Local excitation universal parallel transmit pulses at 9.4T

Ole Geldschläger | Dario Bosch | Steffen Glaser | Anke Henning

1High-Field Magnetic Resonance Center, Max Planck Institute for Biological Cybernetics, Tübingen, Germany
2Biomedical Magnetic Resonance, University Hospital Tübingen, Tübingen, Germany
3Department for Chemistry, Technical University of Munich, Garching, Germany
4Advanced Imaging Research Center, University of Texas Southwestern Medical Center, Dallas, Texas, USA

Correspondence
Ole Geldschläger, High-Field Magnetic Resonance Center, Max Planck Institute for Biological Cybernetics, Max-Planck-Ring 11, 72076 Tübingen, Germany.
Email: ole.geldschlaeger@tuebingen.mpg.de
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Purpose: To demonstrate that the concept of “universal pTx pulses” is applicable to local excitation applications.

Methods: A database of $B_0/B_1^+$ maps from eight different subjects was acquired at 9.4T. Based on these maps, universal pulses that aim at local excitation of the visual cortex area in the human brain (with a flip angle of 90° or 7°) were calculated. The remaining brain regions should not experience any excitation. The pulses were designed with an extension of the “spatial domain method.” A 2D and a 3D target excitation pattern were tested, respectively. The pulse performance was examined on non-database subjects by Bloch simulations and in vivo at 9.4T using a GRE anatomical MRI and a presaturated TurboFLASH $B_1^+$ mapping sequence.

Results: The calculated universal pulses show excellent performance in simulations and in vivo on subjects that were not contained in the design database. The visual cortex region is excited, while the desired non-excitation areas produce the only minimal signal. In simulations, the pulses with 3D target pattern show a lack of excitation uniformity in the visual cortex region; however, in vivo, this inhomogeneity can be deemed acceptable. A reduced field of view application of the universal pulse design concept was performed successfully.

Conclusions: The proposed design approach creates universal local excitation pulses for a flip angle of 7° and 90°, respectively. Providing universal pTx pulses for local excitation applications prospectively abandons the need for time-consuming subject-specific $B_0/B_1^+$ mapping and pTx-pulse calculation during the scan session.

KEYWORDS
9.4T, high-field MRI, local excitation, parallel transmit, pTx, reduced FOV, universal pulses
1 | INTRODUCTION

Operating MRI systems with a $B_0$ field strength of 7T and above (ie, ultra-high field (UHF)), provide higher signal-to-noise ratio, facilitates higher spatial resolutions, and potentially improves diagnostic sensitivity and specificity compared to clinical field strength, such as 1.5T or 3T.\(^1\)\(^3\) However, various technical challenges prevent UHF systems from being used routinely in the clinic.\(^4\) The shorter electromagnetic wavelength at UHF, which results in inhomogeneity of the radiofrequency (RF) field,\(^5\)\(^6\) can lead to spatially varying flip angles (FAs) and, thus, a spatial variation of the image contrast, signal dropouts or brightening. The most flexible approach to overcome this issue is parallel transmission (pTx).\(^7\) PTx enables much-improved control over the spatial and temporal RF field\(^8\)\(^9\) by exploiting the additional degrees of freedom of multiple independent RF transmission channels. Thus, research not only focuses on pulses for homogeneous slice selective\(^10\)\(^11\) or whole volume excitation,\(^12\) but also on pulses that produce local excitation\(^13\)\(^14\) (LEx, also called inner volume or spatially selective excitation) within the scanned object.

In general, pTx pulse design is based on a set of calibration measurements for each individual subject at the beginning of the scan session/experiment. Subject-specific static magnetic field ($B_0$) offset and transmit ($B_1^+$) field distribution maps from each transmit coil need to be acquired before the actual pulse can be calculated. The time needed for $B_0$ and $B_1^+$ map acquisition and pulse calculation is usually between 10 and 15 min,\(^4\) while the subject is already positioned in the scanner. Based on these maps, an RF pulse is calculated, which, usually in conjunction with a gradient waveform, excites a desired spatial pattern in the subject’s tissue. The computational effort of pulse design increases when RF power limitations have to be taken into account. This whole procedure consumes time that gives no clinical information and is a barrier to clinical uptake of the pTx technique.

Recently, Gras et al\(^5\) introduced the concept of “universal pTx pulses” (UPs). The general idea is to collect a database of $B_0$ and $B_1^+$ maps from a representative subject cohort. An RF pulse is designed based on this database and turns out to also perform well on subjects who were not inside the design database. The reliability and benefit of this concept for non-selective and slice selective pulses has been proven for pulses with small and large target FAs as well as their applications in various MRI sequences in the human brain at 7T.\(^16\)-\(^19\) It has been shown that UPs are virtually immune to inter-site differences.\(^20\) Additionally, a feasibility study for UPs calculated and simulated on $B_0/B_1^+$ maps acquired at 9.4T is\(^21\) has been presented. In all of these studies, the used transmit k-space trajectories are either “spokes”\(^22\) or “kT-points.”\(^12\)

