**OTUP: Target specific optimization of the transmit k-space trajectory for flexible universal parallel transmit RF pulse design**

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**Abstract**

Purpose:

To optimize transmit k-space trajectories for a wide range of excitation targets and to design ‘Universal pTx RF pulses’ based on these trajectories.

Methods:

Transmit k-space trajectories (stack-of-spirals and SPINS) were optimized to best match different excitation targets using the parameters of the analytical equations of spirals and SPINS. The performances of RF pulses designed based on optimized and non-optimized trajectories were compared. The optimized trajectories were utilized for universal pulse design. The universal pulse performances were compared with subject specific tailored pulse performances.

The workflow was tested on three test target excitation patterns. For one target (local excitation of a central area in the human brain) the pulses were tested in vivo at 9.4T.

Results:

The workflow produced appropriate transmit k-space trajectories for each test target. Utilization of an optimized trajectory was crucial for the pulse performance. Using unsuited trajectories diminished the performance.

It was possible to create target specific universal pulses. However, not every test target is equally well suited for universal pulse design. There was no significant difference in the in vivo performance between subject specific tailored pulses and universal pulse at 9.4T.

Conclusions:

The proposed workflow further exploited and improved the universal pulse concept by combining it with gradient trajectory optimization for stack-of-spirals and SPINS. It emphasized the importance of a well-suited trajectory for pTx RF pulse design. Universal and tailored pulses performed highly similarly.

The implemented OTUP-workflow and the B0/B1+ map data from 18 subjects measured at 9.4T are available as open source (https://github.com/ole1965/workflow\_gradOptimization\_UPdesign.git).

Keywords: parallel transmit, pTx, universal pulses, local excitation, reduced FOV, high-field MRI, 9.4T, gradient optimization

Introduction

The great potential of MRI scanners operating at ultra high field (UHF) (i.e. a B0 field strength of 7T and above) was extensively discussed (1,2,3). UHF systems provide higher signal-to-noise ratios (4), reduced acquisition times and improved spatial resolutions. However, the shorter electromagnetic wavelength at UHF results in inhomogeneity of the radiofrequency (RF) field. The most promising approach to overcome these issues is the parallel transmission (pTx) technique, as it provides improved control over the spatial and temporal RF field (5,6).

PTx RF pulse design is accompanied with an underlying transmit (or excitation) k-space trajectory spanned by appropriate gradients. Usually the pTx pulse is calculated based on that transmit k-space trajectory. Both are played out simultaneously, resulting in excitation of the spins in a scanned object. For a desired target excitation pattern ‘the choice of a suitable transmit k-space trajectory is crucial’ (7). For non-selective (whole brain) and slice selective excitation, various studies have optimized the positions of ‘kT-points’ (8,9) and ‘spokes’ (10,11) trajectories together with an appropriate RF pulse. RF pulses based on more sophisticated and optimized trajectories such as ‘stack-of-spirals’ (SOS) (12), ‘concentric-shells’ (12) and spiral nonselective (SPINS) (13)-trajectories were also investigated in the past, both in simulations (14,15) and measurements (in rats) (7).

In the first part of the following workflow (called OTUP), we optimized transmit k-space trajectories with a similar approach presented by Davids et al. (15). For three test target excitation patterns, we investigated and optimized four basis trajectories. These trajectories were a single variable density spiral-in trajectory (16,17,18) (1SOS), a two stack of variable density spiral-in trajectory (12,14) (2SOS), a three stack of variable density spiral-in trajectory (3SOS) and a SPINS (13) trajectory. Davids et al. (15) were optimizing these trajectories utilizing certain shape parameters for each trajectory. For each set of shape parameters a set of control points was assigned. Connecting these control points resulted in the final trajectory, based on which a pTx pulse was designed and evaluated. However, the optimized trajectories and resulting pulses were tested only in simulations. In contrast, in the current work we considered the analytical equations of spirals (16) and SPINS (13) in order to create the trajectories. The parameters to be optimized were the parameters of these equations.

During the second part of this study, so-called ‘Universal pTx RF Pulses’ (19) (UPs) based on the optimized k-space trajectories were designed.

Traditionally the transmit RF field (B1+) and the static magnetic field (B0) distribution is measured for each subject and based on this information the pTx RF pulse is calculated during the scan session. The concept of UPs was introduced by Gras et al. (19) to circumvent this pTx inherent lengthy calibration procedure. The major idea of the UP concept is to design RF pulses based on a database of B0/B1+ maps from different subjects prior to pTx scan sessions. Due to the similarity of these maps for most subjects, the UPs also perform well on subjects which were not contained in the pulse design database.

The UP concept was proved (20,21) and developed (9,22,23) for different sequences, applications and RF coils at 7T. These works have in common that they present UPs for nonselective or slice selective excitation, based on ‘kT-points’ (8) or ‘spokes’ (10). Additionally, a recent study performed a combination of UPs and subject specific tailored pulses (TPs) (24) for whole brain excitation using SPINS (13) trajectories.

Most recently, we published a feasibility study for local excitation (LEx) UPs at 9.4T (25). We created LEx UPs based on fixed non-optimized spiral transmit k-space trajectories, which locally excited the visual cortex region of the human brain, while the surrounding tissues experienced only minor excitation.

