RESEARCH ARTICLE

Calibration-free pTx of the human heart at 7T via 3D universal pulses

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Purpose: MRI at ultra-high fields in the human body is highly challenging and requires lengthy calibration times to compensate for spatially heterogeneous $B_1^+$ profiles. This study investigates the feasibility of using pre-computed universal pulses for calibration-free homogeneous 3D flip angle distribution in the human heart at 7T.

Methods: Twenty-two channel-wise 3D $B_1^+$ data sets were acquired under free-breathing in 19 subjects to generate a library for an offline universal pulse (UP) design (group 1: 12 males [M] and 7 females [F], 21-66 years, 19.8-28.3 kg/m²). Three of these subjects (2M/1F, 21-33 years, 20.8-23.6 kg/m²) were re-scanned on different days. A 4kT-points UP optimized for the 22 channel-wise 3D $B_1^+$ data sets in group 1 (UP22-4kT) is proposed and applied at 7T in 9 new and unseen subjects (group 2: 4M/5F, 25-56 years, 19.5-35.3 kg/m²). Multiple tailored and universal static and dynamic parallel-transmit (pTx) pulses were designed and evaluated for different permutations of the $B_1^+$ data sets in group 1 and 2.

Results: The proposed UP22-4kT provides low $B_1^+$ variation in all subjects, seen and unseen, without severe signal drops. Experimental data at 7T acquired with UP22-4kT shows comparable image quality as data acquired with tailored-4kT pulses and demonstrates successful calibration-free pTx of the human heart.

Conclusion: UP22-4kT allows for calibration-free homogeneous flip angle distributions across the human heart at 7T. Large inter-subject variations because of sex, age, and body mass index are well tolerated. The proposed universal pulse removes the need for lengthy (10-15 min) calibration scans and therefore has the potential to bring body imaging at 7T closer to the clinical application.

KEYWORDS
7 Tesla, body MRI, heart, parallel transmission, universal pulse

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1 | INTRODUCTION

Ultra-high field (UHF) MRI has many advantages such as improved SNR and spectral resolution, increased susceptibility sensitivity, and often higher contrast compared to lower field strengths, and, therefore, potentially higher temporal or/and spatial resolution. However, UHF MR is often limited by inhomogeneities of the transmit (Tx) magnetic RF field \((B_1^+)\) yielding spatially variable flip angles (FA) with potential FA voids, and, therefore, a spatially varying contrast. This effect can impact an image-based diagnosis or a quantitative evaluation.

Various techniques exploiting the spatial differences in the \(B_1^+\) maps of the individual Tx channels of a multi-channel Tx coil have been proposed to address the spatial heterogeneities of the FA. A fundamental challenge of such subject-tailored solutions, hampering their wider use and, therefore, the progress of UHF MRI in general, is the need to acquire subject-specific \(B_1^+\) maps, to process them, and to calculate RF pulses or \(B_1^+\) shim solutions, which may require up to 15 min in the human brain. This issue has been successfully addressed by Gras et al using so-called “universal pulses” (UPs). UPs are pre-computed for a library of different \(B_1^+\) maps, and in the same target region, they can be applied to unseen subjects without additional calibration. UPs have been successfully applied for a wide range of pulse designs, sequences and applications in the brain at 7T and have inspired adapted applications including universal RF shims for spectroscopy in the head. Furthermore, a trade-off between UPs and a subject-tailored approach using a spiral nonselective (SPINS) trajectory has recently been demonstrated for brain applications. By combining fast \(B_1^+\) mapping with an RF pulse design initiated by UPs, the pulse’s subject-specific fidelity was increased while calibration time remained below 1 min. Other calibration-free approaches were proposed for the brain using machine-learned slice-by-slice RF shims at 7T or for the liver using dynamic SmartPulses at 3T, but so far not at 7T.

