Preliminary Exam: written component Jinghang Li
Track: Biosignals and imaging
Advisors: Drs. Howard Aizenstein, Tamer Ibrahim

Leveraging B_1^+ Fields on Multi-modal MRI Harmonization Across Imaging RF Coils

SPECIFIC AIMs

Ultra-High Field (UHF) Magnetic Resonance Imaging (MRI) (≥ 7 Tesla) has shown great potential in providing higher resolution, increased signal-to-noise ratio (SNR), and decreased scan time. However, these benefits come with a cost in transmit field (B_1^+) inhomogeneity, which is manifested as high signal in some regions, but low signal in other regions. Transmit field inhomogeneity is one of the major impedances in the UHF MRI. There has been an ongoing effort to reduce the B_1^+ inhomogeneity and localized heating in UHF neuroimaging [1, 2]. Various types of Tic-Tac-Toe (TTT) shaped multi-channel radio frequency (RF) transmit (Tx) coils have been proposed and have successfully demonstrated a more homogeneous transmit field than commercially available RF coils at 7T regardless of the loading shape and size [3, 4]. Currently, a 16-channel transmit array TTT design is being used for more than 30 National Institute of Health (NIH) funded research studies at the University of Pittsburgh. Although, the 16-channel TTT head coil mitigates the B_1^+ field inhomogeneity compared to the commercially available RF coils at 7T, some B_1^+ field improvement is still needed. While introducing another refined head coil improves overall MR signal across the whole head, additional contrast variance would be introduced if the head coil is switched during an ongoing research study [5].

Aside from the transmit fields, the differences in the receive fields would also affect the soft tissue contrast. These field patterns produced by the transmitter and receiver are highly dependent on the RF coil design [6]. For UHF MRI, it's challenging to achieve a homogenous transmit field. Additionally, a homogenous receive field also is not realistic in the real world. To reduce the effect that receive field has on the images, we will first apply bias field correction on all the images across the two domains before the actual image translation [7]. **<u>The primary objective of this work is to leverage deep generative adversarial network (i.e., CycleGAN) and B_1^+ fields to integrate the MR data across domains.</u>** This work aims to reduce soft tissue contrast variation between images acquired using different head coils. A successful implementation of the proposed method ensures smooth transition adopting the newly developed RF head coil from an imaging analysis perspective.

Aim1: Obtain the B1 maps and learn the B1 maps translation across two different head coils

In this work, we will leverage RF coil hardware differences to aid the structural data integration across different head coils. For our load invariant coil design, we believe that there are two transmit field patterns for the two head coils regardless of the shape, size, and the loading position [8]. B1 map measures the general transmit patterns of the loading object and is therefore intrinsically of low resolution. To obtain the B1 maps of the two head coils retrospectively, light weight pix2pix model becomes a good option to infer the transmit pattern from the already acquired structural scans [9]. After obtaining the respective B1 maps, we will implement a CycleGAN to learn the B1 map translation across two different head coils.

Aim2: Implementation and evaluation of the proposed method for data harmonization across structural modalities

MR image contrast variation is a major challenge in multi-site studies. Some major factors that can explain the contrast discrepancy are magnetic field strength, RF coil differences, and pulse sequence design [10]. We believe that the learned B1 map translation can further help the image integration via CycleGAN. Additionally, we want to demonstrate that the proposed method is robust in conversion on various structural modalities (i.e., T1 weighted images, T2 weighted images, etc.). Lastly, we will evaluate the proposed model performance on paired patient images. We expect that our model will have overall lower tissue contrast variation, and closer mean to that of the real images across modalities than the CycleGAN model that is learning without leveraging the B_1^+ map translation.

Research Strategy

A. Significance

Magnetic resonance imaging has been a tremendous tool helping us better identify soft tissue contrast compared to other conventional imaging techniques such as X-ray, and CT [11]. However, differences in hardware design, magnetic field strength, as well as a lack of standardization in acquisition protocols often result in tissue contrast variances between sites [10]. The contrast variation across sites thus requires additional image preprocessing to mitigate the contrast discrepancy, which not only demands additional efforts but also may introduce undesired bias especially in a multi-site study.

Among these major factors, differences in RF coil and magnetic field strength have the most significant impact on the image quality. 7T imaging has an operational frequency of 297.2MHz which translates to an RF wavelength of 13 cm [12]. On average, the adult size head is much larger than the 7T RF wavelength. Consequently, this shortened wavelength leads to nonuniform excitation (B_1^+) and sporadic spots of nonvisible tissue contrast on the MR images [12]. Several generations of TTT shaped RF coil have been developed at the University of Pittsburgh to remedy the B_1^+ inhomogeneity for 7T neuroimaging. These multi-channel RF array designs have demonstrated superior image quality than commercially available RF coils. Some examples that showcase the advantages that TTT coils have over other coils include better subcortical white matter and gray matter contrast and reduced localized RF heating [13].

