PASTEUR: Package of Anatomical Sequences Using Parallel Transmission Universal Pulses Now Available for MAGNETOM Terra

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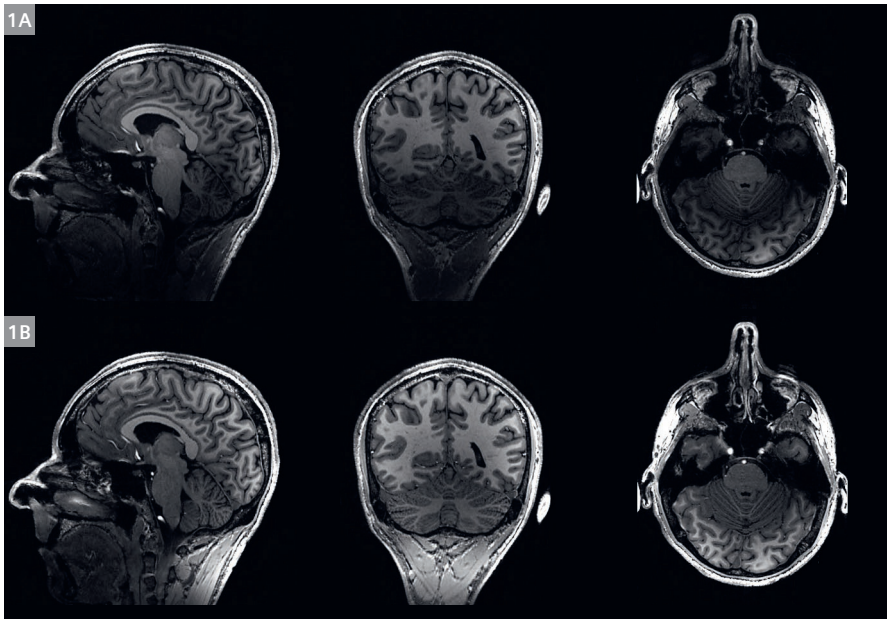
Introduction

In MRI, ultra-high-field (UHF) strengths (≥ 7T) provide a higher signal-to-noise ratio, enabling increased spatial resolution and/or reduced acquisition time as compared to lower-field MR systems [1–3]. As more and more patients have been scanned with UHF systems over the last decade, 7T MRI has markedly demonstrated its added value for diagnosing and characterizing two key diseases of the central nervous system: multiple sclerosis (MS) and focal epilepsy [4, 5]. With MS, 7T structural MRI successfully detects smaller and earlier lesions in both white matter (WM) and gray matter (GM), and provides improved characterization of lesion localization, formation, and resulting damage [4]. As for epilepsy, 7T structural MRI successfully increases the diagnosis success rate in patients with drug-resistant focal onset epilepsy for whom lesions could not be found using lower-field MR systems [5].

However, certain anatomies can be more challenging to acquire with UHF MRI, especially when examining larger volumes. This is due to destructive field interferences that can lead to spatial inhomogeneity in the radiofrequency (RF) excitation profile. In the head, the cerebellum and the temporal lobes can be affected by such inhomogeneities [6].

The use of parallel transmission (pTx) technology with an array of transmit coil elements has proven to be very efficient in addressing these challenges [7]. With pTx, the amplitudes and phases of the RF pulses transmitted by the channels of the coil array are independently modulated in time to homogenize the excitation profile over the volume of interest, provided the actual transmit RF field (B_1^+) and static field offset (ΔB_0) distributions are known. For non-selective excitations used in 3D anatomical MR sequences,



1 T1-weighted MPRAGE (Magnetization-Prepared Rapid Acquisition Gradient-Echo) sequence
(1A) Proposed MPRAGE protocol in TrueForm. **(1B)** Same protocol with Universal Pulses (GRAPE RF pulses were used for magnetization inversion and excitation). Note how GM/WM contrast is specifically improved in the cerebellum and temporal lobes with UP imaging. The sequence SAR is lower using UPs than in TrueForm, since the inversion UP is less energetic than the conventional adiabatic RF pulse.

various parametrization approaches, such as k_T-points [8] or GRAPE [9, 10], have been proposed to design optimized RF and magnetic field gradient waveforms. The design of such subject-tailored RF pulses results in very homogeneous RF excitation profiles, but this is at the cost of the extra scan time required to map the patient field distributions and to design the RF pulses. It also demands specific expertise from the MR user [11, 12].

Alternate methods for a subject-tailored approach can avoid systematic measurement of the RF and static field distributions for each subject and subsequent RF pulse computation. Recently, an original approach that uses "Universal Pulses" (UP) for calibration-free pTx neuroimaging was developed by CEA NeuroSpin [13–15]. To ensure universality, the RF pulses of the PASTEUR package [16] were designed offline using a database of B_1^+ and ΔB_0 brain distributions experimentally acquired from a representative cohort and using state-of-the art optimization algorithms. Several key 3D MR sequences providing anatomical imaging were reprogrammed to host these UPs. The PASTEUR workflow is therefore completely transparent to the 7T radiographer, who can focus on the MR exam with no time penalty or need for advanced sequence parametrization.

In this work, the PASTEUR package, originally designed for the investigational MAGNETOM 7T, was brought to the latest generation of the 7T MR system from Siemens Healthineers: MAGNETOM Terra[1]. To demonstrate the power and versatility of UPs for neuroimaging, the PASTEUR package was deployed in the clinical environment of Poitiers University Hospital (CHU Poitiers) in France. The image quality achieved using conventional TrueForm (i.e., circularly polarized (CP) mode) brain imaging was compared with that from PASTEUR UP brain imaging for MPRAGE, MP2RAGE, FLASH, and SPACE sequences performed on healthy volunteers.