Although the vast majority of the subject-specific and all of the calibration-free parallel-transmit (pTx) methods at 7T have been proposed, investigated, and applied to the human brain, such techniques are even more needed for UHF applications in the body as the \(B_1^+\) heterogeneity is much more pronounced in the thorax and abdomen. Whereas tailored static \(B_1^+\) shimming was proposed for smaller 2D region of interests (ROIs) such as the prostate or the human heart, dynamic pTx showed to further improve excitation uniformity in larger 2D and 3D ROIs in the liver and the heart. The required \(B_1^+\) maps for such optimizations are not straightforward to obtain in the chest and abdomen because of their complex anatomy, larger size, and multiple manifestations of physiological motion. The most common \(B_1^+\) mapping methods used in the brain are sensitive to respiratory and cardiac motion or blood flow, they are incompatible with cardiac triggering or require too much time to be applicable in a single breath-hold. Only recently 3D acquisitions obtained in a non-Cartesian manner under free-breathing have been reported yielding respiration-resolved 3D absolute \(B_1^+\) maps assuming that the sum of the magnitudes of the Tx channels equals the sum of the magnitudes of the Rx channels. The 3D \(B_1^+\) maps were successfully used for static and dynamic pTx in the human heart despite an estimated error of 10% for the used 8Tx/32Rx coil configuration and potential additional errors arising from heart motion and flow. However, although recent progress made calibration times of only 30 s possible for human brain applications including channel-wise 3D multi-slice absolute \(B_1^+\) mapping, the acquisition of channel-wise 3D relative \(B_1^+\) maps of the human body (3 min 35 s) combined with an offline non-Cartesian reconstruction (1 min), manual 3D ROI placement (3 min), pulse design (1 min) plus variable extra time for checking the result still requires calibration times of ~10-15 min.

The need for pTx in the body and the currently long scan times for \(B_1^+\) mapping for these regions make the concept of 3D UP applied to the human body highly appealing. However, a one-size-fits-all solution for the human body or selected 3D regions such as the heart has not been shown yet. Moreover, large inter-subject variations demonstrated at 3T for the human liver required to cluster the subjects in different subgroups using the SmartPulse approach and raised the question of whether only a single class of UPs would work at all in the human body at 7T. It is also unclear how to set up a library for a one-size-fits-all UP in the human heart and how many different \(B_1^+\) data sets would be required to cover the much larger inter-subject \(B_1^+\) variations resulting from a variation of the heart size, heart position, and body-mass-index (BMI) compared to the human head.

This study aimed to investigate the feasibility of using UPs in the human body to achieve calibration-free, homogeneous FA distributions throughout a 3D volume covering the entire heart at 7T. We show that a single class of UPs computed offline using 22 3D \(B_1^+\) maps of healthy subjects with different sex, age, and BMI performs well for both \(B_1^+\) maps from subjects included in the library and unseen subjects. Results obtained by the proposed UP were compared to those obtained by (1) static (magnitude and phase) \(B_1^+\) shimming, (2) dynamic kT-points pulses optimized for a subject-specific 3D heart ROI, and (3) group-specific UPs computed for limited subsets of the library. In vivo data successfully validated the robustness of the UP experimentally at 7T in 9 unseen subjects.

By eliminating the need for a \(B_1^+\) calibration procedure and thereby simplifying the workflow while saving precious scan time, the presented work demonstrates a strong benefit for 3D cardiac MR at 7T, which has the potential to push future 3D body applications at UHF.
2 METHODS

2.1 Subjects and MR scanner hardware

MRI was performed according to an approved Institutional Review Board protocol and after written informed consent in 2 groups of healthy subjects. In the first group, 22 $B_1^+$ data sets from 19 subjects were acquired to generate a library for an offline UP design (group 1: 12 males [M] and 7 females [F], 21-66 years, 19.8-28.3 kg/m²). Here, 3 subjects (2M/1F, 21-33 years, 20.8-23.6 kg/m²) were re-scanned in different scan sessions on different days. In the second group, 9 new and unseen subjects (group 2: 4M/5F, 25-56 years, 19.5-35.3 kg/m²) were scanned using the same scan protocol applied in group 1 plus additional scans were performed with the pre-calculated UP. Therefore, a total number of 31 3D $B_1^+$ data sets was acquired. Although a large range of BMI was investigated, the BMI distribution was slightly skewed distribution toward lower BMI values with a mean of 23.6 kg/m² as compared to the population, because the subjects were recruited from a limited pool of healthy subjects according to our ethical approval.

