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Elevating neuro imaging with an upgrade to SIGNA PET/MR

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When the Charles E. Fipke Integrated Neuroimaging Suite opened in 2019 within the Djavad Mowafaghian Center for Brain Health (DMCBH), it provided new research opportunities to the University of British Columbia (UBC) brain research and neuroimaging community and training for students and post-doctoral scholars. It is home to Canada's first and only simultaneous PET/MR system from GE HealthCare, SIGNA™ PET/MR, dedicated to neuroimaging research.

The scanner can operate in MR only, PET only and simultaneous PET/MR mode, so it is also available for MR-only studies. We are leveraging the simultaneous PET and MR imaging capabilities to study brain function, structure and metabolism. With this advanced technology, our researchers can gain a better understanding of the mechanisms underlying a broad range of neurodegenerative and psychiatric diseases, as well as addiction and aging.

In 2024, our system underwent a significant MR upgrade to SIGNA PET/MR AIR™¹, providing substantial improvements in hardware and software, leading to significantly enhanced MR imaging quality and scan efficiency compared to its original performance. Advanced coil technology enhances SNR to provide sharper and more detailed images.

Key highlights of the upgrade as described by GE HealthCare include:

1. Advanced coil technology: The 48-channel head coil and AIR™ Multi-Purpose (MP) Coils offer excellent image quality, patient comfort and flexibility for diverse applications. The 48-channel head coil is designed for high SNR brain imaging, optimum

parallel imaging and HyperBand simultaneous multi-slice acceleration techniques, and high patient population compatibility. AIR Coils are adaptive and can conform to the patient habitus; they look and feel like a blanket, are lightweight without any concentrated points of pressure and deliver increased acceleration capabilities.

2. Increased digital RF channels (32 to 128): This upgrade to the scanner's core hardware significantly enhances image resolution and reduces noise. Higher channel counts lead to improved image quality and allow for faster scan times through greater acceleration factors.
3. AIR™ Recon DL: This deep-learning-based reconstruction algorithm improves SNR by removing noise and ringing from data. With the higher SNR, superior image quality can be obtained while maintaining similar scan times as before. Alternatively, scan times can be shortened while maintaining similar image quality. In research, shorter scan times can help with subject compliance, particularly when scanning patients with neurodegenerative disease who may be confused or unable to follow instructions.
4. Optimized sequences: Tailored protocols for T1, T2, FLAIR, DTI, fMRI and spectroscopy enable a wide range of research and clinical applications.
5. The upgrade provides higher resolution anatomical and functional imaging, allowing us to:
 - More accurately characterize white matter microstructure with improved diffusion-weighted imaging (DTI, HARDI, NODDI).

- Enhance myelin water imaging sensitivity, expected to enable better differentiation of demyelination versus inflammation.
- Improve lesion conspicuity in T2-weighted and FLAIR imaging, particularly in stroke and multiple sclerosis (MS) studies.

In addition to the MR upgrade, we also evaluated MotionFree Brain, GE HealthCare's fully retrospective and data-driven motion estimation and correction approach for PET brain imaging on the SIGNA PET/MR. MotionFree Brain produces highly accurate (<1 mm) motion estimates with high temporal resolution (~1 second) and no impact on the standard clinical routine (e.g., static FDG scans) without requiring additional scan time. The estimated motion is used for a full event-by-event, motion-corrected list-mode reconstruction, resulting in up to 60% improvement in quantitation accuracy and up to 1.5-times improvement in volumetric accuracy of lesion size, as compared to non-motion corrected images in phantom testing.¹

The new capabilities will enable new research and implementation of more complex multimodal imaging protocols when investigating stroke, neurodegeneration and brain energetics, including the impact of lifestyle on brain function and disease, a topic of great current relevance.

While in clinical settings AIR Recon DL has enabled shorter scan times, in most cases we tend to focus on higher image quality. Often the scanning time is dictated by PET protocols, in our case most often requiring at least 60 minutes of dynamic imaging. This generally allows for sufficient MR data acquisition time.

MotionFree Brain evaluation

We utilized MotionFree Brain on a subject during a 20-minute FDG-PET scan (~60 minutes post injection). The subject was

instructed to remain still for the first half of the scan (10 minutes) and then to move and remain at three other locations within the 48-channel head coil during the second half of the scan.