In contrast to existing approaches, the goal of this study is to investigate the concept of UPs for LEx at 9.4T. In our own preliminary work, it was shown in simulations that it is possible to design pulses that can selectively excite the same 2D\(^23\) or 3D target pattern\(^24\) at 9.4T, as well as at 7T,\(^25\) across multiple subjects. The transmit k-space trajectories in these studies, as well as in the current work, are “spiral” k-space trajectories, which is another difference compared to previous UP studies. The advantages of spirals for LEx were already discussed.\(^26\)

In general, LEx can be used for reduced (or zoomed) field of view (FOV) applications. It allows to reduce the FOV in phase-encoding direction by masking the tissues outside the FOV, which would otherwise fold into the image.\(^27\) Consequently, LEx can reduce the total signal acquisition time and/or increase the spatial resolution which is important for a range of clinical brain and body applications.\(^28\) Furthermore LEx can reduce the distortion in EPI readouts in functional and diffusion-weighted MRI,\(^29\) due to the reduced FOV, especially because the decreased number of points in the readout direction allows shorter inter-echo spacing. LEx pulses were applied within various imaging sequences such as the gradient-echo (GRE) in rats\(^13\) or the fast-spin-echo sequence in the human brain,\(^30\) as well as for diffusion-weighted imaging in human prostate\(^31\) and pancreas.\(^32\) Moreover, LEx has been exploited for MR spectroscopy in the human brain at 3T\(^33\) and 7T\(^34\) to define shaped voxels.

In this work, we demonstrate the feasibility of the combination of LEx and UPs by local excitation of the visual cortex in the human brain with excellent suppression of the remaining brain areas as proof of principle. For that purpose, we collected a database of $B_0$ and $B_1^+$ maps from eight different subjects. We designed pulses that aim to excite a predefined 2D or 3D target excitation pattern (target FA of 90°, FA90), on the database heads. Afterward, the performance of these pulses was tested in simulations and in vivo at 9.4T. In order to show the potential of UPs for LEx, a GRE sequence with a reduced FOV was applied.

2 | METHODS

2.1 | UP calculation

To design UPs that produce the same excitation pattern on different heads, the “spatial domain method”\(^35\) from Grissom et al was applied. Its basic idea is to exploit the linearity of the Bloch equations for small tip angle regimes. Using the small tip angle approximation (STA), Pauly et al\(^26\) derived that the Bloch equation can be approximated by a Fourier integral of any desired (and realizable) excitation k-space trajectory,\(^36\) $k(t)$, weighted by a complex RF pulse $p(t)$, and spatially weighted by the transmit coils complex transmit sensitivity $s(x)$:

$$m(x) = i y m_0 s(x) \int_0^\infty p(t) e^{i \Delta B_0 (x) (t-T)} e^{i k(t)} dt, \quad (1)$$
with \( m(x) \) is the magnetization in voxel \( x \), \( \gamma \) is the gyromagnetic ratio, \( m_0 \) is the equilibrium magnetization magnitude, \( T \) is the pulse length, and \( \Delta B_0(x) \) denotes the field map.

To form an aggregate excitation pattern the single excitation patterns \( s_r(x) \) from the \( R \) transmit coils can be spatially superposed:

\[
m(x) = i \gamma m_0 \sum_{r=1}^{R} s_r(x) \int_0^T p_r(t) e^{i \gamma \Delta B_0(x)(t-T)} e^{i \omega x(t)} dt.
\]  

(2)

Analogously to Yip et al.,\(^3^7\) discretizing time to \( N_I \) samples and space to \( N_J \) voxels yields the following matrix-vector multiplication

\[
m = \sum_{r=1}^{R} S_r A p_r = \begin{bmatrix} S_1 A & \cdots & S_R A \end{bmatrix} \begin{bmatrix} p_1 \\ \vdots \\ p_R \end{bmatrix} = A_{full} p_{full},
\]  

(3)

with \( m \) is the length-\( N_J \) vector of the magnetization from each voxel \( x \) and \( S_r = \text{diag} \{ s_r(x) \} \) is a diagonal matrix containing the sensitivity pattern of transmit coil \( r \). The \((i,j)\)-th element of the \( N_J \times N_T \) system matrix \( A \) is given by:

\[
a_{ij} = i \gamma m_0 \Delta e^{i \gamma \Delta B_0(s_j)}(t_{ij} - T) e^{i \omega x(t_{ij})}.
\]  

(4)

\( A_{full} \) is a vertical concatenation of the matrices \( S_r A \) and \( p_{full} \) is a horizontal concatenation of the length-\( N_T \) vectors \( p_r \) of RF-pulse samples from coil \( r \).

By defining a target excitation pattern \( m_{tar} \) we obtain the optimization problem

\[
p_{TP}^* = \arg \min_p \left\{ \| A_{full} p_{full} - m_{tar} \|^2 \right\}
\]  

(5)

By minimizing this problem in Equation (5), we design the RF pulse \( p_{TP}^* \) that aims to excite the desired target pattern on one specific head (ie, the tailored pulse [TP]).