Acquisitions were carried out on a 7T scanner (Magnetom 7T, Siemens Healthineers, Erlangen, Germany) using an 8-channel transmit array and a whole-body gradient system. The scans were performed with a 32-element body array (MRI.TOOLS, Berlin, Germany) driven in 8Tx/32Rx mode. The coil consists of 1 front and 1 rear segment, each containing 4 dipoles and 12 loops. The 16 channels are arranged in 4 parallel blocks of size 42 cm × 6.7 cm with 3.4 cm spacing between the blocks, each with 3 adjacent loops in head-foot direction and 1 dipole element across this triplet. A single loop covers roughly 1/3 of the dipole along the head-feet direction and has a small overlap with the neighboring loop. For transmission, the relative phases and amplitudes within each block are fixed, making it a single Tx element. The coil was delivered with a declaration of conformity to IEC 60601-1 and IEC 60601-2-33 standards by the manufacturer, certified by an independent test institute (ie, a notified body). Based on these documents, the local ethics board approved its use as an investigational device for studying human subjects. Local/global specific absorption rate limits were incorporated by limiting the RF power of each transmit channel, set to 11.8 W per channel for the 6 min window, in first-level controlled mode, and 23.6 W for the 10 s window.

At the beginning of each session, the posterior coil half was centered on the subject’s heart in head-foot direction whereas the anterior coil half was placed based on anatomic landmarks and feedback from the subject with a 2 cm gap to the subject’s chin. Although we aimed to position the heart in the isocenter, inter-subject variations of the heart size, shape, and position could still be observed in the resulting $B_1^+$ maps.

Reconstructions of the $B_1^+$ maps, manual slice-by-slice selections of the 3D heart ROIs, RF pulse designs, and creation of the pulse files were performed on a separate workstation (12 cores with 2.1 GHz, 128 GB RAM). The optimized static and dynamic pTx pulses and 3D gradient shapes were imported into a customized 3D GRE sequence using a radial phase encoding (RPE) trajectory.

2.2 Adjustments and calibration scans

Relative 3D $B_1^+$ maps of the thorax were acquired for each subject with an RPE trajectory under shallow breathing (nominal FA = 20°, TE/TR = 2.02/40 ms, FOV = (250 × 312 × 312) mm³, resolution = (4 × 4 × 4) mm³, 256 RPE-lines with golden-angle increments, TA = 3 min 35 s). Following the acquisition, the raw data were exported to a remote workstation and reconstructed during the next MR scan (1 min). The reconstruction of non-respiration resolved channel-wise 3D $B_1^+$ maps were completed in <1 min. The reconstructed maps had an isotropic voxel size of 4 mm and showed no visible motion-induced artefacts. The relative $B_1^+$ maps were normalized by the mean value of the sum of magnitudes to be able to use comparable regularization terms and nominal FAs across the different subjects. The sum of magnitudes of the $B_1^+$ maps was used to manually draw an ROI covering the entire heart on a slice-by-slice basis for each subject (3 min). The ROI was then used as a binary mask for static and dynamic pulse design (1 min) followed by variable extra time for checking the results plus creating the RF pulse files and if necessary, the repetition of individual adjustment steps (1-5 min). The total adjustment time to perform tailored static and dynamic pTx including a final check of the RF pulses required 10-15 min.

2.3 Pulse design and evaluation

Four different pulse types have been investigated in this work: (1) default: phase and equal magnitude set by the coil manufacturer to provide sufficient $B_1^+$ throughout the heart and the aorta; (2) tailored-MP: 3D optimized subject-specific magnitude and phase shim settings; (3) tailored-kT: optimized subject-specific kT-point pulses; and (4) UP-kT: optimized universal kT-point pulses for different libraries.

The default shim was set by the manufacturer as a trade-off between $B_1^+$ power efficiency, specific absorption rate efficiency, and avoidance of voids throughout the entire ascending aorta, descending aorta, and the heart based on an electromagnetic simulation of the RF coil. In the following, the number of kT-points and the library size is added to the pulse abbreviations to distinguish between the different pulses used throughout this work. For instance, the proposed
UP22-4kT was computed using a library with 22 $B^+_1$ data sets for 4 kT-points. The tailored-MP and tailored-kT pulses were designed in MATLAB, (The MathWorks, Natick, MA) using the small-tip-angle approximation for the 3D heart volume. Tailored pulses successfully eliminate the dropouts, but require an extra calibration time of ~10-15 min for the acquisition and reconstruction of subject-specific $B^+_1$ maps, manual selection of the heart ROI, and subject-specific RF pulse design.

