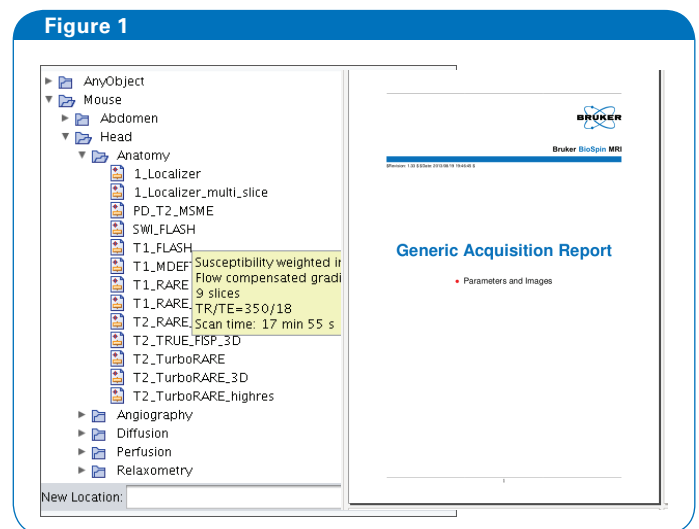


## Consistent Quantification

Regardless of the method, stability and reproducibility are a must for highly meticulous laboratories such as those of pharmaceutical companies. Identical protocols must yield consistent results. Bruker's MRI instruments meet this challenge and provide researchers with the reliability they require.

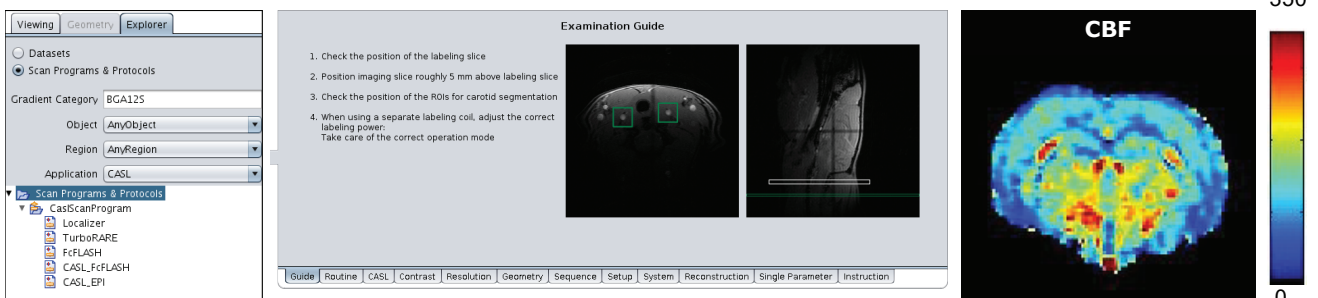
### Pre-optimized Protocols and Scan Programs

This reproducibility has a long history at Bruker. For decades, Bruker's MRI instruments have been delivered with pre-optimized protocols that have been tested on small rodents and categorized according to animal, anatomical region, and application (Figure 1). Use of these stored protocols guarantees that scan parameters are identical from one scan to the next. If parameters are adapted, scan to scan importation of parameters guarantees consistency throughout studies and subjects. ParaVision® 6 marked the introduction of entire scan programs and automatic report generation. These study reports, which can be customized to contain representative images from each scan, ensure that all scan parameters are documented for future reference, maintaining best scientific standards (Figure 1).



Pre-optimized protocols for mice and rats, categorized via anatomical region and application, come standard with the instrument. All parameters and representative images can be saved in the study report.

Figure 2



**1. Pre-prepared, complete Scan Program**

**2. Examination Guide**

**3. Integrated Reconstruction with automatic measurement of Inversion Efficiency and output of quantitative CBF maps**

The CASL workflow package with its pre-prepared, complete scan program, examination guide, and integrated reconstruction with automatic measurement of inversion efficiency and output of quantitative CBF maps provides consistently reliable operator independent data

The CASL Workflow Package was developed in cooperation with Emmanuel Barbier, Grenoble Institute of Neuroscience

Courtesy: E. Barbier, L. Hirschler, J. Warnking, Grenoble Institute of Neuroscience

## Examination Guide with Quantitative Results

Taking the scan programs even further, ParaVision 360 introduces the workflow package for Arterial Spin Labeling (ASL) (Figure 2). This package which yields optimal results when used in combination with a dedicated Arterial Spin Labeling coil, was developed in an industrial-academic cooperation with the Grenoble Institute of Neuroscience<sup>1</sup>. It contains a complete pre-prepared scan program, an examination guide which escorts the user throughout scan preparation, and an integrated reconstruction with automatic measurement of inversion efficiency and output of quantitative Cerebral Blood Flow (CBF) maps.