Theory

To design the non-selective RF pulses of the PASTEUR package, two different *k*-space parametrizations were chosen according to the desired properties of the pulses: k_T-points [8] and GRAPE [9]. Briefly, k_T-points consist of multiple rectangular RF sub-pulses interleaved with gradient blips. The resulting degrees of freedom are therefore amplitude, phase, and the *k*-space position of each RF sub-pulse. The GRAPE pulses are made of simultaneously applied RF and gradient waveforms that vary at every time step. The additional degrees of freedom enable shorter GRAPE pulses compared to the k_T-points.

The MR sequences considered here require diverse RF pulses to influence spin magnetization, and each type has specific properties (e.g., small flip angle (FA), large FA, refocusing, inversion). Nevertheless, the general problem with FA homogenization is relatively similar and related to the pTx MR system, which is equipped with N_c transmitters. It usually involves optimizing the N_c RF complex temporal shapes and the G_X-G_Y-G_Z gradient temporal shapes (defining the locations in *k*-space during transmission) so as to minimize the deviation of the resulting FA map from the desired nominal value (as prescribed in the MR protocol).

For one subject, this problem is often (but not always) written as a magnitude least-squares (MLS) problem [17]. To generalize the concept of simultaneous FA homogenization over multiple subjects and thereby promote universality, the optimal RF / gradient shapes that minimize the root mean square error over N_s subjects are sought [13]. In the case of the PASTEUR package, the database consisted of 20 brain field distributions (male and female Caucasian healthy adult volunteers, age range: between 20 and 50 years old), acquired using MAGNETOM 7T MR systems equipped with 8Tx/32Rx Nova brain coils at CEA NeuroSpin (n = 10) and DZNE Bonn (n = 10). Due to evolutions in MAGNETOM Terra hardware and software, several modifications were made to UPs originally designed for MAGNETOM 7T, in order to update the original RF pulses (details and illustration of these "travelling pulses" are provided in [18]). Lastly, as designed RF pulses must respect hardware and safety limits for all patients [19], a set of explicit constraints on SAR and power per channel should be added [13–16]. For the PASTEUR package currently available for MAGNETOM Terra, the default RF power limits set by Siemens Healthineers were enforced. Design examples of UPs included in the PASTEUR package using GRAPE and k_T-point parametrizations are illustrated in Figure 2.

MR imaging

Data were acquired at CHU Poitiers on a 7T MR system[1] (MAGNETOM Terra, Siemens Healthcare, Erlangen, Germany) equipped with an 8Tx/32Rx transmit/receive coil (Nova Medical, Wilmington, MA, USA). The MR protocol, which consisted of 3D non-selective anatomical sequences, was approved by the local ethics committee. Informed consent was obtained for each subject prior to the MR examination. Exclusion criteria followed the GUFI recommendations [20].

MR sequences supported by the PASTEUR package are MPRAGE [21], MP2RAGE [22], FLAWS [23], FLASH, and SPACE [24], with several magnetization preparations (dark fluid, DIR). The main sequence parameters used at CHU Poitiers are summarized in the table below. Specific

[1] *For MAGNETOM Terra, pTx technology is included in Research mode (as part of the optional Dual mode) and is not intended for clinical use. Research operation may require observation of national regulations.*

sequence information and additional observations are provided, along with images acquired from several healthy volunteers (Figs. 1, 3–9).