However, there also exists different RF transmit field excitation patterns across these TTT head coils. Currently, more than 30 NIH funded neuroimaging research studies have been using our 16-channel Tx coil. With the recent deployment of a 60-channel head coil, all studies are transitioning into using the newly optimized head coil. <u>While the newer generation offers even higher SNR, urgent efforts are needed to mitigate the contrast variation between the MR images acquired using these two distinctive coils.</u>

The objective of this project is to develop a deep learning GAN based model that leverages the RF hardware differences to help integrate MR data regardless of the imaging modalities. In our previous work, CycleGAN has shown great potential in unpaired image translation from 3T to 7T [14]. Thus, we aim to utilize similar model structure while incorporating the transmit field information. We have high confidence that our proposed method will outperform the simple CycleGAN model. <u>A successful deployment of our proposed model will ensure low intra-site image contrast discrepancy. Moreover, some variations of this project will provide much needed support for multi-site MR studies.</u>

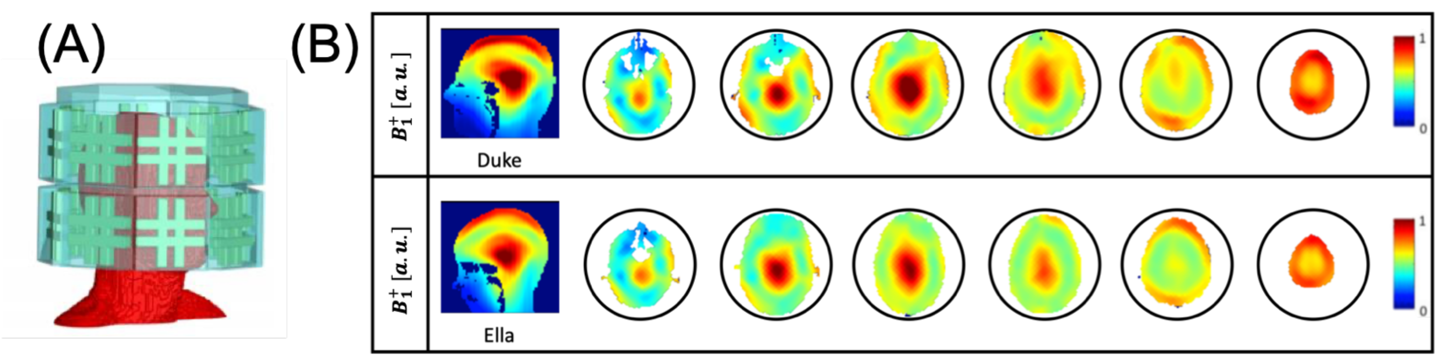

Figure 1 60 Channel-Tx Tic-Tac-Toe (TTT) head coil and B1+ field simulation results. (A) 3D model assembly of the 60 channel TTT coil. (B) Combined transmit field patterns with two different loading cases (i.e., Duke and Ella from the virtual family [15]). The simulation results from these two different loading cases proves that TTT head coil is able to produce similar RF excitation patterns regardless of the loading shape and size.

B. Innovation

While many other studies have used GAN based models to integrate inter-site MR images, the approach proposed in this project will be the first of its kind. Although, many previous works [16, 17] demonstrated remarkable translation across sites, these trained neuro networks are limited within the imaging modality. For example, a network trained on T1-weighted images could only be applied to T1-weighted image translation. We believe that most of the MR image variation could be explained by the underlying RF hardware differences. Deploying such a novel neuro network that inherits these hardware differences enables greater generalizability in MR multi-modal harmonization.