## Superior Image Quality for Streamlined Evaluation

ParaVision 360 also introduced the IntraGateUTE method. It is based on Bruker's patented IntraGate, which is also incorporated into IntraGateFLASH, a method which has been prized by ParaVision users for years. IntraGate based methods are self-gated, requiring no electrodes or external triggering devices. This saves valuable set-up time and also improves animal welfare. Reconstruction of cardiac, respiratory, or cardiac and respiratory cines can be performed and the number of cine frames can be defined after the acquisition has been completed. IntraGateUTE combines the benefits of IntraGate with those of the ultra-short echo time, radial readout UTE method for superior cardiac imaging quality. It can be accelerated up to 8-fold over standard methods and enables full murine heart cine coverage in under 15 minutes (Figure 3). Streamlined evaluation with automatic algorithms is facilitated due its significantly reduced turbulence artifacts.

## Longitudinal Consistency

This excellent cardiac imaging quality is proven to be stable over time, as shown by a research group at the University

of Ulm. In their study using the IntraGateFLASH method, the ejection fraction (EF), end-diastolic volume (EDV), end-systolic volume (ESV), stroke volume (SV), and left ventricular mass (LVM) of five female wildtype C57/B6 mice were measured on five days over the course of more than one year<sup>2</sup>. No significant differences of EF, EDV, ESV, or SV were seen (Figure 4). The LVM increased significantly, as was to be expected with increasing age. This study demonstrates the longitudinal reproducibility of the method and testifies that the reliable hardware and software enable longitudinal studies to be carried out without interruption.

## Multi-site Reproducibility

Such reproducibility is also possible from instrument to instrument and site to site. In their research article titled "Accuracy, repeatability, and reproducibility of longitudinal relaxation rate in 12 small-animal MRI systems"<sup>3</sup>, 11 sites within the United Kingdom, the United States of America, Sweden, Germany, and the Netherlands, headed by Bioxydym Ltd, Manchester, United Kingdom, measured T1 in identical phantoms in order to access reproducibility on preclinical imaging systems (Figure 5). The 11 sites employed 12 MRI systems at field strengths ranging from 3 T to 11.7 T, namely 3 T, 4.7 T, 7 T, 9.4 T, and 11.7 T. The sites were allowed to employ preclinical MRI instruments from any manufacturer of their choice. All sites independently decided to use a Bruker BioSpec or PharmaScan instrument (three of the 12 instruments contained magnets from the former Varian, Magnex or Agilent companies) run on ParaVision software (versions 5.1 to 6.0.1 were used). Each site received 5 phantoms, which were identical from site to site and was requested to measure T1 via the RARE sequence (standard T1map\_RARE protocol) and with a 2-parameter fit in ParaVision in three regions of interest in each of the phantoms. The measurement was repeated on a second day within a three week period, yielding 360 measurements in total. They found a Coefficient of