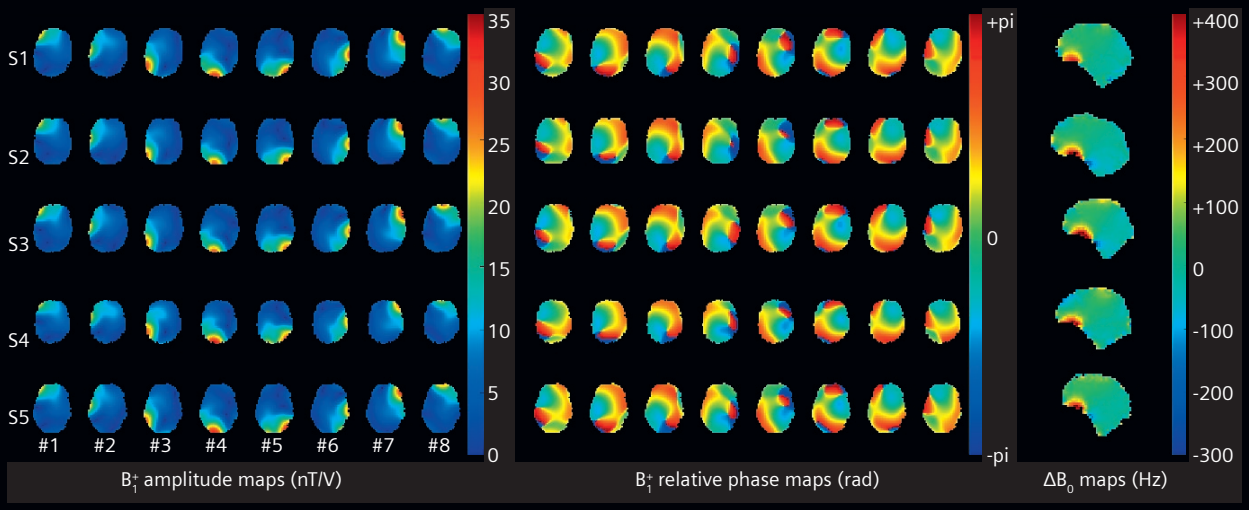
Results

High image quality over the whole brain was obtained for all MR sequences and imaging contrasts when UPs were activated (Figs. 1, 3–9). Where applicable (Figs. 1, 4, 7–9), image quality was significantly improved when compared to conventional TrueForm (i.e., CP: circularly polarized mode). It should be noted that no additional image filters were used to reduce signal bias or to smooth images. Improvements were particularly visually striking in the cerebellum and the temporal lobes, notably on SPACE-based imaging. This is already a well-known phenomenon since the 3D SPACE sequence uses multiple refocusing RF pulses to maintain magnetization along a long echo train. Errors in FA profiles are additive, ultimately creating signal voids within the brain. Regarding sequence-specific absorption rate (SAR), SPACE protocols were usually close to the Level 1 limit. Nevertheless, all MR sequences could be run on millimetric or sub-millimetric spatial isotropic resolution. UP SAR is usually higher than standard rectangular RF pulses, but significantly lower than adiabatic RF pulses. As a result, sequence SAR was sometimes lower when using UPs than with conventional TrueForm (for instance, in MPRAGE or DIR). The radiographers encountered no additional time penalties caused by pTx during the MR exams.

MR sequences	MPRAGE	MPRAGE HR	MP2RAGE	FLAWS	T2* FLASH	T2 SPACE	Dark Fluid $T2_p$ SPACE	DIR SPACE
TA (min)	4:59	9:54	12:20	9:40	5:12	6:00	7:12	7:06
TR (ms)	2600	3000	5000	5000	22	9000	9000	8000
TE (ms)	2.48	3.84	2.06	1.6	16	383	270	320
TI (ms)	1100	1200	740/2430	620/1430	–	–	2300	3500/650
FA (°)	5	6	5/4	4/8	15	T_2 var	T_2 var	T_2 var
FOV (mm^2)	224x224	224x224	230x230	230x230	224x224	230x230	230x230	240x240
Matrix size	320x320	448x448	384x384	288x288	448x376	288x288	288x288	240x240
Resolution (mm^3)	0.7 iso	0.5 iso	0.6 iso	0.8 iso	0.5 iso	0.8 iso	0.8 iso	1.0 iso
Number of partitions	256	320	288	208	320	240	240	192
Parallel imaging technique	GRAPPA	GRAPPA	GRAPPA	GRAPPA	GRAPPA	CAIPIRINHA	CAIPIRINHA	GRAPPA
Parallel imaging factor	3	3	3	3	2x2	3x3	3x3	3x3
Partial Fourier	7/8 (phase)	7/8 (slice)	7/8 (slice)	6/8 (slice)	6/8	allowed	allowed	allowed
Number of averages	1	1	1	1	1	1	1	2
Turbo Factor	256	280	252	156	–	218	180	180
Bandwidth (Hz/px)	210	220	350	500	200	827	599	401

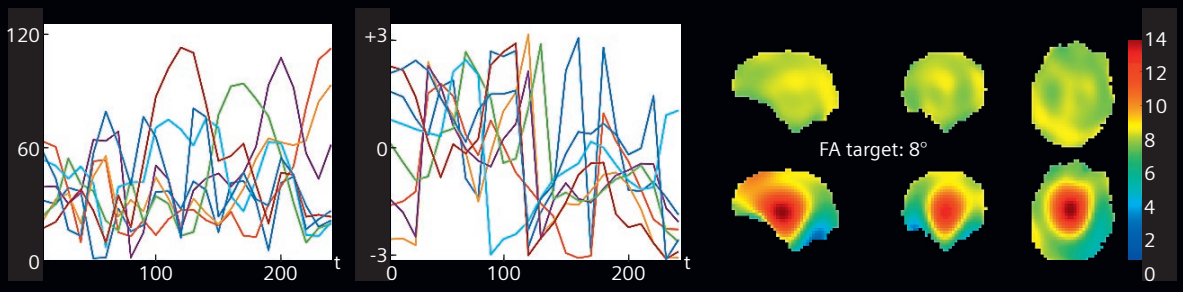
Table 1: The main sequence parameters used at CHU Poitiers.

2A



B_1^+ amplitude maps (nT/V) | B_1^+ relative phase maps (rad) | ΔB_0 maps (Hz)

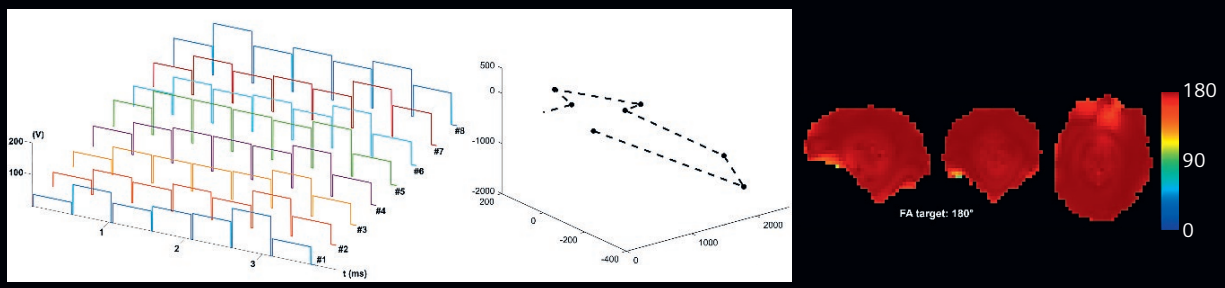
2B



Temporal shapes (amplitude (V) and phase (rad)) of a 240 µs GRAPE excitation pTx RF pulse used in PASTEUR

Bloch simulation of the FA distribution within the brain (in deg) top: GRAPE, bottom: CP-mode

2C



Temporal shapes (amplitude (V)) of a 3.7 ms 7 k_T-points inversion pTx RF pulse used in PASTEUR