While the original “spatial domain method” was intended for designing pulses tailored to one specific subject, we extend this method herein in order to create a pulse \( p_{UP}^* \) that excites the same target pattern on multiple heads (ie, the UP):

\[
p_{UP}^* = \arg \min_p \left\{ \left\| \begin{bmatrix} A_{full,1} \\ \vdots \\ A_{full,NDB} \end{bmatrix} p - \begin{bmatrix} m_{tar} \\ \vdots \\ m_{tar} \end{bmatrix} \right\|^2 \right\},
\]  

(6)

where \( A_{full,p} \) with \( j = 1, \ldots, N_{DB} \), is the full system information matrix of subject \( j \) and \( N_{DB} \) is the size of the design database, ie, the number of subject heads based on which the pulse will be designed. By minimizing Equations (5) or (6) all voxels are weighted equally, ie, no specific weighting function was applied.

The optimization problem in Equation 6 was solved by performing two steps. First, the least-squares method implemented in the lsqr-function\(^3^8\) from MATLAB (MathWorks, Natick, MA) was applied, which solves a system of linear equations. The optimization was stopped after 20 iterations, which was empirically found as a compromise between performance and compute time. Applying higher iteration numbers led to drastically increased pulse voltages with only minor performance improvements, and no regularization term for voltage was applied. Notably, with the least-squares method, it is not possible to exclude the phase of the resulting excitation from the optimization, however, the profiles phase was of no interest during this study. For that reason, in the second step of the UP calculation, the lsqr result was used as an initial guess for the active-set algorithm implemented in MATLAB’s fmincon-function. The cost function used for this optimization is presented in Equation (6), ie, only the magnitude of the profiles are considered. Analogously to the literature,\(^1^5,1^6,1^8,2^1\) the active-set algorithm was chosen because of its speed and robustness.\(^3^9,4^0\) By means of the active-set algorithm, the solution was constrained to a maximum pulse amplitude of 130 Volt at plug level (hardware limit). The optimization was stopped if the improvement of the cost-function values was negligible during 30 consecutive iterations.

Although this approach was introduced for designing small tip angle pulses, it also “holds well at tip angles of 90°.”\(^2^6,3^5,4^1\) For that reason, we designed two different UPs with FA90. The first UP (UP2D) aimed to excite the visual cortex region in the central transversal slice of a head (by means of a 2D target pattern, Figure 1A)) with FA90. The remaining areas within the target slice should not be excited. The UP2D pulse is non-slice-selective and has a fixed duration of 7.96 ms using a 2D spiral-in k-space trajectory (max. amplitude: 23 mT/m, max. slew rate: 150 T/m/s, Figure 1A). That pulse length was chosen as a compromise between sufficient degrees of freedom for the optimization and application possibilities for pulses of that length. Tissue outside of the target slice was not taken into account for designing UP2D. Since UP2D is non-slice selective, a 3D sequence was used for performance evaluation, with frequency encoding along the head-foot direction (see “UP versus TP performance evaluation” section).

Analogously, UP3D aimed to excite the visual cortex area as well with FA90, but by means of a 3D target pattern (Figure 1B) and based on a 3D stack-of-spiral-in trajectory\(^4^2,4^3\) (max. amplitude: 7.4 mT/m, max. slew rate: 150 T/m/s, six spirals, Figure 1B). The pulse duration was 8.18 ms. For both pulses and gradient shapes, the dwell time was 10 μs. The scanner inherent gradient delay of 4 μs was taken into account in the
pulse files. For UP3D (FA90), the deviations between the STA forecasts and the results from the Bloch simulations were compared.

In order to create not only UPs for large tip angles, but also for small tip angles, the calculated UPs for FA90 were scaled down proportionally in order to create UPs with a desired FA of 7° (FA7). We also tested UP calculations directly with a target FA of 7°, but since these pulses did not considerably outperform the downscaled UPs (on the non-database heads, see Supporting Information Figure S1, which is available online, for 2D- and Supporting Information Figure S2 for 3D results), we maintained the downscaled approach.

To create a representative design database for the calculation of the UPs, B_0 and eight single-channel B_1^+ maps were acquired from the heads of eleven different subjects at 9.4T. Eight of the eleven datasets were used for UP design and three for performance evaluation in simulations. These numbers were based on a 7T simulation study in which it was shown that database size of five different heads theoretically is sufficient to design reliable LEx UPs. To increase reliability and since herein the field strength is higher, we wanted to be more conservative and added three more heads to the design database.

To calculate UP2D, the B_0/B_1^+ map information and the resulting excitation pattern from only the central slice of each head were taken into account. After application of the masking routine, each of the eight central slices consisted of between 1942 and 2208 voxels, which resulted in a total of 16533 voxels for all eight heads. For the design of UP3D, the information from the entire heads was employed (57028 to 65801 voxels per head, 487734 voxels for all eight heads).

Both optimization problems were solved on a high-performance-compute system node equipped with an Intel “Haswell” Xeon E5-2698 processor (128 GB RAM, 32 cores with 2.3 GHz each).

The design of UP2D was done using parallel computing on the 32 cores. However, for calculating UP3D, parallel computing was not applied because of RAM limitations.