The tailored kT-points approach has been extended to compute small-tip-angle UP-kT pulses (RF pulses and 3D gradient blips) across multiple $B^+_1$ data sets, inspired by the design of UPs in the human head, solving;

$$\min_{b_\alpha} \frac{1}{2} \left\| m_d - m_p \right\|_{\text{ROI}}^2 + \frac{\beta}{2} \sum_{ch=1}^{N_c} \left\| b_{ch} \right\|^2,$$

with $m_d$ representing the desired (complex) 3D excitation pattern with uniform magnitude (ie, FA magnitude in degree). The phase of $m_d$ in radians is updated in each iteration as used in the MLS approach: $m_p$ represents predicted (complex) 3D excitation pattern (ie, FA magnitude in degree and phase in radians), $N_c$ represents the number of transmit channels, $b_{ch}$ represents the complex channel-wise RF weights (ie, magnitude and phase setting applied at each sub-pulse), and $\beta$ represents the regularization term. $m_p$ is defined for each kT-point as:

$$m_p = \sum_{ch=1}^{N_c} \tilde{B}^+_{1,ch} A(K) b_{ch},$$

with $\tilde{B}^+_{1,ch} = [\tilde{B}^+_{1,ch,1}, \tilde{B}^+_{1,ch,2}, \ldots, \tilde{B}^+_{1,ch,N_n}]$ representing stacked $B^+_1$ data sets of $N_n$ subjects and $A(K)$ representing the Fourier system matrix that is defined by the set of excitation k-space locations $K$ defined by the optimized gradient trajectory. The dimension of $A(K)$ is the number of voxels in the ROI times the number of kT-points.

The used interleaved greedy and local optimization starts with a single kT-point and alternately updates the RF weights and target phase pattern until sufficient reduction of the excitation error is achieved. The excitation k-space location of the next kT-point is selected by a greedy method and the RF weights and target phase pattern are updated until convergence. These steps are repeated alternately until all kT-points have been added to the pulse. A 2-step optimization has been performed to reduce the chance of ending up in an unfavorable local minimum. First, we have computed 200 optimizations with different randomized RF phase vectors for the kT-points. The best result was then used for a full L-curve optimization to tune the regularization parameter $\beta$.

Figure 1 shows FA predictions of the default shim, the required steps to achieve the static or dynamic tailored pulse design and the proposed calibration-free pTx of the human heart at 7T for 1 representative subject. The code for the UP design and the $B^+_1$ data sets can be downloaded from https://github.com/chaigner/UP_body.

The tailored-4kT and UP22-4kT pulses were implemented using four 0.15-ms long square RF pulses and four 0.09-ms long 3D gradient blips, leading to a total duration of 0.96 ms Bloch simulations and subsequent quality checks were performed after optimization before writing the pulse file and exporting them to the MR scanner for qualitative comparison to the prediction in the pulse design.

### 2.4 Statistical analysis

The coefficient of variation (CVs) of the FA predictions of different pulses and groups in the heart ROIs were used to assess the statistical difference by a 1-sample t-test. We performed the t-test with the null hypothesis that the difference of the CVs from 2 groups comes from a normal distribution with a mean equal to 0 and unknown variance. The results were considered statistically significant if $P$ was < .05. Statistically significant results are denoted by a star (*) and not statistically significant results are denoted by “NS” in the figures.

### 2.5 Library design

A total number of 22 different libraries that contain an increasing subset of the 22 $B^+_1$ data sets from group 1 were analyzed to investigate the impact of the number and variability of the different $B^+_1$ data sets on the UP performance. For example, the first library contained only the first $B^+_1$ data set, the second library contained 2 $B^+_1$ data sets (1 and 2) and so on. No educated ordering scheme was used here; instead, the different libraries were created based on the acquisition date in an increasing fashion. The last (ie, the full) library that contained all 22 $B^+_1$ data sets covers a range of sex, body shape, and age (group 1; details are described above) and was used to design the proposed library UP22-4kT. The full library was also used to tune the regularization parameter $\beta$ to achieve a good trade-off between excitation homogeneity and total RF power (Equation 1). The UP22-4kT was computed offline and was used in the experimental validation in 9 unseen test cases (group 2; details are described above). Twenty-two library permutations omitting a different data set of the 22 $B^+_1$ data sets were created (ie, permutation 1 leaves out $B^+_1$ data set 1, permutation 2 leaves out $B^+_1$ data set 2, and so on) to analyze the impact of each $B^+_1$ data set on the robustness of the UPs. All UPs were evaluated using the CV that is defined as the SD of the FA divided by the mean FA in the heart ROI.
2.6 Retrospective simulation studies