3D *k*-space trajectory (mm^{-1}) and localization of the 7 k_T-points

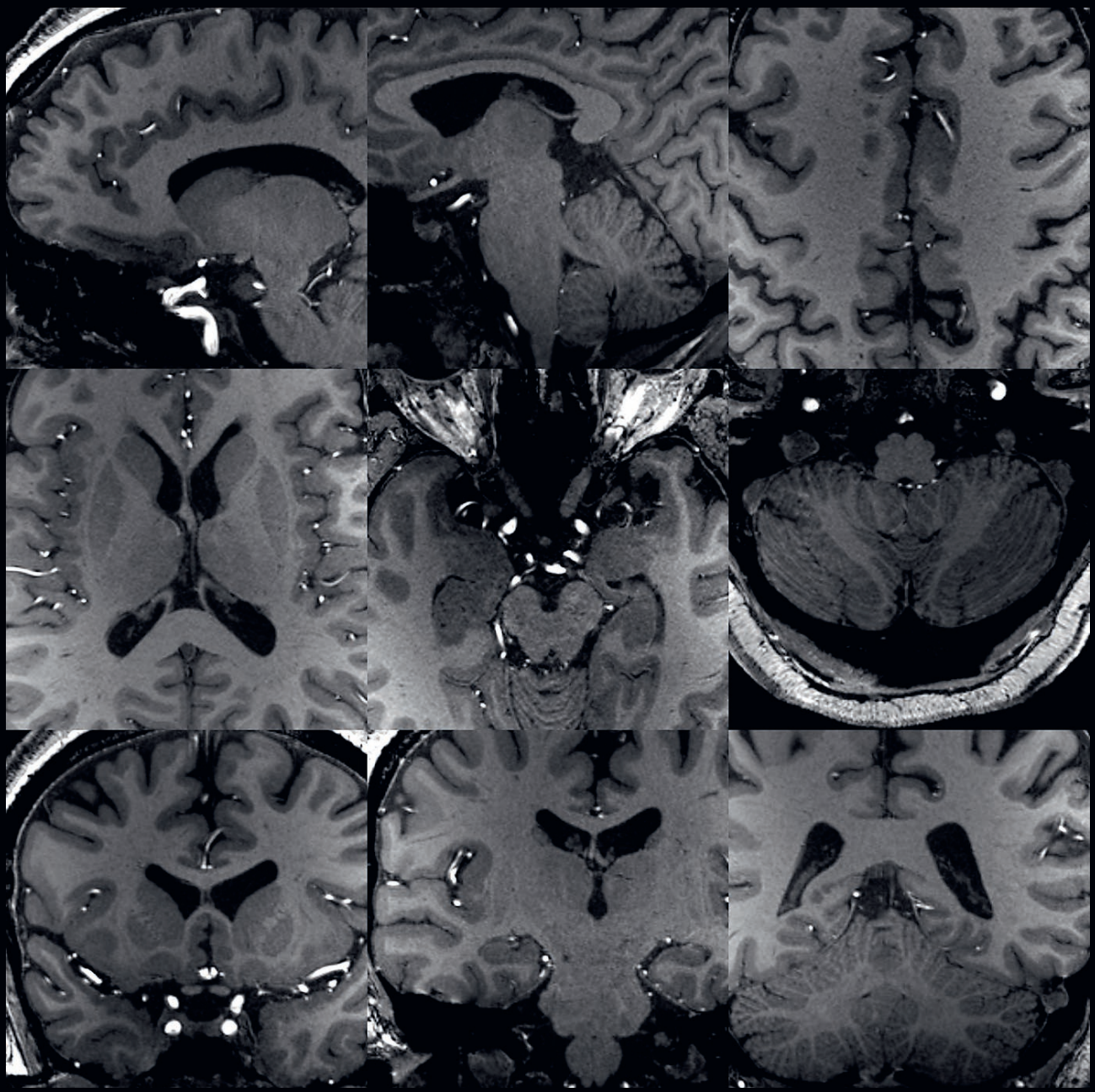
Bloch simulation of the FA distribution within the brain (in deg) for 7 k_T-points inversion

2 Design examples of Universal Pulses of the PASTEUR package using GRAPE and K_T-points

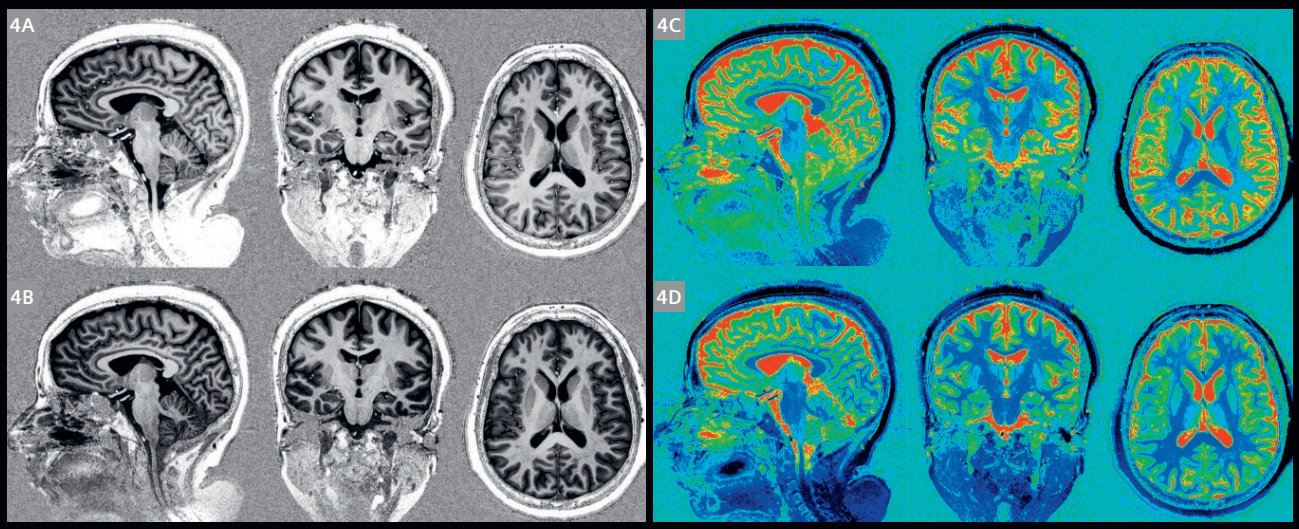
(2A) Extract of the database of brain B_1^+ and ΔB_0 distributions (n = 5 subjects) experimentally acquired on a representative cohort. Measured B_1^+ maps amplitude (nT/V) and relative phase (rad) are displayed in axial view at isocenter. Images are sorted by subjects from top to bottom and by channel indexes from left to right. Measured ΔB_0 offset maps (Hz) are displayed in sagittal view at isocenter. Qualitatively, the B_1^+ maps reveal a high degree of similarity across subjects, with typical spatial correlations of about 0.95 throughout channels. Additional technical details on the database construction can be found in [13].