As the first 10 minutes of the PET scan contained no motion and the FDG distribution was stable one hour after administration, we used this portion of the PET acquisition as the reference/pseudo ground truth for comparison (Figure 1, top row). We retrospectively reconstructed the 20 minutes of imaging data without and with MotionFree Brain (Figure 1, middle and bottom rows, respectively) to demonstrate MotionFree Brain's impact.

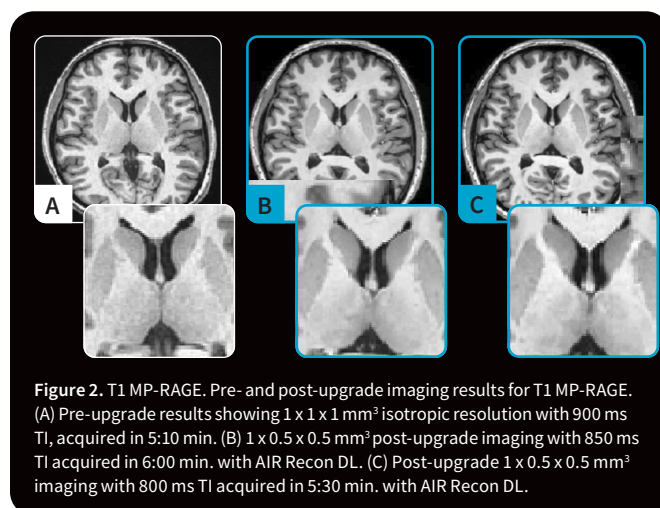
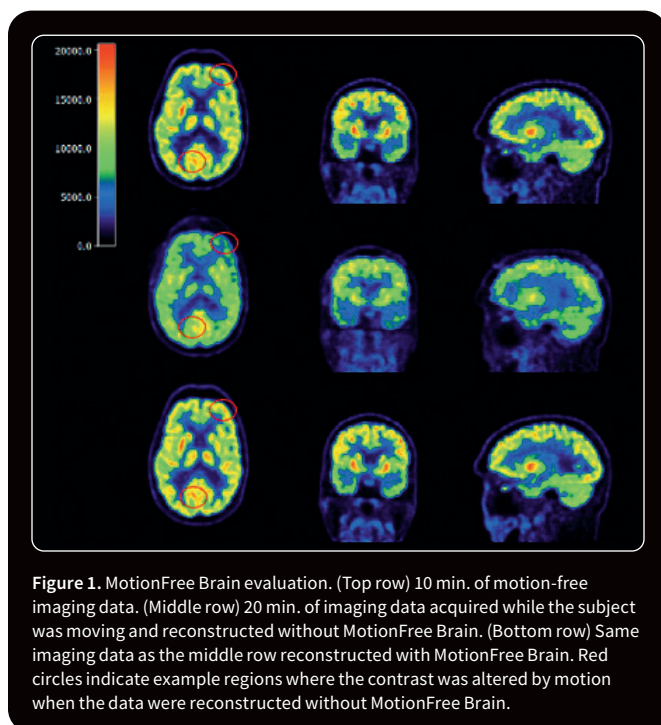
The difference between the images reconstructed with and without motion correction can be observed in Figure 1. As indicated by the red circles in Figure 1, the contrast is altered by motion in some of the brain areas and, thus, the PET uptake pattern becomes less symmetric. With the motion correction, the image acquired when the subject was moving looks nearly identical to the one without motion. Quantitatively, the regional SUV estimated for the region of interest placed on the putamen was reduced by ~30% without motion correction and restored to within 3% after motion correction, as compared to the motion-free data. In general, quantification within smaller structures with relatively high PET uptake is affected more by motion compared to that within larger structures.

MR upgrade test and validation

Extensive testing and verification procedures were conducted to assess the performance of the upgraded scanner and optimize acquisition sequences. Both qualitative and quantitative (such as contrast vs. noise, segmentation and metric scan-to-scan reproducibility as well as accuracy of distortion correction) comparison approaches were employed. AIR Recon DL was used to enhance all compatible sequences unless noted otherwise.