Figure 3

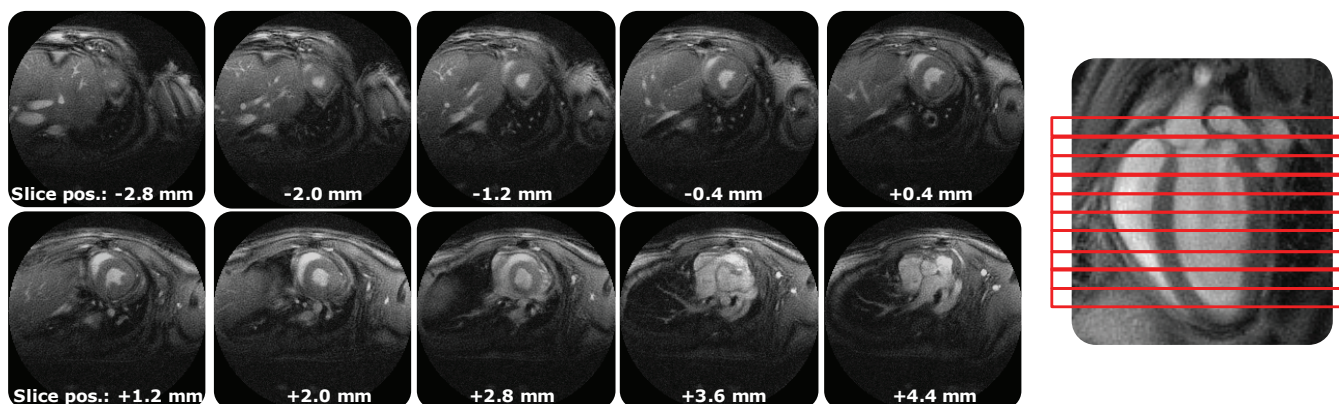
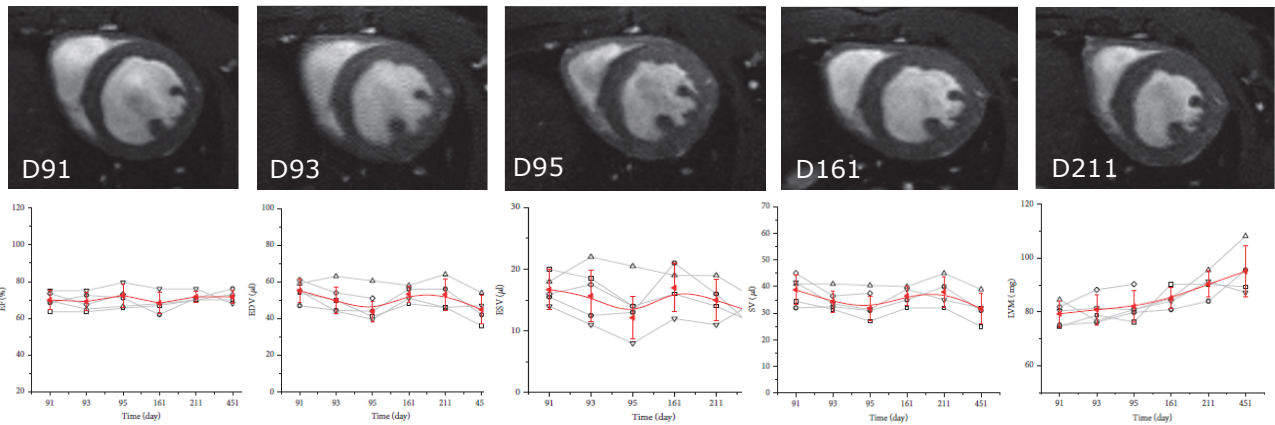


Figure 4



IntraGateFLASH measurement of cardiac parameters over course the of one year. Top: IntraGateFLASH images at days 91, 93, 95, 161, and 211. Bottom from left to right: ejection fraction (EF), end-diastolic volume (EDV), end-systolic volume (ESV), stroke volume (SV), left ventricular mass (LVM) versus time.

Courtesy: V. Rasche, Core Facility Small Animal Imaging, Ulm University, Ulm, Germany

Reference: Z. Zuo, et al., BioMed Research International, 2017

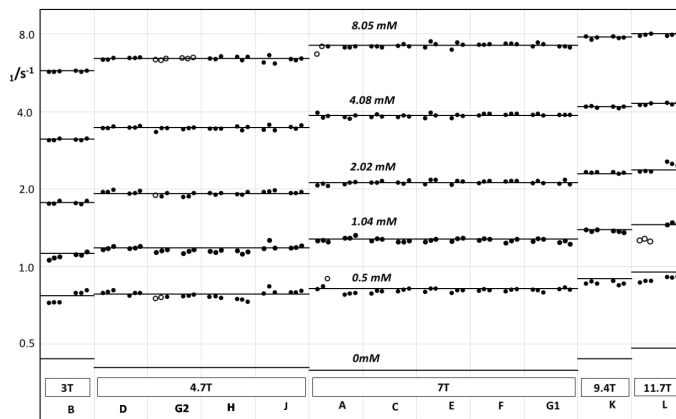
Variation (CoV) of 1.43% between sites, which is significantly better than CoVs of 5.5%-8.2% reported in similar studies performed with clinical systems. This reinforces the feasibility of T1 as a biomarker in studies of, for example, cardiac and liver diseases, neurology, oncology, as well as in diseases such as in myocardial fibrosis or multiple sclerosis, where smallest changes in T1 may prove to be clinically significant. Furthermore, it clearly demonstrates the extremely reliable reproducibility of Bruker MRI instruments.