(2B) Example of excitation UP RF temporal shapes designed with the GRAPE algorithm (different color indicates different transmit channel), along with the corresponding FA distribution in the brain simulated with Bloch equations (results from TrueForm – circularly polarized mode – are also provided below to demonstrate the expected improvement).

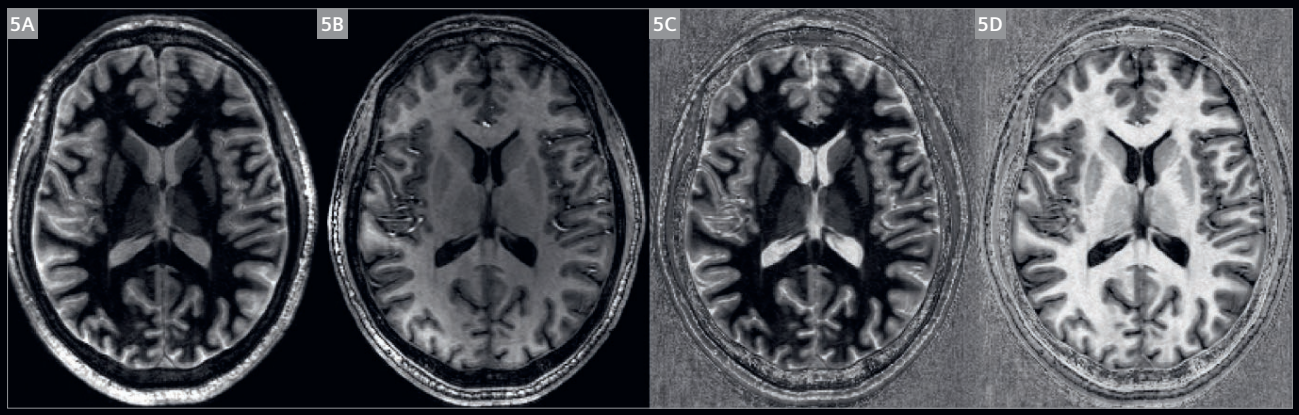
(2C) Example of inversion Universal Pulses RF temporal shapes and *k*-space trajectory designed with k_T-points, along with the corresponding FA distribution in the brain simulated with Bloch equations.



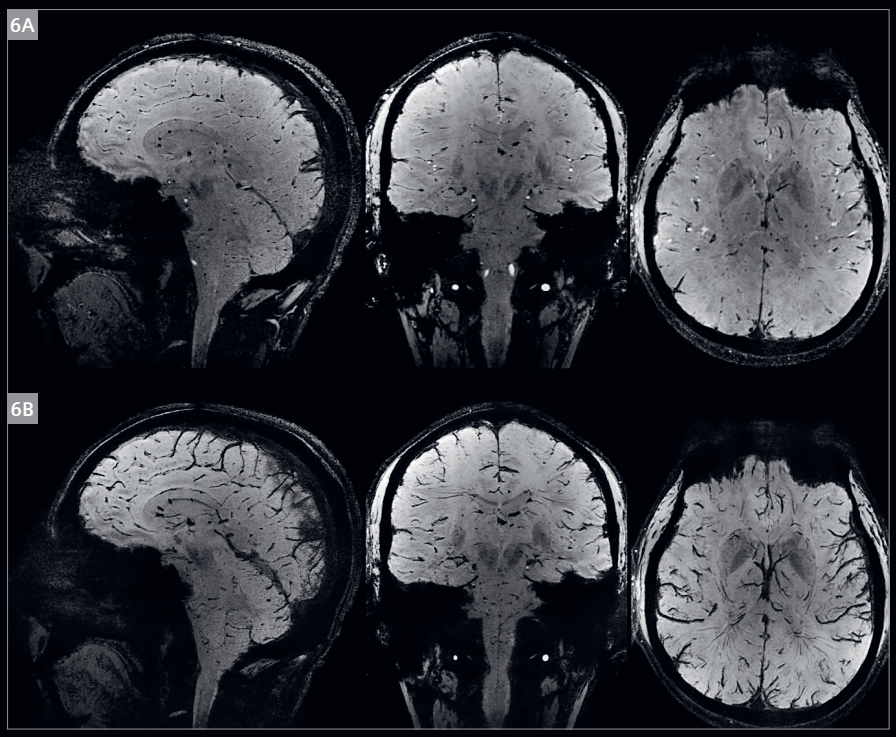
3 **High-resolution T1-weighted MPRAGE imaging using PASTEUR package**
Representative zoomed images in all orientations (sagittal, transverse, coronal) of a 500 µm isotropic spatial resolution MPRAGE sequence acquired in 10 minutes with Universal Pulses. Note the very high image quality over the whole brain, which could be further improved using image filters to mitigate the reception field bias.