During this study, the subject-specific TPs were calculated as a reference by solving the optimization problem in Equation (5) with MATLABs lsqr-function. As mentioned before, the lsqr-function does not allow to exclude the excitation phase from the optimization. However, only lsqr was used for TP design, due to time limitations for online pulse design (20 iterations ~ 0.7 (19) seconds for 2D (3D)). It should be noted that the TPs for FA7 were not downscaled FA90 pulses, but directly designed with a target FA of 7°. In case the maximum pulse amplitude exceeded the limit of 130
2.2 UP versus TP performance evaluation

Bloch equations were used to simulate the magnetization profiles of each RF pulse (using the corresponding $B_0/B_1^+$ maps of the heads). For simplicity, relaxation effects during the RF pulse dynamics were ignored but could be incorporated with knowledge of T1/T2 maps. The magnetization profiles were converted to FA profiles afterward. For each FA profile the normalized root mean square error (NRMSE) between the profile and the target excitation FA pattern, respectively, was determined, in order to evaluate the overall performance of a pulse. Additionally, the mean FA in the target excitation and non-excitation areas, respectively, were calculated for each profile to also verify the background suppression performance.

Before the application of TPs and UPs at the scanner, both, global SAR and maximum local SAR for each pulse were calculated using the VOP method. None of the pulses calculated during this study exceeded any of the SAR regulation limits. However, SAR constraints were not incorporated in the pulse design algorithm.

To test the pulses in vivo at 9.4T, all FA7 pulses (ie, UP2D/UP3D and the corresponding TPs for FA7) were applied on three non-database subjects in a T2*-weighted 3D short repetition time (TR) GRE-sequence (voxel size: $0.8 \times 0.8 \times 0.8$ mm$^3$, matrix size: $224 \times 280 \times 280$ (head to feet), 3D encoding direction: left to right, phase-encoding direction: anterior to posterior, frequency encoding direction: head to feet, TR = 18 ms, echo time (TE) = 8 ms, bandwidth (BW) = 260 Hz/px, GRAPPA$^{47} 2 \times 2$. To further prove the performance of the pulses, UP3D for FA7 was applied in a GRE-sequence with a reduced FOV (voxel size: $0.4 \times 0.4 \times 0.4$ mm$^3$, matrix size: $224 \times 162 \times 200$, TR = 18 ms, TE = 8 ms) on one non-database subject.

All FA90 pulses (ie, UP2D/UP3D and the corresponding TPs for FA90) were applied on three non-database subjects with a sequence analog to the one used for acquisition of the $B_0/B_1^+$ maps (see “Volunteer scans” section). For that purpose, the FA90 pulses were used as preparation pulse in the TurboFLASH sequence, in order to create their FA maps. Applying FA90 pulses to the short TR GRE-sequence was not possible due to conservative SAR constraints, which lead to long TRs and, thus, unrealistic scan times.

![FIGURE 2](image-url) Bloch simulated FA profiles of the TPs for FA90 (first row of profiles), UP2D for FA90 (second row of profiles), the TPs for FA7 (third row), and UP2D for FA7 (fourth row). The eight columns on the left present the database heads. The three columns on the right present the non-database heads. The upper numbers within each profile depict the mean FA and the corresponding SD in the non-excitation region. The lower numbers within each profile depict the mean FA and the corresponding SD in the excitation region. The bar plot below the profiles illustrates the NRMSEs between the target pattern and resulting profile for each pulse and head.
2.3 Volunteer scans

All measurements were performed on a 9.4T whole-body MR scanner (Siemens Healthcare, Erlangen, Germany) equipped with an SC72 whole-body gradient system, with a maximum amplitude and slew rate of 40 mT/m and 200 mT/m/ms, respectively. An in-house-built 16 channel tight-fit array coil, consisting of eight transceiver surface loops and eight additional receive-only loops was used. All experiments were performed with the approval of the local Ethics Committee. Informed signed consent was obtained from each volunteer, before each MR experiment.

A 3D presaturated TurboFLASH (satTFL) sequence was used for interferometric individual-channel $B_1^+$ mapping\(^4\) (TR = 2.44 ms, TE = 0.75 ms, BW = 700 Hz/Px, asymmetric echo, elliptical k-space acquisition, GRAPPA $2 \times 2$, recovery time between acquisitions = 7.5 s, nominal FA saturation = 60°, FA readout = 4°). An additional scan with 500 µs prolonged TE was used to calculate $B_0$ maps, from the phase evolution between the two different echo times. All maps were recorded with 3.5 mm isotropic spatial resolution and a matrix size of 64 × 64 × 64. Note that, as most FA mapping methods, this sequence allows for measuring accurate FA maps within the range of ~30-150°.\(^5\) The acquired $B_0$/$B_1^+$ maps of each database head (central transversal slice) is visible in Supporting Information Figure S3.

To guarantee that all heads were positioned highly analogous relative to the coil and the isocenter of the scanner, the top of each head was aligned to a marker inside the coil. Furthermore, all scans were executed with the same pad underneath the head. Scanning was performed in the head-first supine position.

Based on a reference image of the $B_1^+$ mapping data, tissue masks were created using a neural network implemented in MATLAB, which was trained on five manually segmented datasets. The major purpose for creating these tissue masks was to exclude the voxels in the skull bone positions, for which contribution to the signal is negligibly low. Here, the $B_0$ maps change rapidly, which makes pulse design particularly difficult in those regions. Since these voxels do produce almost no signal in the MR acquisition, they can be neglected in the pulse design. It should be noted that only the skull bone voxels were masked out, not the subcutaneous fatty tissue voxels (Figure 1).