T1-weighted imaging — MP-RAGE

The Magnetization Prepared Rapid Acquisition Gradient Echo (MP-RAGE) sequence is commonly used to visualize anatomical structures and is sensitive to tissue contrast, particularly between gray matter and white matter.



For post-upgrade T1 MP-RAGE optimization, parameters such as acquisition orientation, slice coverage, inversion time (TI), etc. have been chosen to obtain the best compromise between contrast, noise, scan time and image artifacts.

Visual inspection was conducted to assess the white-to-gray-matter contrast, noise and artifacts between different acquisition orientations (e.g., axial vs. sagittal). Special attention was given to optimizing the contrast ratio between cerebral white matter and caudate putamen regions, as the striatal regions typically contain worse contrast compared to the rest of the gray matter regions in the T1 image.

Protocol improvements included shorter TRs and TE_s, sub-millimeter reconstruction voxel size and higher matrix size.

T2-weighted imaging — T2 Cube

T2 Cube provides detailed anatomical information, especially for visualizing fluid-filled structures like the ventricles and spinal cord. We compared healthy controls pre- and post-upgrade and a stroke patient post-upgrade. Improvements to the sequence include shorter TR, echo train length (ELT) and scan time.

With the protocol improvements and 48-channel head coil, streaking artifacts observed prior to the upgrade were no longer visible and excellent T2 contrast was observed in the stroke patient between the stroke region and the rest of the brain (Figure 3).

T2 FLAIR

This sequence suppresses the signal from the cerebrospinal fluid, making it useful for detecting lesions or abnormalities in the brain. We maintained the same parameters pre- and post-upgrade to demonstrate the improvement in SNR and image quality with AIR Recon DL. In the images obtained from healthy controls, we can better differentiate the white and gray matter post-upgrade

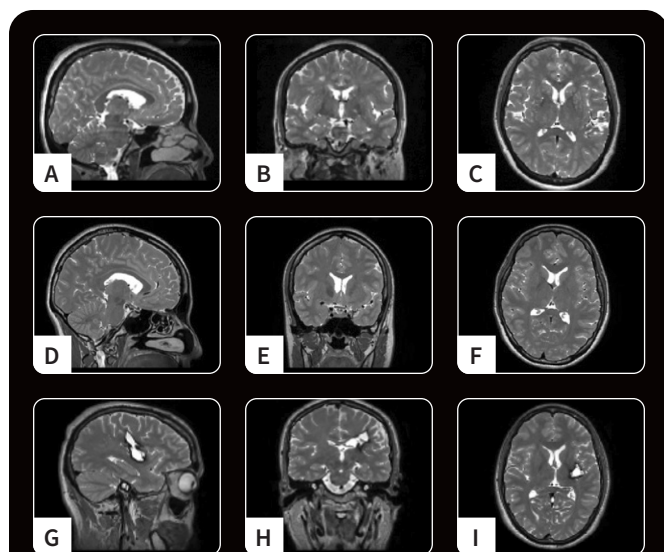


Figure 3. (A-C) A healthy control pre-upgrade. (D-F) In a different healthy control post-upgrade, the T2 image with the 48-channel head coil was observed to be less noisy as well as free from previously observed streaking artifacts pre-upgrade. (G-I) Stroke patient post-upgrade with excellent T2 contrast clearly observed between the stroke region and the rest of the brain.

(Figure 4A-C vs. 4D-F). In the image obtained from the stroke patient, the regions with stroke can be easily identified in the T2 FLAIR image (inverse contrast compared to T2) (Figure 4G-I).