In addition to the evaluation in group 1 (library) and group 2 (unseen test cases), the impact of different sub-groups on the performance of the UPs has been analyzed in 4 retrospective simulation studies. For this purpose, 4 additional groups were created with different compositions using all 31 $B_1^+$ data sets: (group 3) library-male, 13 $B_1^+$ data sets of male subjects; (group 4) library-female, 18 $B_1^+$ data sets of female subjects; (group 5) library-low BMI, 16 $B_1^+$ data sets of 8 male and 8 female subjects with a BMI <23.5 kg/m$^2$; and (group 6) library-high BMI, 15 $B_1^+$ data sets of 10 male and 5 female subjects with a BMI >23.5 kg/m$^2$. The UPs were optimized as described above. The different UPs were evaluated using the CV for the predicted $B_1^+$ maps in the heart ROIs.

2.7 Experimental validation

Isotropic, high-resolution 3D image data sets were acquired with tailored-4kT and precomputed UP22-4kT pTx pulses to validate the FA predictions in the unseen test cases (group 2) using RPE-trajectory based 3D gradient-echo scans (nominal FA = 10°, TE/TR = 1.75/3.7 ms, FOV = 250 × 312 × 312 mm$^3$, resolution = 1.4 × 1.4 × 1.4 mm$^3$, 256 RPE lines separated by the golden angle, TA = 3 min 35 s). The acquired 3D RPE data sets were binned into 4 respiratory motion states using self-navigation. The respiratory motion surrogate was obtained from the central k-space line ($k_x = k_z = 0$) of each radial spoke. The underlying motion field was estimated via image registration based on the aforementioned reconstructions and was used to correct the respiratory motion. The resulting respiratory corrected
3D data set was then used to qualitatively validate the \(B_1^+\) predictions.

## RESULTS

### 3.1 Performance of tailored kT-point pulses

Figure 2A shows the CVs of the tailored-MP and tailored-kT pulses, which were optimized for and applied to each of the 22 \(B_1^+\) data sets of group 1. Compared to the default phase setting with a median CV of 44.7%, tailored-MP pulses reduce the median CV to 14.9% and the performance increases further by adding more kT-points. In 4 subjects, however, the tailored-MP pulse was not sufficient to reduce the CV below 20% and FA dropouts remained in the 3D FA-predictions (not shown). For tailored-4kT pulses, we observe a median CV of 7.2% with a range of 5% to 10% across all 22 \(B_1^+\) data sets. Figure 2B shows the performance of tailored-MP and tailored-kT pulses that were optimized for the \(B_1^+\) data set of subject 1 and then, applied to all 22 \(B_1^+\) data sets of group 1. Applying tailored pulses to the \(B_1^+\) data set of subject 1 yield CV values of 6% to 12%, depending on the number of chosen kT-points. In contrast, if this pulse is applied to \(B_1^+\) data sets 2-22, a large CV variation between 15% and 55% was observed, a direct consequence of large inter-subject variabilities and resulting differences in the channel-wise \(B_1^+\) maps. The same observation has been made when the \(B_1^+\) map for optimization was used from a subject other than subject 1.