The UPs in the current study were calculated based on the optimized k-space trajectories. As UPs can be calculated offline with (theoretically) no time limitation, additional computation time to optimize the trajectories next to the actual RF pulse is not problematic. The entire OTUP workflow was tested on three different target excitation patterns (two LEx- , one ‘whole brain like’-target pattern). For one target the resulting RF pulses and transmit trajectories were applied in vivo at 9.4T for proof of principle. The OTUP code was made available as open source.

Methods

*Test target patterns*

The following three target excitation patterns (Figure 1) were created in order to test the workflow:

* ‘targetNuclei’: A small central region encompassing the red nuclei should be excited with a homogenous flip angle (FA) of 7° in eight consecutive transversal slices. The surrounding voxels within these slices should not experience excitation. The voxels directly adjacent to the excited region were excluded from the pulse design mask, to avoid a direct transition from excitation to non-excitation regions, thereby reducing the complexity of the optimization problem. The red nuclei are small structures in the human rostral midbrain involved in motor coordination (26). This structure is of special interest for research on Parkinson’s disease (27,28) and may be of interest for practical reduced FOV application.
* ‘targetM’: The letter ‘M’ should be excited with a FA of 7° in one central transversal slice. The surrounding voxels within these slices should experience no excitation. Desired excited and non-excited voxels are directly adjacent. This target pattern served as a ‘proof of concept’ pattern.
* ‘targetWB’: All brain voxels located in 16 consecutive transversal slices should be excited with a homogenous FA of 7° (i.e. there are no voxels which were not allowed to experience excitation). Excitation of the whole brain was not possible as the coverage of the utilized RF coil was not sufficient to reach the upper and lower brain (see B1+ maps in the supporting information Figure S1).

All target patterns had in common, that the transversal slices located above or below the slices of interest (see red horizontal lines in Figure 1) are excluded from the pulse design mask, i.e. the performance of the pulse in these excluded slices is neither evaluated nor optimized by the pulse design algorithm. This approach is feasible since the head to feet direction was chosen as the frequency encoding direction for in vivo imaging. Thereby, folding artifacts from tissues above and below the red lines would not appear.

For each of the three targets pattern the OTUP workflow consisting of ‘Gradient Trajectory optimization’ and ‘Final UP calculation’ was tested. The workflow was implemented in Matlab (MathWorks, Natick, MA) and is available as open source (https://github.com/ole1965/workflow\_gradOptimization\_UPdesign.git):

Gradient Trajectory optimization

In order to save computation time, we optimized the transmit k-space trajectory based on only one head from the design database. Afterwards the UPs were designed on B0/B1+ maps from the entire design database using the resulting optimal k-space trajectories (see ‘Final UP calculation’ section).

Four different basis k-space trajectories were chosen: A single variable density spiral-in trajectory (16,17,18) (1SOS), a two stack of variable density spiral-in trajectory (12,14) (2SOS), a three stack of variable density spiral-in trajectory (3SOS) and a spiral nonselective trajectory (SPINS) (13).

A single variable density spiral-in trajectory (16) can be represented by:

|  |  |  |
| --- | --- | --- |
|  |  | Eq. 1 |

with where is the length, is the radial extent of the spiral, is the density variable and with is the number of turns.

For 1SOS Eq. 1 was implemented in a cost-function having the equation parameter and the position of the spiral on the kz-axis as input parameter. Within the cost-function, the spiral was created based on these input parameters. For that trajectory, a RF pulse was designed based on the B0/B1+ map of one subject. For RF pulse design the ‘Spatial domain method’ (29) was utilized because of its speed, due to the small tip angle approximation (30) of the Bloch equations. The output parameter of the cost-function was the root mean squared error (RMSE) between the FA profile predicted by Bloch simulations and the target excitation pattern.

For 2SOS and 3SOS the procedure was analogous with the only exception that two or three spirals were designed, respectively. For 2SOS the cost-functions input parameter were ,, for the first spiral and ,, for the second spiral, as well as and as the positions on the kz-axis. For 3SOS a third spiral with corresponding input parameters for the cost-function was added.

A SPINS trajectory (13) can be created using Eq. 2-4:

|  |  |  |
| --- | --- | --- |
|  |  | Eq. 2 |
|  |  | Eq. 3 |
|  |  | Eq. 4 |

Where is the radial coordinate and and are the polar and azimuthal angles. The parameter is the maximum radial extent, and are the respective angular velocities and is the length of the trajectory. Additional parameters are . Similar to 1SOS, 2SOS and 3SOS a cost-function with the SPINS parameter () as input parameter was implemented in order to create a SPINS trajectory for each set of parameters and to design a pulse based on this trajectory.

Trajectories that exceeded the maximum gradient amplitude or slew rate were punished with a very high cost-function output value, in order to prevent the optimization from considering these trajectories as optimum. The maximum allowed trajectory duration was 10ms. Reasonable lower and upper bounds for the input parameters were found empirically. Each basis k-space trajectory was optimized separately. From the four optimized trajectories the one that enabled the lowest RMSE performance or a considerably shorter duration with similar RMSE, was considered for UP calculation.