### Functional Imaging Robustness

This reproducibility is not limited, however, to phantom studies, but is found even in such challenging studies such as fMRI. In their 2018 ISMRM contribution titled "Multi-centre resting-state fMRI comparison reveals common functional net-

works in the mouse brain"<sup>4</sup>, resting state fMRI data obtained from C57B6/J mice on Bruker MRI instruments located at 12 different sites within Singapore, Italy, Belgium, Canada, Germany, Australia, the United Kingdom, France, Switzerland, and China was compared. The data was obtained under various conditions concerning field strength (4.7 T, 7.0 T, or 9.4 T), coil type (room temperature or MRI CryoProbe), and anesthesia type (isoflurane, halothane, medetomidine, or a combination of isoflurane and medetomidine). Functional Connectivity (FC) values were determined from two Region of Interests (ROI), in the contralateral and posterior cingulate cortex, based on seed points located at anterior S1 and the anterior cingulate, respectively. Significant contralateral FC for the anterior S1 seed was seen in 60-80% of the datasets, while FC reproducibility for to the anterior cingulate seed ranged between 40-60%. The dependence of the FC data on the variations in setup

Figure 5



R1 vs. field strength, measured on centrally prepared phantoms on 12 different Bruker MRI instruments at 11 different sites

Reference: J.C. Waterton, et al., Accuracy, repeatability, and reproducibility of R1 in 12 small-animal MRI systems, BCISMRM 2018, P019

Courtesy: J.C. Waterton CSci FRSC(UK), Tristan Consortium

mentioned above was investigated and a positive correlation was found between FC for the anterior S1 and SNR (which in turn had a positive correlation with field strength and coil type (MRI CryoProbe yielding higher SNR)). Anesthesia type was identified to have an effect on FC in both ROIs. These data from world-wide imaging sites show robustness of fMRI and demonstrate that taking study setup into consideration, data obtained within international collaborations can be reliably compared.

## Conclusions

The consistency of data obtained with Bruker MRI instruments run on ParaVision, allows researchers to be confident of their results when comparing them with international reports and to trust that their instruments will perform over time, allowing them to carry out longitudinal studies reliably and without interruption. The highest quality of the images enables evaluation via automatic algorithms, eliminating variation of outcomes arising from user dependencies. Thanks to pre-optimized protocols and scan programs, this quality is easily and reliably reproduced, measuring up to the standards of even the most stringent laboratories.

## References

1. Hirschler L, Debacker CS, Voiron J, Köhler S, Warnking JM, Barbier EL (2017) Interpulse phase corrections for unbalanced pseudo-continuous arterial spin labeling at high magnetic field. *Magnetic Resonance in Medicine* 79(3)1314-1324
2. Zuo Z, Subgang A, Abaei A, Rottbauer W, Stiller D, Ma G, Rasche V (2017) Assessment of Longitudinal Reproducibility of Mice LV Function Parameters at 11.7 T Derived from Self-Gated CINE MRI. *BioMed Research International* 2017
3. Waterton JC, Hines CDG, Hockings PD, Laitinen I, Ziemian S, Campbell S, Gottschalk M, Green C, Haase M, Hassemer K, Juretschke HP, Koehler S, Lloyd W, Luo Y, Persson IM, O'Connor JPB, Olsson LE, Pindoria K, Schneider JE, Sourbron S, Steinmann D, Strobel K, Tadimalla S, Teh I, Veltien A, Zhang X, Schütz G (2019) Repeatability, and reproducibility of longitudinal relaxation rate in 12 small-animal MRI systems. *Magnetic Resonance Imaging*, <https://doi.org/10.1016/j.mri.2019.03.008>
4. Grandjean J, Canella C, Anckaerts C, Ayrancı G, Coletta L, Gallino D, Gass N, Hübner N, Kreitz S, Mechling AE, Strobel S, Wu T, Wank I, Chakravarty M, Chang WT, von Elverfeldt D, Harsan LA, Hess A, Keliris G, Rudin M, Sartorius A, Jiang T, Van der Linden A, Verhoye M, Weber-Fahr W, Wenderoth N, Zerbi V, Gozzi A (2018) Multi-centre resting-state fMRI comparison reveals common functional networks in the mouse brain. *ISMRM* (2018) 1108

## Optimal Performance and Uptime

For peace of mind when carrying out longitudinal studies, Bruker offers its professional Services and product Lifecycle Support. Vital instrument components are monitored at regular intervals. In addition, preventative maintenance protects researchers' investments for the long run and guarantees optimal performance and uptime. It lets researchers know that they can rely on their instrument to perform throughout the course of their studies, providing the reproducibility they require.