Myelin water imaging

The Myelin-GRASE sequence, a technique used to assess myelin water content in tissues, is available on the scanner. In 1994,

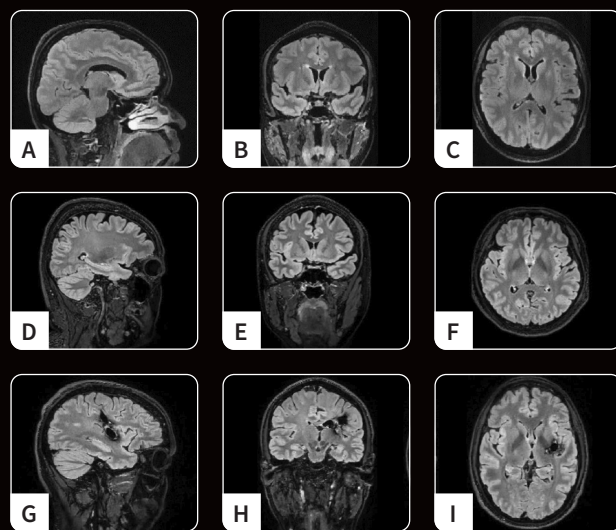


Figure 4. (A-C) A healthy control pre-upgrade. (D-F) Another healthy control post-upgrade. (G-I) A stroke patient post-upgrade with the regions of stroke easily identified in the T2 FLAIR image (inverse contrast compared to T2).

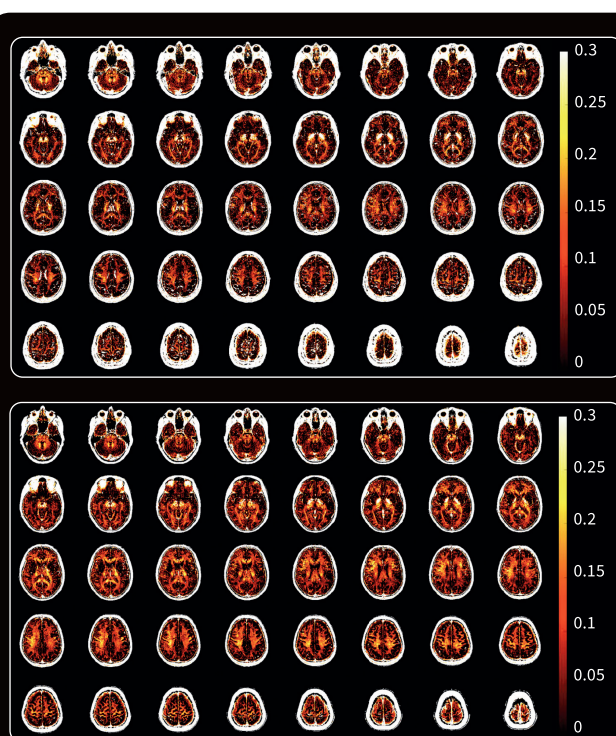
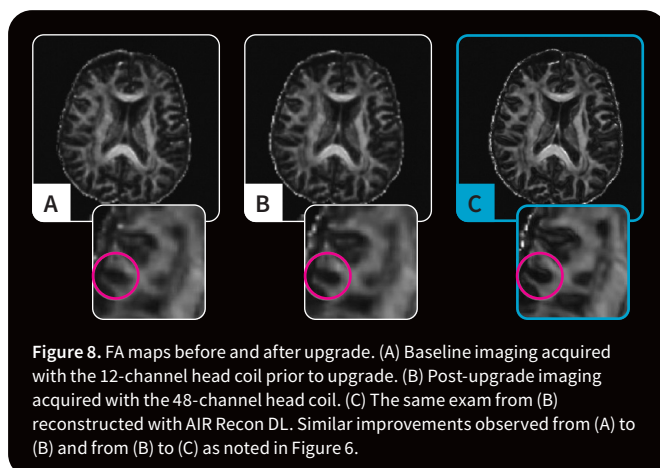
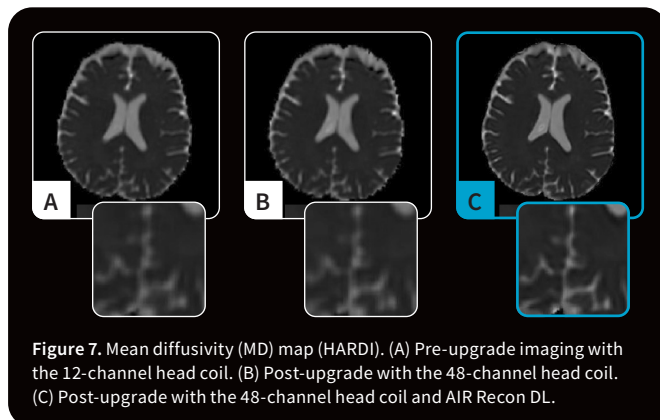
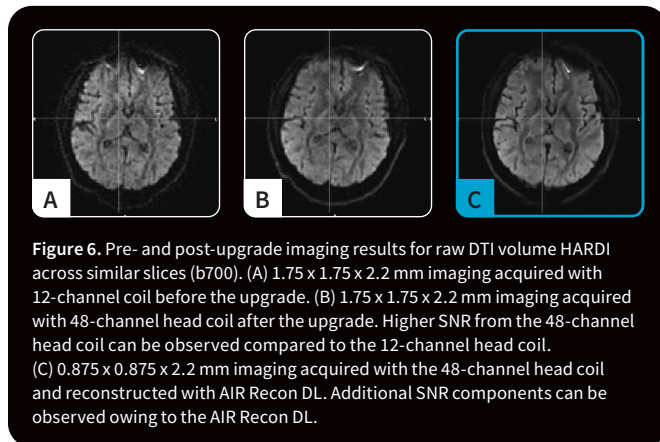