To solve the four optimization problems the ‘Particle swarm optimization’ (31), implemented in Matlabs *particleswarm* function was utilized. Particle swarm optimization ‘works by maintaining a swarm of particles that move around in the search-space influenced by the improvements discovered by the other particles’ (32). This optimization routine was chosen because it creates a reliable overview on the entire search-space and it does not require an initial guess, which would be hard to find in this case. As this algorithm is stochastic and non-deterministic the calculated optimum of the *particleswarm* function can differ from one call to another. For that reason, the *particleswarm* function was executed 20 times for each cost-function mentioned above. From the 20 optimized parameter sets, the one that provided the lowest RMSE was utilized for further RF pulse calculation. In case several parameter sets provided equal or highly similar RMSE values, the one that produced the shortest trajectory duration was used further.

In order to show the influence of the underlying transmit trajectory on the RF pulse performance, we tested each of the optimized trajectories for each of the test targets, respectively. For instance, for targetWB, we calculated pulses based on the optimal trajectory for targetNuclei, targetM and targetWB, respectively. The pulses were calculated and applied on one example subject using Bloch simulations.

Final UP calculation

Analog to the own preliminary work (25) the following optimization problem was considered:

|  |  |  |
| --- | --- | --- |
|  |  | Eq. 5 |

where , with , is the full system information matrix (29) of subject and is the size of the design database, i.e. the number of subject heads based on which the pulse will be designed. This approach is an extension of the spatial domain method (29).

For each test target and optimized trajectory, we solved this optimization problem in Eq. 5 with a combination of the ‘magnitude least squares’ (MLS) optimization (33) and the active-set algorithm implemented in Matlabs *fmincon*-function.

The MLS optimization relies (similar to the spatial domain method) on the small tip angle approximation (30) but considers only the resulting magnetization profile’s magnitude in the optimization process. The spatial domain method used within the gradient optimization was drastically faster but includes the profile’s phase and magnitude in the optimization. However, the profile’s phase was of no interest during this study. Considering only the profiles magnitude and not the phase in the pulse design results in an improved pulse performance for applications where the profile’s phase is of no relevance (33).

Similar to the own preliminary work (25) the MLS result was post processed in order to potentially further improve the pulse performance. The MLS pulse was utilized as the initial guess for the active-set algorithm. Within the cost-function minimized by this algorithm the FA profile for a given pulse was simulated with Bloch equations (without relaxation). The output parameter of the cost-function was the RMSE between the resulting FA profile and the target FA pattern.

In line with the literature(19,20,22,21), the active-set algorithm was chosen because of its speed and robustness(34,9). With the *fmincon*-function the solution was constrained to a maximum pulse amplitude of 130 Volt at plug level (hardware limit). The optimization was stopped if further improvement on 30 consecutive iterations was negligible.

The final UPs were simulated on 7 non-database heads using Bloch-equations. Their performances were compared with the corresponding TP performances. The TPs were calculated with the MLS method only.

For all of the mentioned calculations a target FA of 7° was set. In the ‘Results’-section we will only focus on the results for that FA. However, we ran analogous calculations for targetNuclei for a FA of 180° (results are shown in the supporting information Figure S4).

The UP design database consisted of the B0/B1+ maps from 11 different subjects. The 11 datasets were randomly chosen from the 18 overall acquired B0/B1+ maps at 9.4T. In the supporting information we provide an ‘Analysis of database size’, where we explain why the design database contains 11 heads.

All calculations (gradient trajectory optimization, analysis of database size (supporting information) and final UP calculation) were performed on a high-performance-compute system node equipped with an Intel Xeon IceLake Platinum 8360Y processor (256 GB RAM, 72 cores with 2.4 GHz each) exploiting parallel computing.

*Measurement system and data acquisition*

All measurements were performed on a 9.4T whole-body MR scanner (‘Magnetom 9.4T’, Siemens Healthcare, Erlangen, Germany) equipped with a SC72 whole-body gradient system, with a maximum amplitude and slew rate of 40mT/m and 200 mT/m/ms, respectively. An in-house-built 16 channel tight-fit array coil (35), consisting of eight transceiver and eight receive-only loops was used. All experiments were performed with approval of the local Ethics Committee. Informed signed consent was obtained from each volunteer, before each MR-experiment.

Individual-channel B1+ mapping was performed using a 3D presaturated TurboFLASH sequence (36) (TR=2.44ms, TE=0.75ms, BW=700Hz/Px, asymmetric echo, elliptical k-space acquisition, GRAPPA (37) 2x2, recovery time between acquisitions=7.5s, nominal FA saturation = 60°, FA readout = 4°). For B0 mapping an additional scan with 500µs prolonged TE was utilized. B0 were then calculated from the phase evolution between two different echo times. All maps were acquired with a 3.5mm isotropic spatial resolution and a matrix size of 64x64x64. With these scanning procedure 18 different subjects were measured. The resulting B0/B1+ maps can be seen in the supporting information Figure S1.

Tissue masks were created using a masking routine based on a neuronal network (25).