### 3.2 Tuning and evaluating UP pulses

Figure 3A shows the CV for the UP-4kT as a function of the number of \(B_1^+\) data sets included in the library. Note that the evaluation was always performed on all 22 \(B_1^+\) data sets. As expected, adding more \(B_1^+\) data sets to the library decreases the median CV measured across 22 \(B_1^+\) data sets from 31.2% (UP1-4kT) down to 12.8% (UP22-4kT) with a range of 10.7% to 15.8%. However, the question of the optimal or minimal number of \(B_1^+\) data sets in the library remains unanswered. The median value remains constant after including 10 \(B_1^+\) data sets in the library, but at least 1 outlier has been observed up to a library size of 20 \(B_1^+\) data sets. Three subjects were re-scanned with a slightly different coil position (\(B_1^+\) data sets 12, 19, and 20). Figure 3B shows the double-logarithmic L-curve plots of the root-mean-square RF power and the nominal FA root-mean-square error for the tuning of the regularization parameter. Figure 3C shows the evaluation of UP21-4kT pulses from 22 different data set permutations omitting 1 of the 22 \(B_1^+\) data sets each and then applying them.
to all 22 $B_1^+$ data sets. Three $B_1^+$ data sets (2, 13, and 17) have a stronger impact on the overall performance, because leaving out these subjects leads to at least 1 outlier with a CV $>$20%. However, no explanation was found why these 3 $B_1^+$ data sets (3 male subjects with a BMI of 19.7, 24, and 28.4 kg/m$^2$) are different compared to the other 19 $B_1^+$ data sets.

### 3.3 Performance of static and dynamic UPs

Figure 4 shows the performance of UP-4kT and UP-kT examples with a varying number of kT-points designed using the full library of group 1 with all 22 $B_1^+$ data sets. All UPs applied to the 9 test cases of group 2 ($B_1^+$ data sets 23-31), which had not been included in the library for pulse design, yielded CVs comparable to the 22 $B_1^+$ data sets of the used library. The UP-MP pulse results in a median CV of 25% (range = 18.5%-34%), which is consistently better than the default setting with a median CV of 44% (range = 33%-65%). However, 6 FA predictions using the UP-MP pulse still result in unfavorable CVs larger than 30%. The performance of the UP-kT examples improves, as expected, with an increasing number of kT-points and results in a median CV of 16% for 2 kT-points and 12% for 5 kT-points with comparable CV variations.
3.4 Impact of group-specific UP libraries

Figure 5 depicts the resulting CV values of 5 different UP-4kT pulses designed for different subgroups of the database. For example, the UP designed based on $B_1^+$ data sets from female subject (Figure 5B) yields median CV values of 10.4% (range = 8.8%-15.9%) for this group, but results in elevated median CV values of 18.2% in the male group (range = 9%-32.1%). A similar trend was observed for all 4 group-specific UPs.
3.5 Performance of the precomputed UP in unseen test cases

Figure 6 shows representative RF and gradient vectors of $B_1^+$ data set 23; unseen test case in group 2. The different RF pulse amplitudes were scaled to achieve the same mean nominal FA of $10^\circ$ in the 3D heart ROI to allow quantitative comparisons of RF voltages between pulses. For the tailored-MP pulse, the RF power is distributed unevenly across the channels with a 3-fold higher peak voltage for channel 7 (located posterior to the heart) as compared to the second-highest amplitude. Across all 31 $B_1^+$ data sets, we found on average a 4-fold increase of the peak voltage of the tailored-MP and a 3-fold increase of tailored-4kT and UP22-4kT pulses compared to the default pulses. Compared to the tailored-MP pulses, the tailored-4kT and UP22-4kT pulses consistently result in a more evenly distributed RF power across the different RF channels. Comparable peak RF voltage was observed between tailored-4kT and UP22-4kT pulses. However, the tailored-4kT pulses show different complex RF weights and 3D gradient blips compared to the UP22-4kT pulse. The optimized phase encodes and complex RF weights of UP22-4kT are summarized in Supporting Information Figure S2.

Figure 7A,B depicts the predicted CV in the 3D heart ROI for $B_1^+$ data sets obtained from the library (group 1) and unseen test cases (group 2) using 4 excitation settings: default, tailored-MP, tailored-4kT and UP22-4kT. In group 1, UP22-4kT yields lower median CVs than tailored-MS (12.8% vs. 18%) and does not result in severe signal drops in the heart, typically indicated by elevated CV values >25% in our experience. As expected, further improvement in CV was achieved in group 1 by using tailored-4kT pulses with a median CV of 7%. The same trend was observed in group 2 for the 9 unseen test cases. Although 7 test cases result in CVs of <13%, 2 resulted in a higher CV up to 18%. However, the tailored-4kT pulse resulted in relatively higher CV values of up to 12%.