Figure 5. Transaxial image slices displaying the MWF from a healthy control subject (top) pre-upgrade and (bottom) post-upgrade for a different healthy control subject. Less noisy MWF maps can be observed post-upgrade compared to pre-upgrade.

UBC's Alex MacKay, PhD, Professor of Physics and Astronomy and Director of the UBC MRI Research Centre, and his team developed the myelin water imaging technique and improved the sensitivity of MR in distinguishing between inflammation, demyelination, remyelination and axonal damage in diseases such as MS. Examples of Myelin-Water-Fraction (MWF) map of healthy control subjects pre- and post-upgrade are shown in Figure 5. Higher SNR in the MWF map with the 48-channel head coil post-upgrade can be observed compared to the MWF map with the 12-channel head coil pre-upgrade.

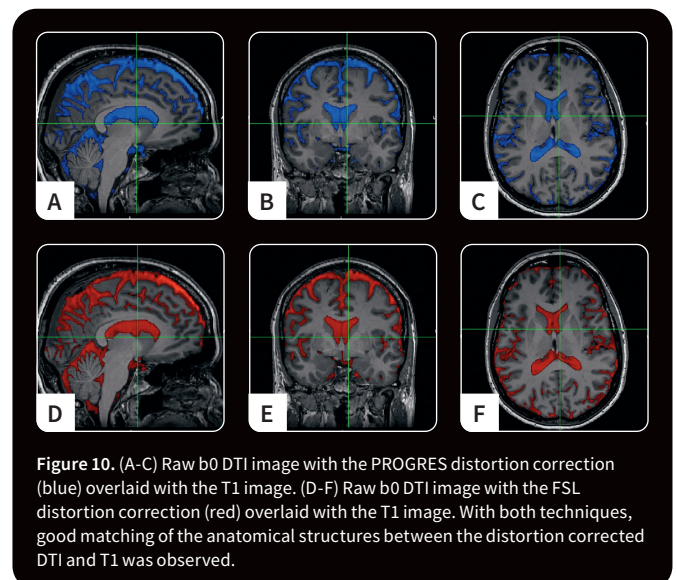
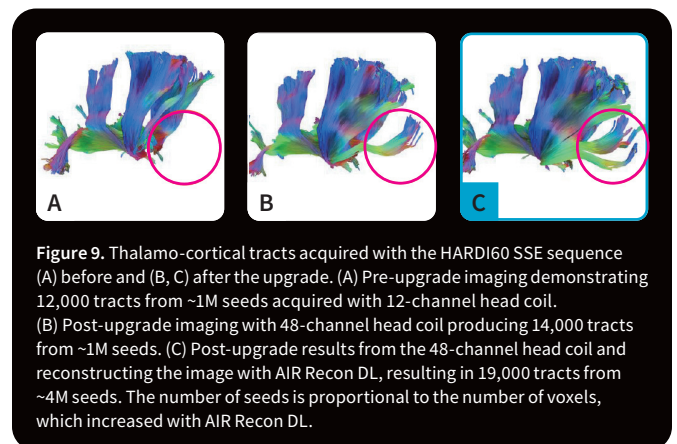


Diffusion tensor imaging (DTI)

DTI provides detailed information on the structure and integrity of white matter tracts in the brain that are important for brain function. DTI can detect changes in diffusion anisotropy due to damage to white matter tracts from stroke, MS and traumatic brain injury. The sequence is also being used to study changes in white matter structure that occur in neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease.