The final UP for targetNuclei was applied in vivo at 9.4T as proof of principle example. In order to test the in vivo performance for targetNuclei, the calculated pulses were applied in a T2\*-weighted 3D short TR spoiled GRE-sequence (voxel size: 0.8x0.8x0.8mm3, matrix size: 224 (left to right) x 280 (anterior to posterior) x 280 (head to feet), 3D encoding direction: left to right, phase encoding direction: anterior to posterior, frequency encoding direction: head to feet, TR=18ms, TE=8ms, BW=260Hz/px, GRAPPA 2x2).

Global and local SAR were supervised using the VOP method (38,39). The dwell time for RF pulses and gradient shapes was 10 μs. The scanner inherent gradient delay of 4μs was taken into account in the pulse files.

Results

*Gradient Trajectory optimization*

Figure 2 shows the optimized transmit k-space trajectories. It should be noted that all plots have the same kx and ky axes limits, however, for the sake of clarity the limits of the kz axes of the SPINS plots differs from the limits of the kz axes of the SOS plots. The RMSE values next to each plot are based on the difference between the target FA profile and the respective Bloch simulated FA profile (i.e. the unit of the RMSE is degree).

For targetNuclei the 1SOS optimization resulted in a 9.44ms long spiral located on -3m-1 on the k-space z-axis. The spiral had an extent of approximately ±80m-1 on the kx and ky axis. The first of the two spirals from the 2SOS result (6.5ms) had the same extent. The extent of the second spirals is approximately half of the extent of the first spiral. One spiral of the 3SOS result (8.37ms) had an extent of ±100m-1 in kx and ky direction. Next to a second, smaller spiral, the optimization created an additional very short third spiral shaped like an arc or a half-turn, rather than a full spiral. The SPINS optimization resulted in a trajectory (9.38ms) similar to a concentric 3D-shell (7).

As the 2SOS trajectory enables the shortest duration (6.5ms), while having a similar RMSE as the other trajectories (0.26), it was chosen for UP calculations for targetNuclei.

The trajectories for targetM extended further into the outer k-space compared to the targetNuclei trajectories. The 1SOS and the 2SOS results were very similar having one large spiral reaching ±150m-1 on the the kx and ky axis (one spiral of the 2SOS result is only an arc). The 3SOS result consisted of a big low density spiral having the same kx and ky extend as 1SOS and 2SOS and smaller spiral underneath. The third spiral, again, was only an arc. The SPINS result had a similar extend on the kx and ky axis, but a large extend on the kz axis (from 0m-1 till -400m-1).

Again, all four results were similarly well suited for RF pulse design, i.e. all four RMSE values were between 0.15 and 0.17. All trajectories exploited the maximum allowed duration of 10ms. The SPINS result was considered for further pulse calculations for targetM because it showed the best performance.

For targetWB all trajectories exhibited a drastically lower extend in k-space compared to the targetNuclei and targetM trajectories. Additionally, the durations are shorter compared to the durations from the other trajectories. As the 3SOS result constituted the best compromise between duration (3.96ms) and RMSE (0.36) this trajectory was chosen for further pulse calculations for targetWB.

The calculation time for each of these k-space trajectory optimizations was below 24 hours, respectively (depending on the target (Figure 1)).

As Figure 3 shows, for each target pattern the associated optimal transmit trajectory enabled the best performing RF pulse. However, if the underlying trajectory was not designed for the respective target pattern, the RF pulse performance diminished. This effect is most pronounced in case the optimal trajectory for targetM pattern is applied to the targetWB pattern and vice versa. The maximum pulse voltages were relatively low if the RF pulse was designed based on the trajectory designed for a certain target. Utilizing a suboptimal trajectory can lead to dramatically higher pulse amplitudes (for instance, 586V for targetWB using the targetM trajectory, 24V using the targetWB trajectory).

*Final UP calculation*

For targetNuclei, the *fmincon* function was stopped after 395 iterations (~9 days). Figure 4 presents a comparison between the simulated performances of the UP and the corresponding TPs on seven non-database heads. The TPs were slightly outperforming the UP. The computation time of each TP was ~24 seconds (pulse length: 6.5ms). The FA profiles resulting from the TPs exhibited a uniform excitation of the desired excitation area with mean FAs close to 7°. The desired non-excitation areas were in some voxels only very slightly excited with mean FAs close to 0°. The mean RMSE performance of the TPs (UP) was 0.25 (0.52). For the UP the mean FAs in the nuclei area were between 6° and 7° (except of head 14) and the excitation in the desired non-excitation areas was close to 0°.

Analogously, Figure 5 displays the TP and UP performances for targetM. The mean TP (UP) RMSE performance was 0.14 (0.53). Each TP created an excitation perfectly shaped like an ‘M’. For the UP (*fmincon* function was stopped after 820 iterations, ~6days) the transition between desired excitation and non-excitation voxels was not as sharp as for the TPs (computation time per TP was approximately 5 seconds, pulse length: 9.92ms). The mean UP excitation within the ‘M’ is mostly between 6° and 7.5°. However, for head 14 the mean excitation was 5.3°.