Figure 7C shows 1 representative unseen subject ($B_1^+$ data set 23) for all 4 excitation settings. UP22-4kT resulted in smooth FAs even though $B_1^+$ data set 23 was not included in the library. This effect is further highlighted for all 9 unseen test cases in Figure 8A that qualitatively illustrates the FA predictions for a sagittal slice using the default and the proposed UP22-4kT to achieve a nominal FA of $10^\circ$ in the 3D heart ROI. Note, that homogeneity is achieved in all test cases despite the large inter-subject variations. An overview of all 31 $B_1^+$ data sets is shown in Supporting Information Figure S1. Quantitative FA distributions within the 3D heart ROIs are depicted in a boxplot showing the 4-fold reduction of FA spread in all $B_1^+$-data sets.

**Figure 6** Pulse diagram showing the complex RF voltages (magnitude and phase) and 3D gradient blips of the tailored-MP, tailored-4kT and UP22-4kT of unseen $B_1^+$ data set 23. The relative RF voltage of each pTx pulse was scaled to achieve a nominal FA of $10^\circ$ in the 3D heart ROI. The tailored-MP pulse was realized as a series of 4 block pulses to compare the relative RF peak voltage and RF power to the tailored-4kT and UP22-4kT pulses.
AIGNER ET AL.

Figure 9 illustrates the respiratory corrected 3D GRE images acquired with UP22-4kT of 2 unseen subjects (23 and 24) in comparison to the FA predictions based on the acquired $B_1^+$ maps. Qualitatively, a close match between FA predictions and the 3D GRE images were observed, demonstrating the feasibility of calibration-free pTx in the human heart.

3.6 Application of the precomputed UP compared to tailored pulses

Figure 10 shows respiratory motion-corrected 3D GRE images acquired with the default setting, tailored-4kT and precomputed UP22-4kT of 2 unseen test cases (23 and 24). The 3D images acquired with UP22-4kT result in a comparable image quality as tailored-4kT pulses, which demonstrates the feasibility of mitigating the RF field inhomogeneity problem (indicated by yellow arrows) while eliminating the need for lengthy (10-15 min) calibration times.

4 DISCUSSION

The proposed UP optimized for a 3D region covering the whole heart provided consistently low CV values across all 22 $B_1^+$ data sets in the library (median in group 1: 12.8%) and, importantly, across all 9 unseen cases. Such CV values were lower and, therefore, yielded improved FA homogeneity as compared to the tailored-MP pulses (median in group 1: 18%). Even lower CV values (median in group 1: 7%) were only achieved by tailored-4kT pulses. Qualitatively, no degraded image quality was observed when 3D GRE images acquired with UP22-4kT were compared to acquisitions using tailored-4kT pulses although numeric simulations had suggested stronger FA variations. Therefore, although UP22-4kT results in a comparable image quality as tailored-4kT pulses, they do not require lengthy (10-15 min) calibration times.

This work was initially motivated by the observation that pTx in the human body can be very challenging and time-consuming. Subject motion between calibration and pTx application is another potential pitfall for the application
of tailored pTx. However, because of large anatomic inter-subject variations of the heart, it was not a priori clear if UPs would work well, and whether calibration-free pTx in the heart would require an approach that takes inter-subject variations into account, as suggested for the liver at 3T. To achieve robust UPs, a library of 22 $B_1^+$ data sets from subjects with different sex, age, and BMI was created. Multiple subsets of this library were created as proposed in to qualitatively and quantitatively evaluate the robustness of UPs computed for different sub-groups. As expected, group-specific UPs work well, but even more astonishingly, they produced only marginally better FA homogeneity compared to the one-size-fits-all UP computed for all 22 $B_1^+$ maps.

The stronger inter-subject variations of the heart size and position in the thorax are a potential explanation for the need for a much larger library size as compared to the UP design in the human head where 6 subjects were used. The 22 $B_1^+$ data sets used in this work allowed us to show the general feasibility of applying a robust UP in the heart at 7T. However, an even larger number of data sets or data sets with a larger variety in the library would further improve the robustness of the UPs. This, of course, is not a methodologic issue, but rather a logistical challenge. To reduce extra costs, one might speculate that the measured maps may be merged with simulated $B_1^+$ maps of the same coil and with different body models and positions.