3 RESULTS

3.1 UP2D – 2D target pattern

After 716 iterations of the active-set algorithm, the optimization was stopped because the cost-function values did not decrease further. The average duration of one iteration was 3.5 min. The resulted UP2D for FA90 applied within the TFL sequence produces a maximum local specific energy dose (SED) of 2.65 J/kg. Herein, SAR is not a meaningful measure, as the pulse is played out only once in the TFL sequence. UP2D for FA7 produces a maximum local SED of 0.02 J/kg, a maximum local SAR of 0.89 W/kg, and a global SAR of 0.07 W/kg within the GRE sequence (TR = 18 ms).

Figure 2 shows simulated FA profiles of the eight databases and three non-database heads. For both FA90 and FA7, the profiles resulting from the TPs and from UP2D are very similar. The respective TPs deliver only a slightly better performance compared to the UP2D performance. The mean FAs for the TPs and UP2D are highly similar, while the SD is slightly higher for most UP2D profiles. For non-database heads, the NRMSE values of UP2D are increased compared to database heads, but the resulting profiles are still highly similar to the TP profiles. For non-database heads, UP2D...
performs with a mean NRMSE of 0.069 ± 0.005 for FA90 and 0.069 ± 0.009 for FA7. The mean TP performance for these heads is 0.035 ± 0.002 for FA90 and 0.033 ± 0.001 for FA7. Notably, without optimizing UP2D with the active-set algorithm, the mean NRMSE on non-database heads would have been 0.087 ± 0.008 for FA90 and 0.087 ± 0.009 for FA7.

Figure 3 presents images recorded with a GRE sequence at 9.4T applying UP2D for FA7 and the respective TPs, for the three non-database heads. The image quality in the target excitation region and the background suppression resulting from the TPs and UP2D are very similar. Confirming the simulation results from Figure 2, it is visible that the areas where no excitation is desired, contribute very little signal. The visual cortex area is excited almost exclusively. The TPs outperform UP2D at the subcutaneous fatty tissue regions.

By applying UP2D with FA90 and the respective TPs in the satTFL sequence (for three non-database heads), we obtain the FA maps visible in Figure 4. Again, the performance of UP2D and the TPs is similar. Excitation occurs mainly in the visual cortex area; however, there is some lack of FA homogeneity within that region. While the TPs performance is close to the desired FA90, the UP2D causes a slightly too high FA in some of the excited voxels. In the remaining areas, the shown FAs are below 30° for most voxels. As mentioned before, for observed FAs of below 30° the satTFL-sequence results are not reliable⁵⁰ (ie, the observed FAs of approximately 20° on the green and blue profile line in Figure 4 are most likely not the actual FAs). Supporting Information Figure S5 shows the mean FAs in the target excitation and non-excitation areas, respectively.

### 3.2 | UP3D – 3D target pattern

Each iteration of the active-set optimization for UP3D took 2:19 h:min on average. The algorithm was stopped after 175 iterations, as the further improvement was expected to be negligible. The resulted UP3D for FA90 applied within the TFL sequence produces a maximum local SED

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**Figure 4** The central box of images shows FA profiles (central transversal slice, respectively) acquired in vivo with the satTFL $B^+$ mapping sequence from the three non-database heads. Both the respective TPs and UP2D for FA90 were applied on each head. The line charts above and below the FA profiles, show the FAs in the respective voxels in the FA profiles (marked by the colored lines in the images).
of 0.65 J/kg. UP3D for FA7 produces a maximum local SED of 0.004 J/kg, a maximum local SAR of 0.22 W/kg, and a global SAR of 0.016 W/kg within the GRE sequence (TR = 18 ms).

Figure 5 displays the simulation results for the pulses with a 3D target pattern. Due to space limitations in the figure, only the FA profiles from three representative database subjects and three non-database subjects are depicted. Comparing the pulse performances, both UP3D and the TPs have some lack of homogeneity in the excited areas and achieve a mean FA below the desired 90° or 7°. In the center of the target excitation area, the FA is generally higher compared to the peripheral regions of the excited areas. On the non-database heads, UP3D for FA90 (FA7) creates a mean FA in the target excited areas of ~70° (~6°), while the corresponding TPs for FA90 (FA7) on the non-database heads only achieve a mean FA of ~49° (~4°). The FA SD is in general slightly higher for UP3D, compared to the TPs (Supporting Information Figure S4 depicts the mean FAs and SD in the excited/non-excited areas, respectively). Notably, the TPs for FA7 are not downscaled from the TPs for FA90, but directly designed with a target FA of 7°. Furthermore, UP3D outperforms the corresponding TPs in the overall performance which is visible observing the NRMSE values: For most database and non-database heads (FA90 and FA7) the NRMSEs from UP3D are lower than the NRMSEs from the TPs. For non-database heads, UP3D performs with a mean NRMSE of 0.114 ± 0.007 for FA90 and 0.115 ± 0.009 for FA7. The mean TP performance for those heads is 0.129 ± 0.004 for FA90 and 0.128 ± 0.004 for FA7. Without optimizing UP3D with the active-set algorithm, the mean NRMSE on non-database heads would have been 0.133 ± 0.004 for FA90 and 0.133 ± 0.005 for FA7. In general, the NRMSEs are higher, compared to the NRMSEs for the 2D target pattern (Figure ).