In Figure 6 pulse performances for targetWB are depicted. The TPs reached a mean excitation of 7° on all heads, the mean RMSE performance was 0.38. The computation time per TP was approximately 22 seconds (pulse length: 3.96ms). The mean RMSE for the UP was 0.81 (*fmincon* function was stopped after 950 iterations, ~11days). It was striking that especially on head 14 the UP performance was insufficient, but also on head 12 and 13 the RMSEs differ drastically between UP and the corresponding TPs. For heads 15-18 the UP performance could be deemed acceptable.

The targetNuclei UP performance was satisfactory on all non-database heads. It provided the lowest difference between the mean RMSE TP value and the mean RMSE UP value (0.27). For that reason, the pulses for targetNuclei were tested in vivo at 9.4T. Additionally, targetNuclei was tested for calculation of pulses with a FA of 180° in the target excitation area. The results are presented in the supporting Figure S4.

In Figure 7 GRE images of two different non-database subjects with targetNuclei excitation are visible. For both subjects, UP and TPs images appeared almost identical. The central voxels containing the nuclei were excited relatively uniformly, while excitation in the surrounding tissues (in the slices of interest) was visible, but drastically lower compared to the desired excitation area. The mean excitation values and standard deviation were highly similar. For the UP, the mean excitation in the desired excitation area was 0.33 for the one subject and 0.40 for the other subject. In the desired non-excitation areas the excitation was 0.04 and 0.05 (only about 12% of the excited region). For the TPs these values were very similar.

Discussion

This work presents the OTUP workflow to optimize the underlying transmit k-space trajectory for pTx UPs and through that further exploit the advantages of the UP concept.

As the theoretically unlimited computation time is one of the main advantages of UP design, the underlying transmit k-space trajectories is optimized to achieve the best possible match with the excitation target (up to 24hours) before the actual UP design process started. For each of three test target excitation patterns (Figure 1), four basis transmit trajectories were optimized, respectively. The optimization procedure was also utilized for subject specific TP designed herein for comparison.

The optimized k-space trajectories revealed that with increasing complexity of the target excitation pattern the extent of the optimized trajectories in kx and ky direction in k-space increased. For the least complex targetWB (i.e. excitation of 16 entire transversal brain slices) the optimized trajectory ran close to the k-space center, covering only low frequencies. For that reason, the targetWB trajectory is unsuitable for excitation of targetM (i.e. the most complex target pattern exciting only the voxels along an area shaped like the letter ‘M’) (Figure 3).

For targetM, a very sharp transition between excitation and non-excitation between adjacent voxels needed to be achieved. The optimized targetM trajectory covered high frequencies and expanded till ±150m-1. That resulted in a k-space FOV of 300m-1 in kx and ky direction. Converting this value to the voxel size in the image space (i.e. calculating the reciprocal of the k-space FOV) results in the utilized voxel size of the B1+ maps of 3.5mm approximately. As visible in Figure 3, such high frequencies are unsuited for excitation of targetWB.

As some of the spirals in the SOS trajectory optimization reduced to arcs (i.e. the shortest possible spiral) the number of spirals could be included as another parameter to be optimized in future optimizations.

Interestingly, the SPINS trajectories had completely different shapes for the three tested excitation targets. Although originally thought to be well suited for entire brain slices (13), the proposed optimization method created a SPINS trajectory that was also well suited for the complex LEx targetM. In general, SPINS tend to have a longer duration for similar RMSEs as SOS trajectories.

While in the current work the underlying transmit trajectories were optimized, the following two and numerous other pulse design studies (29,33,40,41,7) have in common, that the respective transmit trajectories were only adapted to a given target pattern, field of view and matrix size, rather than an actual trajectory optimization. Any RF pulse calculations started only after the transmit trajectories were fixed.

Shao et al. (14) presented the concept of transmit k-space trajectory container ‘that shapes and forms the candidate trajectory’ (14) based on which the RF pulse will be designed later. In Malik et al. (13), the study that introduced the SPINS trajectory, the parameters of the analytical equation of the SPINS were adapted in order to match the excitation target pattern (homogenous excitation of five brain slices). For instance, ‘ was chosen to cover sufficiently high spatial frequencies to correct for typical variations across the adult brain’ at 3T. With that approach a 1ms SPINS trajectory were designed that enables a subject specific tailored RF pulse performing with a normalized RMSE (NRMSE) of 5.5% on the whole brain at 3T (target FA: 8°). The mean TP performance for targetWB with the optimized 3SOS from the current study was also 5.5% (mean TP RMSE of 0.38 divided by the FA of 7°), but the utilized field strength of 9.4T was drastically higher.

An actual optimization of the k-space trajectory was performed for spokes (11,42,10,43)- and kT-points-trajectories (9), where the location of the spokes and the kT-points is optimized simultaneously with the RF pulse for non-selective or slice selective excitation.

In a 7T study (19), 0.7ms long kT-point TPs performed with ~7% (NRMSE) for a target FA of 9° for whole brain excitation. Davids et al. (15) presented a NRMSE of 6.2% for whole brain excitation with a 4.5ms optimized shells trajectory. The 3SOS TPs for targetWB from the present study (NRMSE: 5.5%) outperformed these two NRMSEs from the literature, but has a considerably longer duration as the kT-point pulse (3.96ms versus 0.7ms).