Overall, the results are convincing with respect to the observed flexibility, robustness, and performance of a one-size-fits-all universal pulse in the human body. This is even more astonishing considering the structure of the used 32-channel body coil. Each of the 8 transmit modules consists of 4 coil elements, 1 dipole, and 3 loop elements that are located at different positions along the dipole in head–foot direction resulting in phase changes along this direction. Despite the observed robustness, major changes of the positions (e.g., larger shifts in head–foot direction) or major variations in the subject’s size may result in more pronounced inter-subject variations.

Based on the observations made in the heart, we expect that for other organs of comparable or smaller size the UP concept should perform similarly well. For larger 3D geometries such as the liver or the entire human body, in contrast, this may no longer be the case as reported by SmartPulses at 3T and more investigation would be needed to fully answer this question at 7T.
Another useful extension would be the design of UPs with large tip angles as proposed for the human head.\textsuperscript{14} At present, however, peak $B_1^+$ limitations of the used coil did not permit higher FAs than $\sim 5$ to $10^\circ$ without substantially increasing the non-selective, rectangular-shaped RF subpulses that collide with the aim for short RF pulse durations to limit the sensitivity to off-resonance effects. The short pulse durations of 0.96 ms allowed to neglect off-resonance effects.\textsuperscript{29} For longer pulse durations, however, subject-specific 3D $B_0$ maps might be needed to compensate for potential off-resonance effects as shown in the human brain.\textsuperscript{12} Furthermore, the low actual FAs allowed us to perform the pulse design based on relative $B_1^+$ maps. Because we are mostly interested in FA variations, we also decided to use the CV as a metric to quantify the homogeneity rather than the root-mean-square error that was used in the optimization. This has the limitation that systematic changes (eg, offsets of the average FA) are not covered by this analysis. Nevertheless, large FA pulses seem to be essential for cardiac imaging to introduce tissue contrast. The computationally intensive optimization would further benefit from an offline pre-calculation. Because computation time is not a limiting factor in the offline computation, it would be also interesting to add hardware constraints in the pulse design\textsuperscript{37} or to investigate the impact of gradient imperfections on the optimized pulses,\textsuperscript{38} especially when designing a simultaneous RF and gradient application such as 3D SPINS pulses.\textsuperscript{9}

Although non-respiration resolved channel-wise $B_1^+$ maps were suitable for shallow breathing for 3D cardiac RF pulse design,\textsuperscript{29} stronger respiration requires performing respiration-resolved reconstructions to generate $B_1^+$ maps free of breathing artefacts.\textsuperscript{31} Preliminary data suggest that tailored-4kT pulses designed for 1 respiration state might result in reduced performance if applied to the other respiration states.\textsuperscript{30} The design of respiration-specific and respiration-robust 3D tailored-4kT pulses using respiration-resolved 3D $B_1^+$ maps seem to compensate for differences between the respiration states\textsuperscript{30} in the case of strong respiration patterns. However, we saw that UPs can be robust to changes between subjects and, therefore, expect that they are also more robust to respiration. Nevertheless, further investigation is required to determine how much impact the respiration has on the performance of the UPs designed for a set of non-respiration resolved $B_1^+$ maps and if the performance could be increased using respiration resolved maps to cover such changes as well.
This study demonstrates in vivo that universal pulses with 4kT-points (UP22-4kT) are highly suitable for calibration-free 3D heart FA homogenization at 7T despite large inter-subject variations because of sex, age, and BMI. The proposed use of UPs allows calibration-free pTx without the need for a lengthy and challenging calibration process.

5 | CONCLUSION

This study demonstrates in vivo that universal pulses with 4kT-points (UP22-4kT) are highly suitable for
and has the potential to push the limits of body imaging at 7T and above.

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**SUPPORTING INFORMATION**

Additional Supporting Information may be found online in the Supporting Information section.

**FIGURE S1** Sagittal slice of the 3D FA predictions using the default setting (left) and the UP22-4kT (right) for 31 $B_1^+$ data sets (library: $B_1^+$ data sets 1-22, unseen test cases are $B_1^+$ data sets: 23-31). The 4kT-UP results in a homogeneous FA in the heart ROI of all 9 test cases.

**FIGURE S2** Optimized phase encodes ($k$-locations) for each gradient axis ($k_x$, $k_y$, and $k_z$) and optimized complex RF weights (magnitude and phase angle) for each of the 8 transmit channels and 4 kT-points of UP22-4kT.

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