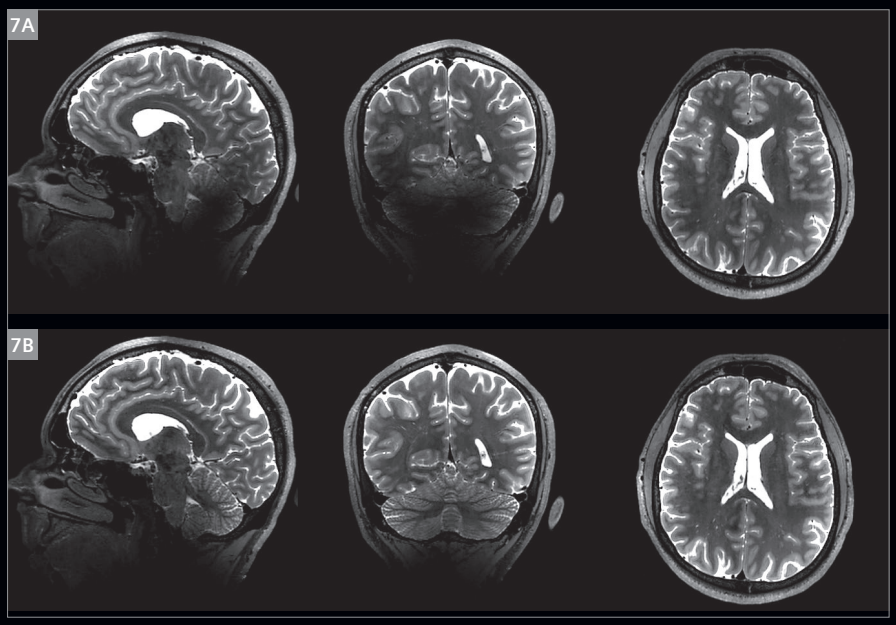
4 **T1-weighted MP2RAGE (Magnetization-Prepared 2 Rapid Acquisition Gradient-Echoes) sequence**
(4A) Uniform (UNI) images obtained with the proposed MP2RAGE protocol in TrueForm. Note that MP2RAGE UNI images are inherently corrected for reception bias field, so the resulting signal inhomogeneity only comes from B_1^+ excitation bias. **(4B)** UNI images obtained with the same protocol using Universal Pulses. Signal homogeneity within the brain is improved (see, for instance, the signal homogeneity of the cortex). **(4C)** Associated quantitative T1 map (in ms) in colormap obtained with TrueForm imaging. **(4D)** Associated T1 map obtained with UPs. The improvement in excitation homogenization significantly improves the accuracy of T1 measurement, as T1 values are computed with Bloch equation integration, notably in the WM and in the cortex.



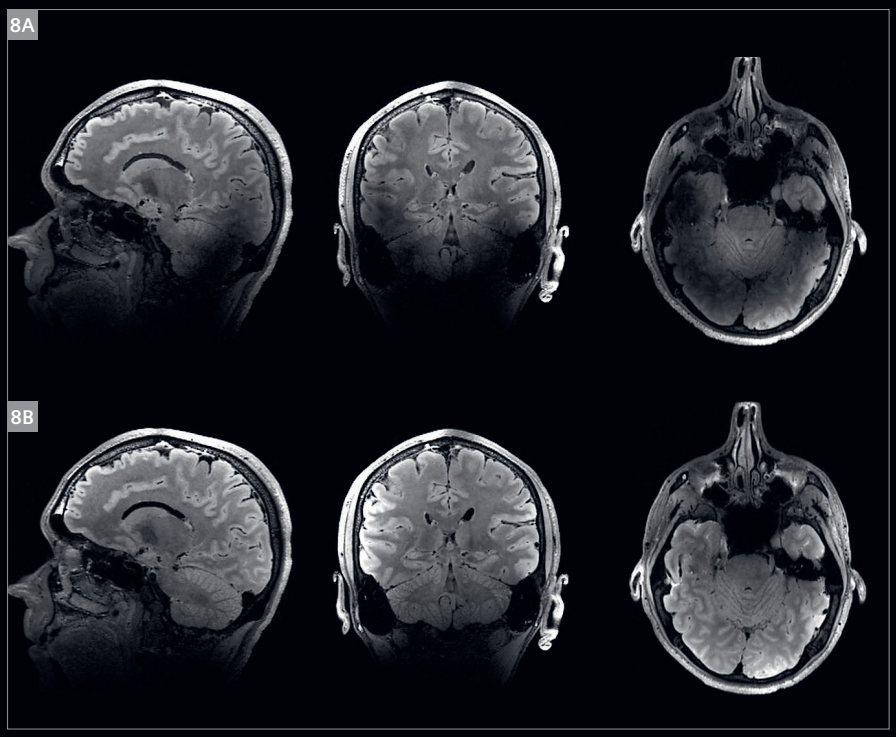
5 **T1-weighted FLAWS (FLuid And White matter Suppression) sequence**
Proposed protocol with Universal Pulses. **(5A)** Inversion 1 volume (equivalent to fast gray matter acquisition T1 inversion recovery, FGATIR), **(5B)** Inversion 2 volume (equivalent to MPRAGE), **(5C)** synthetic high contrast (HC), and **(5D)** synthetic high contrast opposite (HCO). Note that synthetic contrasts were computed offline. These synthetic contrasts are relevant for deep brain structure and/or cortex visualization, though they do amplify image noise [23].