Furthermore, Davids et al. (15) tested a LEx target pattern exciting a cube at the back of the head (NRMSE: 3.6%, duration: 5ms). This cube target is comparable with respect to its complexity to targetNuclei from this work (NRMSE: 3.7%, duration: 6.5ms).

In order to create and optimize the k-space trajectories SOS, shells and cross, Davids at al. (15) assigned a set of up to 50 control points for each set of certain shape parameters for the respective basis trajectory. These control points needed to be connected afterwards with further software (44). In contrast, in the current work, the trajectories were created by analytical equations for given parameters, what is more straightforward and easier to implement as the approach in the literature.

It should be noted, that none of the presented performance values from the literature is directly comparable to the values from the current work, as the utilized coils, target pattern and field strengths differed, respectively. However, the OTUP workflow yielded optimized transmit trajectories and RF pulses that produces similar or improved performances compared to the approaches in the literature. Only for whole brain excitation, optimized kT-points trajectories seems to have considerably advantages in terms of the pulse duration.

For each test target, the optimal trajectory was utilized to calculate UPs. Considering the UP results for targetWB it was conspicuous that the UP performance on head 14 is drastically lower as the performance on the remaining non-database heads. Taking all heads except of head 14 into account the mean RMSE (NRMSE) is 0.72 (~10%). Head 14 exhibited a different head size and shape compared to the other heads which is most likely the reason for the bad UP performance on that head. In order to avoid such suboptimal performances in the future, different UPs for different head sizes and shapes should be designed.

The UP performances for targetWB (without consideration of head 14) slightly outperformed the kT-point UPs for whole brain excitation from Gras et al. (19) (mean UP NRMSE of 12% for a target FA of 9° on non-database heads). However, as already mentioned, the duration of the kT-point trajectory (0.7ms) is drastically lower as the duration of 3SOS trajectory utilized in the current study (3.96ms). For MR sequences that demands a pulse duration of under 1ms, the application of kT-points for whole brain excitation may be advantageous over sophisticated trajectories such as the 3SOS trajectory.

In an own previous study (25) we presented UPs for LEx of the visual cortex in the human brain, based on non-optimized transmit trajectories (duration: 8.18ms). These UPs performed with a mean NRMSE of 11.4% on non-database heads. This visual cortex target is comparable to targetNuclei from the present work. With optimized transmit trajectories we were able to outperform the UPs from the previous study, as we achieved a mean UP NRMSE for targetNuclei of 7.4% and a pulse duration of 6.5ms. To our knowledge, there are no further works on UPs for LEx, yet.

The GRE acquisitions in Figure 7 demonstrate that the experimental results confirm the simulation results and that the presented UP design software is fully functional. The power of the UP concept with optimized transmit trajectories is clearly demonstrated: Although the depicted subjects were non-database subjects, the UP had a highly similar in vivo performance at 9.4T as the subject specific TPs. Before the TP could be applied, subject specific B0/B1+ mapping and pulse calculation needed to be performed, while the UP could be applied immediately. In all images the red nuclei are excited. For UP and TPs, there is some slight excitation in areas were no excitation was desired. Especially in the TP simulations (Figure 4) this excitation was not visible at all. That leads to the assumption that there are experimental inaccuracies in the transmission of the RF pulse or the execution of the gradient waveform. B0/B1+ map inaccuracies may also be possible (36,45). The calculated pulses itself should not be responsible for the unwanted excitation, even if it is only slight. These problems should be further investigated and addressed in the future.

Conclusion

We introduced and validated a new pTx pulse design method that optimizes the transmit k-space trajectory (SOS and SPINS) to best match the excitation target of interest prior to calculation of respective UPs or subject specific TPs. OTUP was demonstrated for three different target excitation patterns. The importance of utilizing an optimized target dependent k-space trajectory was emphasized.

For one of the target patterns the resulting pulses were tested in vivo at 9.4T as proof of principle for the integrity of the design method. TPs and UP produced highly similar GRE images, proofing the power of the UP-concept. Both excited the target excitation area, while the surrounding tissues experienced only minor excitation.

The workflow code and the B0/B1+ map data from 18 subjects measured at 9.4T are available online as open source.