Figure 6B compares the NRMSE values between the STA forecast and the Bloch simulation for UP3D (FA90) for the eight database heads, respectively. The biggest NRMSE difference is visible for h1 (0.0026). In the example FA profiles in Figure 6A, differences between the STA and the Bloch profile are barely visible. A lack of excitation uniformity in the excitation area occurs in both profiles. In the voxel-wise difference map of STA profile and Bloch profile, discrepancies

\[\text{FIGURE 5} \quad \text{Bloch simulated FA profiles of the TPs for FA90 (upper left sector), UP3D for FA90 (lower left sector), the TPs for FA7 (upper right sector), and UP2D for FA7 (lower right sector). Depicted are just three database heads (h1, h4, h8) and the three non-database heads (h9, h10, h11). For each head, a transversal, a sagittal, and a coronal slice are depicted (see Figure 1B for the slice positioning). The different colormaps for the FA90 and FA7 profiles are worth noting. The bar plot below the profiles illustrates the NRMSEs between the target pattern and resulting profile for each pulse and head.}\]
of a maximum of 12° mainly in the excited area are observable. In the non-excited area, there are almost no differences between STA and Bloch profile. For the remaining database heads, the results are similar to the shown representative example h6.

Figure 7 depicts in vivo GRE imaging results of UP3D and the corresponding TPs for FA7 (for the three non-database subjects). On all three comparisons, UP3D and the TPs perform similarly well. UP3D delivers a slightly higher signal in the visual cortex area compared to the TPs, while there is very little signal in the remaining areas for both pulses.

In Figure 8, in vivo FA maps acquired with the satTFL B<sub>1</sub> mapping sequence by applying UP3D and the respective TPs for FA90, are shown. The FAs resulting from the TPs are mostly below the desired FA90. UP3D outperforms the TPs as the FA in the excited areas is in general closer to 90° (see Supporting Information Figure S5 for the mean FAs in the target excitation and non-excitation areas, respectively).

In order to further demonstrate the performance of UP3D, GRE images with a reduced FOV compared to the FOVs from Figures 3 and 7, were acquired (Figure 9). Since the two phase-encoding directions were anterior to posterior and left to right, folding artifacts would have occurred, if the signal from outside the FOV were not suppressed sufficiently. In fact, folding artifacts are negligible.

4 | DISCUSSION

This work demonstrated that the concept of UPs is applicable for LE<sub>x</sub>. For a 2D and a 3D target pattern, UPs based on eight database heads were designed. The UPs delivered a good performance in simulations and in vivo on database heads and non-database heads for small and large FAs.

The pulses in this study were designed by means of an extension of the “spatial domain method.”<sup>35</sup> This approach is based on the small-tip-angle approximation<sup>26</sup> of the Bloch equations. Nevertheless, it was also possible to design large FA LE<sub>x</sub> pulses with this method. However, when simulated with full Bloch equations it is revealed that the pulse performance is slightly lower than predicted by the STA method. Figure 6 shows that this decrease is minor for LE<sub>x</sub> patterns with a relatively small excited area. In the non-excited area, there are almost no differences between STA and Bloch profile, which was expected since this is inside the small-tip-angle regime. Performing pulse optimization exploiting full Bloch simulation in the active-set algorithm, was not feasible during this study, as replacing the matrix multiplication by full Bloch simulations would lead to immensely increased optimization time for a database of eight heads and a pulse length of 8 ms (for 3D target patterns, ~22 h per iteration).

Despite the slight difference between the STA profile and Bloch profile, the introduced method produced UPs with excellent performance. For the 2D target pattern, the respective TPs perform just slightly better than UP2D (Figure 2) on non-database heads. The mean NRMSE difference between TPs and UP2D is 0.034 ± 0.004 for FA90 and 0.036 ± 0.008 for FA7. The simulated FA profiles are very similar. That is confirmed in the in vivo measurement results (Figures 3 and 4), where TP and UP2D acquisitions are akin. Both have very low excitation in the desired non-excitation areas and good excitation in the visual cortex area. However, in the satTFL FA profiles (Figure 4) UP2D exceeded the desired 90° in some voxels, which explains the higher NRMSEs for UP2D compared to the TPs. In the GRE results in Figure 3, UP2D delivers a slight unwanted excitation of the subcutaneous fatty tissue next to the visual cortex area. A possible reason why this is not visible in simulations (Figure 2) could be inaccuracies in the B<sub>0</sub> field measurements of these tissues or nonlinearities in the gradient system of the scanner.

The simulated FA profiles resulting from UP3D and the respective TPs are similar as well (Figure 5). Interestingly, UP3D performs slightly better than the respective TPs. The mean NRMSE difference between TPs and UP3D on non-database heads is 0.015 ± 0.011 for FA90 and 0.013 ± 0.013 for FA7. That is most likely due to the fact that UP3D was
calculated without incorporating the excitation phase in the optimization, while it was included for the TP calculations. For that reason (and for the non-existing compute time limitations, theoretically) UP3D produces better results, although the optimization takes eight complete heads at the same time into account. The Supporting Information Figure S6 presents simulated 3D profiles for TPs that were calculated with the magnitude least-squares optimization in order to exclude the phase from the calculation. As the computation time for this approach (~ 6:48 min:sec for a 3D TP) was considerably higher compared to the solely least-squares approach, the resulted pulses were not measured in vivo in this study.