DTI HARDI60_SSE is a high angular resolution diffusion imaging acquisition with 60 directions and single-shot EPI (SSE) for fast image acquisition. This sequence measures the diffusion of water molecules in the brain, providing information about white matter tracts.

In general, the 48-channel head coil produces images with better SNR compared to the 12-channel head coil. AIR Recon DL further reduces noise and results in even cleaner images without altering the contrast (Figures 6-8). Additional fiber tracts derived from DTI images were observed post-upgrade compared to pre-upgrade, with AIR Recon DL achieving the highest number of tracts for the same subject as shown in Figure 9.



PROGRES for DTI

PROGRES is a distortion correction for DTI sequences available on the MR system. We cross-validated the correction with the equivalent one from the FMRIB Software Library (FSL) using our data. DTI images were acquired with the scanner distortion correction. The same subject DTI sequence was repeated without the scanner distortion correction. Together with the PEPolar sequence, post-processing distortion correction using FSL was applied to the uncorrected DTI images. The distortion corrected DTI images obtained with both versions of distortion correction (PROGRES vs. FSL) were compared in terms of qualitative and quantitative similarities. Fractional anisotropy (FA) maps derived from the DTI images were also compared. The two distortion correction approaches were found to give comparable results (Figures 10 and 11).

Multi-shot DTI with MULTIPLEXED Sensitivity-Encoding (MUSE)

MUSE allows for the acquisition of high-resolution diffusion-weighted images with reduced scan time and improved image quality. It is particularly useful for studying complex brain structures and connectivity. Images obtained with this sequence are currently

being evaluated at UBC; preliminary results indicate improved performance compared to single-shot DTI acquisition described above (Figures 12 and 13).

DTI Multishell 106 (NODDI_SSE) and 128

With the upgrade, we now have access to more advanced DTI techniques (Figure 14) that allow for the quantification of neurite density and orientation distribution function (ODF).

Gradient echo imaging, neuromelanin

Gradient echo imaging for neuromelanin is a specialized GE HealthCare product sequence that highlights neuromelanin-rich structures, such as the substantia nigra and locus coeruleus. Comparable image quality was observed pre- and post-upgrade (Figure 15).

Susceptibility weighted imaging

The susceptibility weighted imaging (SWI) sequence is sensitive to blood products and iron, making it useful for detecting microhemorrhages and iron deposition (Figure 16).

Perfusion – pCASL

Pseudo-Continuous Arterial Spin Labeling (pCASL) is a non-invasive, perfusion-weighted imaging technique to measure cerebral blood flow using arterial spin labeling (ASL). For the global average percentage signal change during breath hold, the 12-channel data with the HNU pre-upgrade had an average signal change of 1.19%, whereas the 48-channel head coil data had 1.43%, for a 20% improvement in signal change with the new coil after the upgrade (Figure 17).

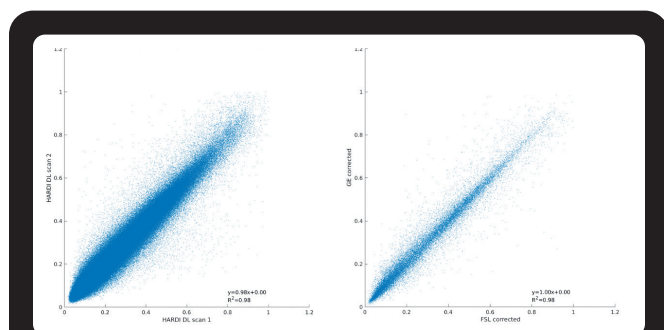


Figure 11. (Left) Scatter plot comparing FA maps derived from two DTI scans (both with the FSL distortion correction) of the same subject (i.e., scan-to-scan variability) and (right) scatter plot comparing FA maps derived from one DTI scan with the scanner distortion correction and the same scan with the FSL distortion correction of the same subject. The variability in FA values due to the difference between the two versions of the distortion correction was observed to be negligible compared to the scan-to-scan variability.