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# References

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| 1. | Uğurbil K. Imaging at ultrahigh magnetic fields: History, challenges, and solutions. NeuroImage. 2018 Mar; 168: 7–32. |
| 2. | Budinger TF, Bird MD, Frydman L, Long JR, Mareci TH, Rooney WD, et al. Toward 20 T magnetic resonance for human brain studies: opportunities for discovery and neuroscience rationale. Magnetic Resonance Materials in Physics, Biology and Medicine. 2016 May; 29: 617–639. |
| 3. | Nowogrodzki A. The world's strongest MRI machines are pushing human imaging to new limits. Nature. 2018 Oct; 563: 24–26. |
| 4. | Pohmann R, Speck O, Scheffler K. Signal-to-noise ratio and MR tissue parameters in human brain imaging at 3, 7, and 9.4 tesla using current receive coil arrays. Magnetic Resonance in Medicine. 2015 Mar; 75: 801–809. |
| 5. | Katscher U, Börnert P, Leussler C, van den Brink JS. Transmit SENSE. Magnetic Resonance in Medicine. 2002 Dec; 49: 144–150. |
| 6. | Zhu Y. Parallel excitation with an array of transmit coils. Magnetic Resonance in Medicine. 2004; 51: 775–784. |
| 7. | Schneider JT, Kalayciyan R, Haas M, Herrmann SR, Ruhm W, Hennig J, et al. Inner-volume imaging in vivo using three-dimensional parallel spatially selective excitation. Magnetic Resonance in Medicine. 2012 Jun; 69: 1367–1378. |
| 8. | Cloos MA, Boulant N, Luong M, Ferrand G, Giacomini E, Bihan DL, et al. kT-points: Short three-dimensional tailored RF pulses for flip-angle homogenization over an extended volume. Magnetic Resonance in Medicine. 2011 May; 67: 72–80. |
| 9. | Gras V, Luong M, Amadona A, Boulant N. Joint design of kT-points trajectories and RF pulses under explicit SAR and power constraints in the large flip angle regime. Journal of Magnetic Resonance. 2015 Dec; 261: 181-189. |
| 10. | Zelinski AC, Wald LL, Setsompop K, Goyal VK, Adalsteinsson E. Sparsity-Enforced Slice-Selective MRI RF Excitation Pulse Design. IEEE Transactions on Medical Imaging. 2008 Sep; 27: 1213–1229. |
| 11. | Grissom WA, Khalighi MM, Sacolick LI, Rutt BK, Vogel MW. Small-tip-angle spokes pulse design using interleaved greedy and local optimization methods. Magnetic Resonance in Medicine. 2012 Mar; 68: 1553–1562. |
| 12. | Irarrazabal P, Nishimura DG. Fast Three Dimensional Magnetic Resonance Imaging. Magnetic Resonance in Medicine. 1995 May; 33: 656–662. |
| 13. | Malik SJ, Keihaninejad S, Hammers A, Hajnal JV. Tailored excitation in 3D with spiral nonselective (SPINS) RF pulses. Magnetic Resonance in Medicine. 2011 Aug; 67: 1303–1315. |
| 14. | Shao T, Xia L, Tao G, Chi J, Liu F, Crozier S. Advanced Three-Dimensional Tailored RF Pulse Design in Volume Selective Parallel Excitation. IEEE Transactions on Medical Imaging. 2012 May; 31: 997–1007. |
| 15. | Davids M, Schad LR, Wald LL, Guérin B. Fast three-dimensional inner volume excitations using parallel transmission and optimized k-space trajectories. Magnetic Resonance in Medicine. 2015 Nov; 76: 1170–1182. |
| 16. | Kim Dh, Adalsteinsson E, Spielman DM. Simple analytic variable density spiral design. Magnetic Resonance in Medicine. 2003 Jun; 50: 214–219. |
| 17. | Schröder C, Börnert P, Aldefeld B. Spatial excitation using variable-density spiral trajectories. Journal of Magnetic Resonance Imaging. 2003 Jun; 18: 136–141. |
| 18. | Liu Y, Feng K, McDougall MP, Wright SM, Ji J. Reducing SAR in parallel excitation using variable-density spirals: a simulation-based study. Magnetic Resonance Imaging. 2008 Oct; 26: 1122–1132. |
| 19. | Gras V, Vignaud A, Amadon A, Bihan DL, Boulant N. Universal pulses: A new concept for calibration-free parallel transmission. Magnetic Resonance in Medicine. 2016 Feb; 77: 635–643. |
| 20. | Gras V, Boland M, Vignaud A, Ferrand G, Amadon A, Mauconduit F, et al. Homogeneous non-selective and slice-selective parallel-transmit excitations at 7 Tesla with universal pulses: A validation study on two commercial RF coils. PLOS ONE. 2017 Aug; 12: e0183562. |
| 21. | Wiggins C, Poser B, Mauconduit F, Boulant N, Gras V. Universal Pulses for MRI at 9.4 Tesla - a Feasibility Study. In 2019 International Conference on Electromagnetics in Advanced Applications (ICEAA); 2019 Sep: IEEE. |
| 22. | Gras V, Mauconduit F, Vignaud A, Amadon A, Bihan DL, Stöcker T, et al. Design of universal parallel-transmit refocusing kT -point pulses and application to 3D T2 -weighted imaging at 7T. Magnetic Resonance in Medicine. 2017 Nov; 80: 53–65. |
| 23. | Gras V, Pracht ED, Mauconduit F, Bihan DL, Stöcker T, Boulant N. Robust nonadiabatic T2 preparation using universal parallel-transmit kT -point pulses for 3D FLAIR imaging at 7 T. Magnetic Resonance in Medicine. 2019 Jan; 81: 3202–3208. |