In vivo (Figures 7 and 8), the performance of the corresponding TPs and UP3D (FA7 and FA90), again, is similar. Analog to the 2D results (Figure 3) it is visible for FA7 that the excitation in the target non-excitation areas is very low. Since the satTFL-sequence results (Figures 4 and 8) are not reliable for FAs of below 30° and since the simulations (Figures 2 and 5) and the GRE results for FA7 (Figures 3 and 7) show a very low excitation in the target non-excitation areas, it leads to the assumption that this is also true for the UP2D- and UP3D-FA90 in vivo results.

The FAs in the visual cortex resulting from the TP in Figure 8 are mostly below the desired FA90, while UP3D is in general closer to FA90. The deviation in terms of excitation uniformity in the excitation area which is visible in FA profiles in simulations (Figure 5) and in the satTFL acquisitions (Figure 8) for TPs and UP3D can be deemed acceptable as the GRE sequence (Figure 7) as well as “most neuroimaging applications exhibit some resilience against moderate FA variations.” It should be noted, that this offset in the simulations is not a result of the slight discrepancy between STA forecast and Bloch simulation. Both profiles exhibit this offset problem, as visible in Figures 5 and 6A. For the 2D results (Figure 2), this offset is very small, as the optimization problem is not as difficult as for the 3D case. For the same reason, the 2D TPs were still outperforming UP2D, even though they incorporated excitation phase optimization.

This offset for 3D target pattern pulses is one of the future challenges that need to be addressed. Increasing the pulse length or applying pulse oversampling are options to increment the degrees of freedom. However, they also have their own drawbacks, such as increasing T1/T2 effects and elevated computational burden. A further solution could be

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**FIGURE 7** The central box and the two boxes on the right-hand side show in vivo GRE images (represented by three slices respectively, slice positioning according to Figure 1B) from the three non-database heads. Both the respective TPs and UP3D for FA7 were applied to each head. The line charts left and above the central box show the normalized signal strengths in arbitrary units in the respective voxels in the GRE images of the central box (marked by the colored lines in the images).
using another pulse design method, such as optimal control approaches,\textsuperscript{44,52,53} which show good performance for designing LEx TPs at 7T. Extending the k-space domain parallel transmit pulse design method\textsuperscript{54} for UP calculation could also be an option. Another possibility is the application of joint optimization methods that optimize the RF pulse shape and the k-space trajectory simultaneously.\textsuperscript{55-57} In addition, using variable-density spiral k-space trajectories,\textsuperscript{58,59} or completely different trajectories such as SPINS\textsuperscript{60} or concentric shells,\textsuperscript{13} could be worth investigating to excite a more accurate pattern.

Furthermore, the subject positioning procedure could be improved. Instead of aligning the top of the head, the subjects’ eyes can be used as a reference for the position, in order to be more robust toward different head sizes/shapes. Another topic for future examinations could be to search for the optimal database size for designing LEx UPS at 9.4T.

The UP concept was originally invented for whole-brain excitation to mitigate the RF field inhomogeneity at 7T.\textsuperscript{15-19} All of these studies are using kT-point\textsuperscript{12} k-space trajectories based on which the pulse is optimized. During the design, the kT-points amplitudes, as well as their positions in the transmit k-space, are optimized simultaneously. By means of that approach, the authors created UPS for whole-brain excitation at 7T, which perform with an NRMSE of between 0.08 and 0.11 for non-database subjects. In the respective 9.4T feasibility study,\textsuperscript{21} a whole-brain excitation UP with a target FA of 5° (180°) and a pulse length of 0.83 ms (3.98 ms), performs with an NRMSE of 0.129 (0.063) for the one tested head that was not contained in the design database. The average NRMSEs (0.114 for FA90, 0.115 for FA7) from UP3D for non-database heads for LEx we obtained in this study is in good agreement with the whole-brain excitation values from the literature. However, the values for the whole-brain excitation UPS and the LEx UPS are only partially comparable, as the whole brain UPS are shorter and just the kT-points’ amplitudes and positions are optimized. For LEx UPS, we optimize the complete pulse shape sampled in 10 μs steps based on the spiral k-space trajectory, which is not changed during the optimization. Furthermore, a LEx target pattern creates a significantly more difficult optimization problem, as not every voxel is allowed to be excited. Only an area in the volume should be excited, while other areas should experience no excitation. Using kT-points pulse design for LEx applications is not possible due to the complexity of the optimization problem.

**FIGURE 8** The central box and the two boxes on the right-hand side show FA profiles (represented by three slices respectively, slice positioning according to Figure 1B) from the three non-database heads, acquired in vivo with the satTFL $B_0^+$ mapping sequence. Both the respective TPs and UP3D for FA90 were applied to each head. The line charts left and above the central box show the FAs in the respective voxels in the FA profiles of the central box (marked by the colored lines in the images)
Another interesting outcome of this study is that using spiral k-space trajectories for excitation seems to be more robust toward gradient nonlinearities than it is known from readout spirals. A possible reason for that observation may be that the RF pulse has a more significant influence compared to the applied transmit trajectory.