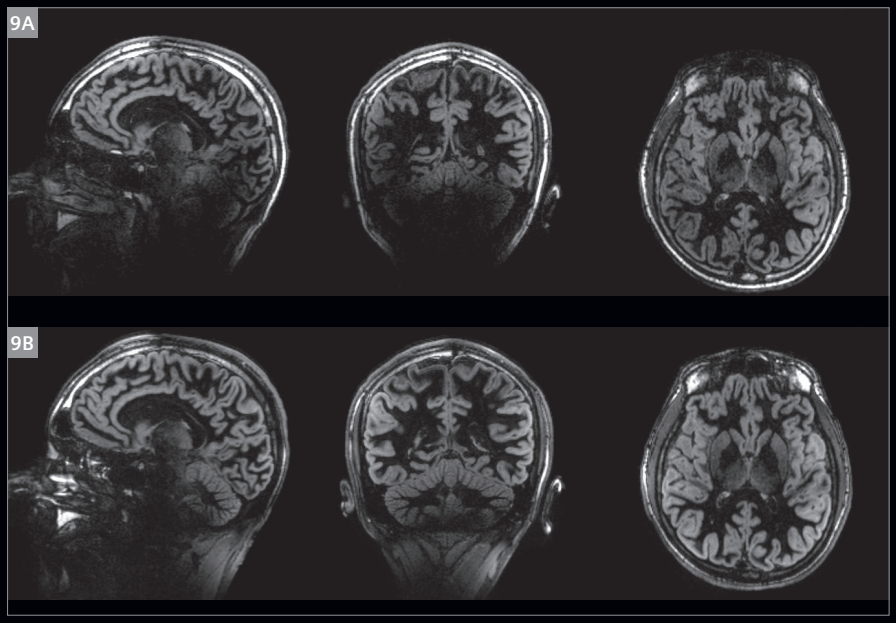
6 T2*-weighted FLASH sequence (6A) Proposed GRE protocol with Universal Pulses. **(6B)** Associated minimum-intensity projection (minIP), with 4 mm slice thickness. Note the high image quality, including in the lower part of the brain. This type of protocol could be used for quantitative susceptibility mapping (QSM).



7 T2-weighted SPACE (Sampling Perfection with Application optimized Contrasts using different flip angle Evolution) sequence (7A) Proposed protocol in TrueForm. **(7B)** Same protocol with Universal Pulses. The 3D SPACE sequence generates one T2-weighted volume. The chosen refocusing train option was T2 var (with target T1: 1400 ms, target T2: 50 ms). The improvement in excitation and refocusing homogenization significantly enhances signal homogeneity, notably in the cerebellum and temporal lobes.



8 Dark fluid T2-weighted SPACE sequence with T2 magnetization preparation
(8A) Proposed protocol in TrueForm. **(8B)** Same protocol with Universal Pulses. This sequence generates one T2-weighted volume with suppressed cerebrospinal fluid (CSF) signal. The preparation consisted of a 90°-τ-180°-τ-90° module (τ = 50 ms) to achieve an effective inversion of the CSF signal and a saturation in the brain tissues. This module is described in detail in [25]. The chosen refocusing train option was T2 var (with target T1: 1400 ms, target T2: 50 ms). The multiple improvements in preparation, excitation, and refocusing RF pulses results in an efficient signal restoration in the cerebellum and temporal lobes.



9 Double Inversion Recovery (DIR) SPACE sequence
(9A) Proposed protocol in TrueForm. **(9B)** Same protocol with Universal Pulses. The 3D SPACE sequence generates one T2-weighted volume with both WM- and CSF-suppressed signals. The chosen refocusing train option was T2 var (with target T1: 1400 ms, target T2: 50 ms). The sequence SAR is lower with UP than with TrueForm, since the inversion GRAPE pulses are less energetic than the standard adiabatic RF pulses. The multiple improvements in preparation, excitation, and refocusing RF pulses significantly enhances signal homogeneity and achieves efficient signal restoration in the cerebellum.