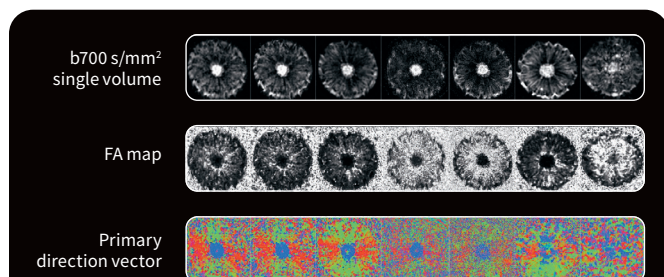


Figure 12. Pineapple HARDI 60 scans used to determine the number of shots and voxel size for multi-shot DTI acquisition. Although 2-shot with smaller voxel size (i.e., 2-shot HR) acquisition appeared to have higher resolution in the raw DTI image, the corresponding FA map contained substantially more outlier/white voxels (i.e., >1.0) and the corresponding primary direction vector map was the noisiest. For number of shots higher than two, the primary direction vectors appeared to be more corrupted.

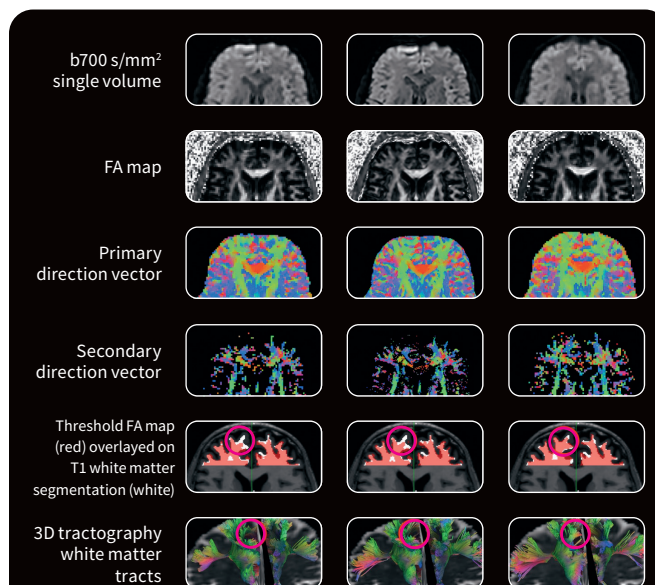


Figure 13. Qualitative visual comparison. Advanced distortion reduction (i.e., 2-shot) produced raw DTI images and FA maps with better anatomical matching with respect to structural T1, as well as more fiber tracts than standard DTI with or without advanced de-noising (i.e., 1-shot without AIR Recon DL). Note that all DTI images shown included the reverse-polarity distortion correction.

MR spectroscopy (MRS)

MRS provides information about the chemical composition of tissues. The scanner can acquire single- and multi-voxel spectroscopy using semi-LASER to detect the following metabolites: N-acetyl aspartate (NAA), choline and creatinine, and we are currently optimizing detection of lactate.

fMRI

Single-echo fMRI: A basic fMRI technique that measures blood-oxygen-level-dependent (BOLD) contrast to map brain activity.

Multi-echo fMRI: An advanced fMRI technique that allows for improved sensitivity and quantification of hemodynamic responses. We are currently optimizing the sequence parameters for our tasks.

Conclusion

The hardware and software upgrade implemented on the SIGNA PET/MR was found to lead to significant improvements in MR image quality. MotionFree Brain PET was found to accurately correct for motion when imaging with a tracer with relatively stable spatial distribution, especially relevant when imaging subjects prone to motion. Collectively, these improvements significantly enhance the overall imaging performance of the scanner, thus enabling more complex research studies, which will ultimately lead to a better understanding of brain function and disease. **S**

Reference

1. Spangler-Bickell MG, Hurley SA, Pirasteh A, Perlman SB, Deller T, McMillan AB. Evaluation of Data-Driven Rigid Motion Correction in Clinical Brain PET Imaging. J Nucl Med. 2022 Oct;63(10):1604-1610.