We demonstrated that UP3D can be used for reduced FOV acquisitions (Figure 9). Taking no acceleration methods (ie, GRAPPA) into account and assuming the same spatial resolution of $0.4 \times 0.4 \times 0.4 \text{ mm}^3$ for full FOV (Figure 9A) and reduced FOV (Figure 9B) measurement, the scan time duration of the full FOV acquisition theoretically would have been 75:16 min:sec (matrix size: $448 \times 560 \times 560$ (3D phase encoding, phase encoding, frequency encoding), TR = 18 ms). For the reduced FOV the scan duration was 10:53 min:sec (matrix size: $224 \times 162 \times 200$ (3D phase encoding, phase encoding, frequency encoding), TR = 18 ms). For an application in which only a certain transversal (here: the central transversal slice) is of interest, UP2D could also have been used, instead of UP3D.

A conventional way to image the visual cortex area as shown in Figure 9 would be to apply a coronal slab selective sinc pulse to excite a subvolume including the target. By again choosing the H->F direction as the frequency encoding direction, folding artifacts would be avoided in this direction. However, the FOV still needs to cover the entire L->R direction (448 steps) in order to avoid folding artifacts. For a slab sized equally to the reduced FOV scenario, that would result in 162 3D-encoding lines, respectively a scan duration of 21:46 min:sec (ie, twice of the reduced FOV scan time).

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**FIGURE 9** A, In vivo GRE images (represented by three slices respectively, slice positioning according to Figure 1B) from one non-database head acquired with UP3D (FA7) with full FOV. The yellow boxes in A mark the positioning of the reduced FOV applied in B. B, GRE image analog to A, but acquired with a reduced FOV. The white arrow depicts a slight folding artifact.
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**ORCID**

Ole Geldschläger [https://orcid.org/0000-0002-8400-0635](https://orcid.org/0000-0002-8400-0635)

Dario Bosc [https://orcid.org/0000-0002-6537-6370](https://orcid.org/0000-0002-6537-6370)

Steffen Glaser [https://orcid.org/0000-0003-4099-3177](https://orcid.org/0000-0003-4099-3177)

Anke Henning [https://orcid.org/0000-0002-2267-4861](https://orcid.org/0000-0002-2267-4861)

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SUPPORTING INFORMATION

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

**FIGURE S1** A: First row: Bloch simulated FA profiles of the FA90 UP2D (downscaled to FA7). Second row: Bloch simulated FA profiles of a UP directly designed with target FA of 7°. B: Mean and standard deviation bars of the FAs in the simulated FA profiles of a UP directly designed with target FA of 90° (FA90 UP2D, downscaled to FA7). C: Bar plot illustrating the NRMSEs between the directly designed FA7 UP2D (legend with the downscaled UP2D, the blue markers depict the values achieved with the downscaled UP2D, the blue markers depict the values achieved with the directly designed UP2D, the blue markers depict the values achieved with the directly designed FA7 UP2D, the blue markers depict the values achieved with the directly designed FA7 UP2D). FIGURE S1 A: First row: Bloch simulated FA profiles of the FA90 UP2D (downscaled to FA7). Second row: Bloch simulated FA profiles of a UP directly designed with target FA of 7°. B: Mean and standard deviation bars of the FAs in the simulated FA profiles of a UP directly designed with target FA of 90° (FA90 UP2D, downscaled to FA7). C: Bar plot illustrating the NRMSEs between the directly designed FA7 UP2D (legend with the downscaled UP2D, the blue markers depict the values achieved with the directly designed FA7 UP2D). FIGURE S2 C: First row: Bloch simulated FA profiles of the FA90 UP3D (downscaled to FA7). Second row: Bloch simulated FA profiles of a UP directly designed with target FA of 7°. Three representative database heads and all non-database
heads are shown. A: Mean and standard deviation bars of the FAs in the excited (upper values) and non-excited regions (lower values) of each head. The green markers depict the values achieved with the down-scaled UP2D, the blue markers depict the values achieved with the directly FA7 designed UP2D (legend visible in B). B: Bar plot illustrating the NRMSEs between target pattern and resulting profile for each pulse and head

**FIGURE S3**
A: $B_0$ map of the central transversal slice of each database head in Herz. B: $B_1^+$ map from each transmit channel of the central transversal slice of each database head in nano Tesla per Volt

**FIGURE S4**
A: Mean FAs and standard deviation bars in the respective excitation or non-excitation regions in the Bloch simulated FA profiles for UP3D (FA90) and the respective TPs. B: Analog to A, but for FA7

**FIGURE S5** Left: Mean FAs and standard deviation bars in the respective excitation or non-excitation regions from the in vivo 2D FA maps from Figure 4. Right: Mean FAs and standard deviation bars in the respective excitation or non-excitation regions from the in vivo 3D FA-maps from Figure 8

**FIGURE S6** Analog to Figure 5 from the main document, except that the TPs were designed by means of the magnitude least-squares optimization

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