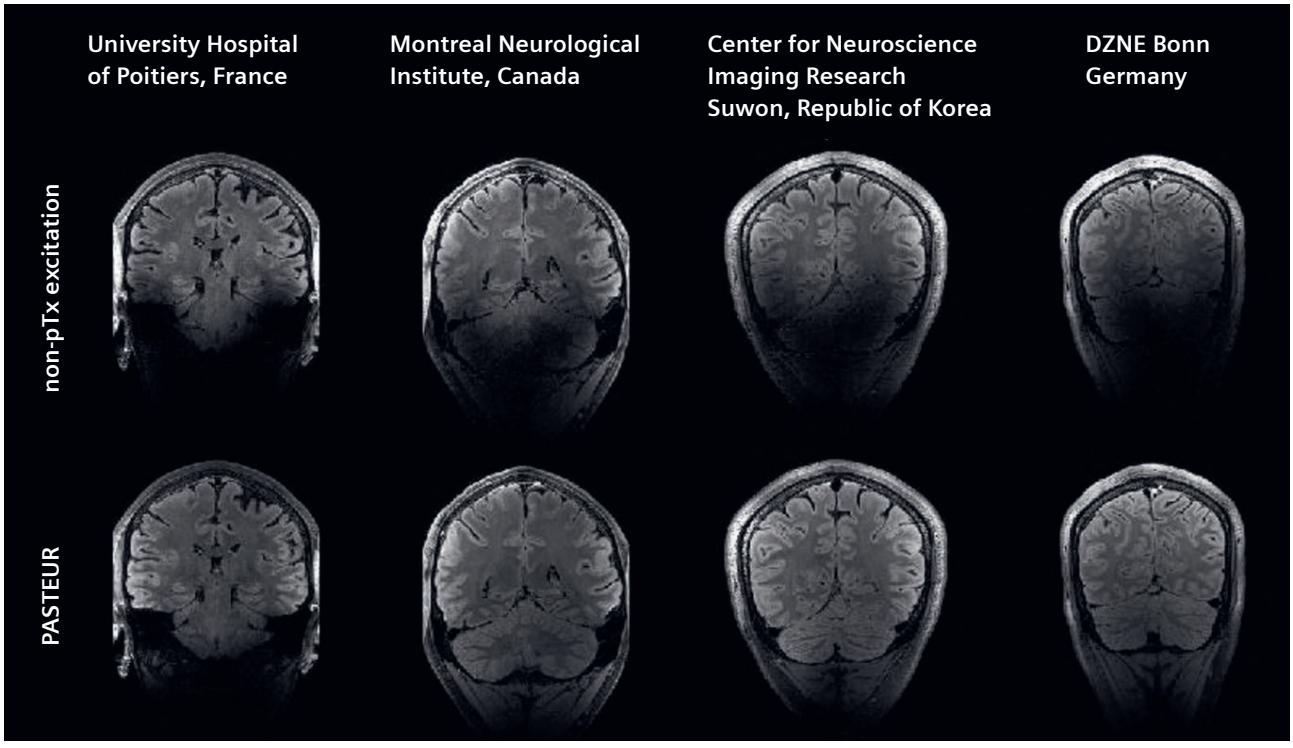
Discussion

In this work, the PASTEUR package was successfully deployed in a clinical site equipped with a MAGNETOM Terra and with no previous expertise in pTx or RF pulse design. The easy-to-use package allowed the team to acquire high-quality, high-resolution, whole-brain 3D structural images from several healthy volunteers, with various clinically relevant MR contrasts and at strictly zero workflow penalty. The results were very favorably received by the local radiologists, who concluded that typical UHF image artifacts were "gone for good".

The Universal Pulses presented here rely on a representative field database acquired in advance, and designed offline once by MR experts using thorough optimization approaches (since the offline computation time is irrelevant, increased pulse-design performance was achieved). UPs are thus valid for a given field strength (7T), body part (head), patient position (headfirst supine), and pTx RF coil. Assuming a certain degree of similarity in the B_1^+ and ΔB_0 maps among the population, UPs could be successfully applied to new patients without personalized field map measurements and RF pulse calculations. The PASTEUR package therefore makes the use of the underlying pTx hardware completely transparent to the operator.

While earlier work showed that increasing the size of the database improves UP robustness, the pulses' universality appears to converge rather quickly with the number of subjects [13]. Nevertheless, the idea of introducing database subgroups based, for instance, on gender, age, body mass index, or disease condition should be investigated in the future. Additional improvements could be made to further improve the universality, based on either of the following:

1. the latest machine-learning approaches to categorize the patients (Smart Pulse) [26];
2. fast subject- and exam-specific calibration using standardized UPs (SUPs) [27];
3. a combination of UPs with fast, tailored approaches (FOCUS) [28].



10 Dark fluid T2-weighted SPACE imaging with PASTEUR in four testing sites
Comparisons of standard non-pTx excitation and PASTEUR images from several research centers equipped with MAGENTOM Terra and MAGENTOM 7T^{Plus} systems (Figure adapted from [18]), illustrating the universality and reliability of UPs. From left to right: University Hospital of Poitiers in France; Montreal Neurological Institute in Canada; Center for Neuroscience Imaging Research in Suwon, Republic of Korea; and German Center for Neurodegenerative Diseases (DZNE) in Bonn, Germany.

Lastly, UP advantages were soundly demonstrated for brain imaging [9, 13–16, 25], yet other organs could likely also benefit from this approach, accounting for increased anatomical variability [29].

As already stated, image quality of the whole brain was always significantly improved with UPs compared to TrueForm, in all considered imaging contrasts. Occasionally, small image artifacts remained in UP imaging. These hyper-signal artifacts arise from very localized and strong off-resonance effects, which have more variability among individuals (see also Figure 2). This is a known limitation of UPs, and radiologists should be aware of it. Note that the proposed imaging protocols could likely be improved, especially to reduce acquisition time. For instance, the latest acceleration techniques, such as compressed sensing, were not yet available for MPRAGE and MP2RAGE [30].

Additional MR sequences and supported features are planned for the PASTEUR package in the future: Several non-selective 3D MR sequences could be added, an important milestone would be the ability to excite arbitrary slabs with UPs [31], and 2D imaging should also be addressed while still maintaining the universality of the approach [32]. Importantly, all PASTEUR developments will be deployed to operate on the Iseult MAGNETOM 11.7T MRI system [33] recently installed at CEA NeuroSpin, a world-leading R&D collaboration between CEA and Siemens Healthineers.

The PASTEUR package is currently available for the 7T MAGNETOM Terra on the C2P platform[2] from Siemens Healthineers. At the time of writing, the PASTEUR package has already been distributed to 15 sites around the world (Fig. 10). Its adoption by the UHF community could help pave the way for pTx integration in clinical workflows.

Acknowledgments

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[2]Access to the C2P platform from Siemens Healthineers is possible for collaboration partners who have signed the associated IDEA agreement. Please contact your local collaboration manager for more information.

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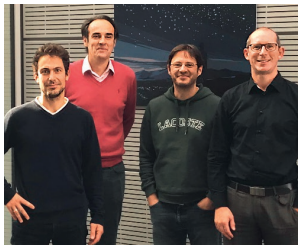

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