| 24. | Herrler J, Liebig P, Gumbrecht R, Ritter D, Schmitter S, Maier A, et al. Fast online-customized (FOCUS) parallel transmission pulses: A combination of universal pulses and individual optimization. Magnetic Resonance in Medicine. 2021 Jan; 85: 3140–3153. |
| 25. | Geldschläger O, Bosch D, Glaser S, Henning A. Local excitation universal parallel transmit pulses at 9.4T. Magnetic Resonance in Medicine. 2021 Jun. |
| 26. | Cacciola A, Milardi D, Basile GA, Bertino S, Calamuneri A, Chillemi G, et al. The cortico-rubral and cerebello-rubral pathways are topographically organized within the human red nucleus. Scientific Reports. 2019 Aug; 9. |
| 27. | Lewis MM, Du G, Kidacki M, Patel N, Shaffer ML, Mailman RB, et al. Higher iron in the red nucleus marks Parkinson\textquotesingles dyskinesia. Neurobiology of Aging. 2013 May; 34: 1497–1503. |
| 28. | Philippens IHCHM, Wubben JA, Franke SK, Hofman S, Langermans JAM. Involvement of the Red Nucleus in the Compensation of Parkinsonism may Explain why Primates can develop Stable Parkinson's Disease. Scientific Reports. 2019 Jan; 9. |
| 29. | Grissom W, Yip Cy, Zhang Z, Stenger VA, Fessler JA, Noll DC. Spatial domain method for the design of RF pulses in multicoil parallel excitation. Magnetic Resonance in Medicine. 2006; 56: 620–629. |
| 30. | Pauly J, Nishimura D, Macovski A. A k-space analysis of small-tip-angle excitation. Journal of Magnetic Resonance. 1989 Jan; 81: 43–56. |
| 31. | Kennedy J, Eberhart R. Particle swarm optimization. In Proceedings of ICNN\textquotesingle95 - International Conference on Neural Networks: IEEE. |
| 32. | Pedersen ME. Good Parameters for Particle Swarm Optimization.: Luxembourg: Hvass Laboratories; 2010. |
| 33. | Setsompop K, Wald LL, Alagappan V, Gagoski BA, Adalsteinsson E. Magnitude least squares optimization for parallel radio frequency excitation design demonstrated at 7 Tesla with eight channels. Magnetic Resonance in Medicine. 2008; 59: 908–915. |
| 34. | Hoyos-Idrobo A, Weiss P, Massire A, Amadon A, Boulant N. On Variant Strategies to Solve the Magnitude Least Squares Optimization Problem in Parallel Transmission Pulse Design and Under Strict SAR and Power Constraints. IEEE Transactions on Medical Imaging. 2014 Mar; 33: 739–748. |
| 35. | Avdievich NI, Giapitzakis IA, Pfrommer A, Borbath T, Henning A. Combination of surface and `vertical' loop elements improves receive performance of a human head transceiver array at 9.4 T. NMR in Biomedicine. 2017 Dec; 31: e3878. |
| 36. | Bosch D, Bause J, Ehses P, Zaiss M, Scheffler K. Rapid pre-saturated TFL transmit field mapping with an optimized 3D centric single-shot readout. In Proceedings of the International Society for Magnetic Resonance in Medicine Meeting 2020 (Virtual Conference), #3703. |
| 37. | Griswold MA, Jakob PM, Heidemann RM, Nittka M, Jellus V, Wang J, et al. Generalized autocalibrating partially parallel acquisitions (GRAPPA). Magnetic Resonance in Medicine. 2002 Jun; 47: 1202–1210. |
| 38. | Eichfelder G, Gebhardt M. Local specific absorption rate control for parallel transmission by virtual observation points. Magnetic Resonance in Medicine. 2011 May; 66: 1468–1476. |
| 39. | Hoffmann J, Henning A, Giapitzakis IA, Scheffler K, Shajan G, Pohmann R, et al. Safety testing and operational procedures for self-developed radiofrequency coils. NMR in Biomedicine. 2015 Apr; 29: 1131–1144. |
| 40. | Xu D, King KF, Zhu Y, McKinnon GC, Liang ZP. Designing multichannel, multidimensional, arbitrary flip angle RF pulses using an optimal control approach. Magnetic Resonance in Medicine. 2008 Mar; 59: 547–560. |
| 41. | Setsompop K, Wald LL, Alagappan V, Gagoski B, Hebrank F, Fontius U, et al. Parallel RF transmission with eight channels at 3 Tesla. Magnetic Resonance in Medicine. 2006 Nov; 56: 1163–1171. |
| 42. | Dupas L, Massire A, Amadon A, Vignaud A, Boulant N. Two-spoke placement optimization under explicit specific absorption rate and power constraints in parallel transmission at ultra-high field. Journal of Magnetic Resonance. 2015 Jun; 255: 59–67. |
| 43. | Yip CY, Grissom WA, Fessler JA, Noll DC. Joint design of trajectory and RF pulses for parallel excitation. Magnetic Resonance in Medicine. 2007; 58: 598–604. |
| 44. | Davids M, Ruttorf M, Zollner FG, Schad LR. Fast and Robust Design of Time-Optimal k-Space Trajectories in MRI. IEEE Transactions on Medical Imaging. 2015 Feb; 34: 564–577. |
| 45. | Pohmann R, Scheffler K. A theoretical and experimental comparison of different techniques for B 1 mapping at very high fields. NMR in Biomedicine. 2012 Sep; 26: 265–275. |
| 46. | Mitchell M. An Introduction to Genetic Algorithms: ‎MIT Press; 1996. |

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