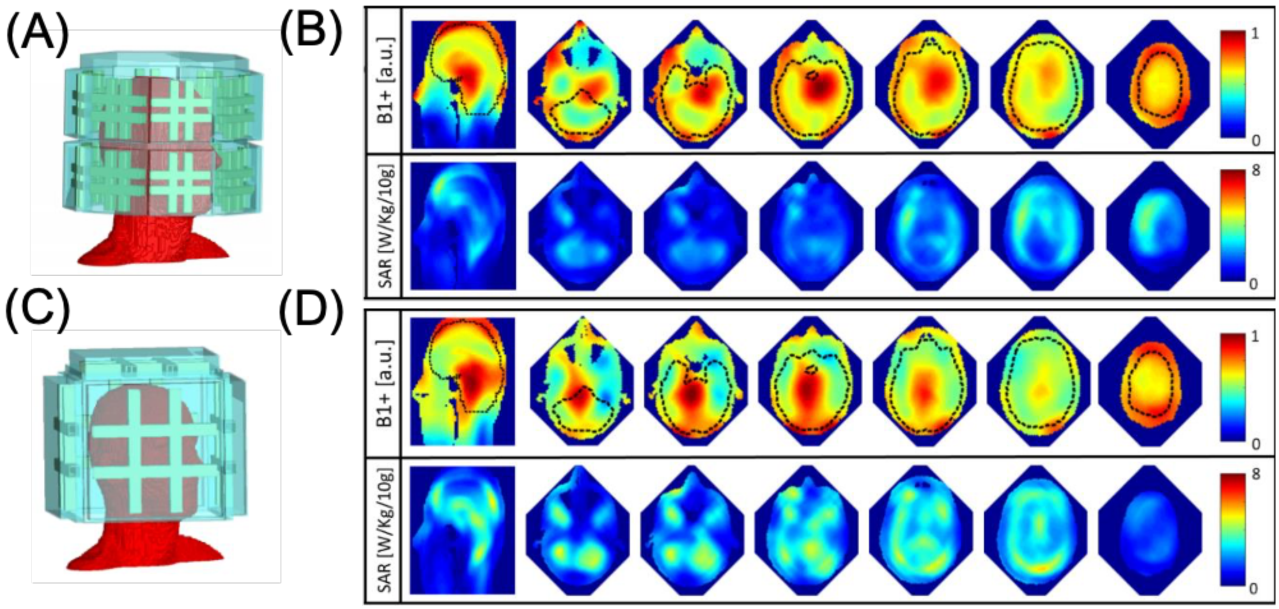

Figure 2 Electromagnetic (EM) simulation results from the two generations of TTT head coils. (A) 3D model assembly of the 60 channel TTT coil. (B) Duke model EM simulation results from the 60-channel head coil. (C) 3D model assembly of the 16 channel TTT coil. (D) Duke model EM simulation results from the 16-channel head coil. The two respective EM simulation results show that there exist two homogenous yet distinctive transmit patterns, which result in tissue contrast variation on structural images [13].

C. Approach

<u>Aim1: Obtain the B1 maps and learn the B1 maps translation across two different head coils</u>

Aim1a: Obtain the B1 maps via pix2pix GAN and structural MR images

Before learning the transmit pattern discrepancies, B1 maps from the two different head coils should be collected. Although, B1 map sequence is crucial during the coil development period, very few in-vivo B1 maps were collected for a research study. To construct a generative model that infers the RF excitation pattern from the structural scans, some paired in-vivo images should be collected. We plan on acquiring T1-weighted MPRAGE and B1 map on volunteers using the two head coils respectively. The number of volunteers needed will be determined by the model performance. However, we do not expect to recruit more than 50 volunteers. After the data collection, B1 map will be synthesized using a 3D pix2pix GAN illustrated in the figure below (Figure 3). We decide to utilize Pix2Pix GAN because it is less memory intensive than other GAN architectures (i.e., CycleGAN) and assumes no pre-defining relationship on the paired images [9]. Although Pix2Pix model struggles to generate fine details on images, it is still able to capture the main features of the images, thus making it the perfect option for our task. Normally Pix2Pix model is applied to 2D image translation (i.e., gray scale images) or small-scale 3D image translation (i.e., color images). In this aim, we believe a 3D Pix2Pix model is more suitable because 2D model might fail at preserving connections between slices.

The most common loss function implemented in deep learning-based models is binary cross entropy (BCE). However, due to the presence of the stochastic noise on the B1 maps, BCE loss should be re-assessed. Recent years, a new loss function that quantifies the differences of two distributions has appeared in some of the GAN research studies. Wasserstein loss, or commonly referred as Earth Mover's Distance, measures the distance between two probability distributions [18]. It could be informally interpreted as the minimum energy required to move pile of dirt in the shape of one probability distribution to the shape of the other distribution.

W-Loss can be described like the following expression: $\boldsymbol{min_g max_c}\mathbb{E}(\boldsymbol{c}(\boldsymbol{x})) - \mathbb{E}(\boldsymbol{c}(\boldsymbol{g}(\boldsymbol{z})))$, where $\boldsymbol{g}$ is the generator, $\boldsymbol{c}$ is the critic/discriminator, $\boldsymbol{z}$ is the bottleneck information, and $\boldsymbol{x}$ is the real images. Intuitively, in W-loss, the generator wants to minimize the fake image distribution distance from the real images, whereas discriminator aims to maximize the distance between the two distributions. One limitation of the W-loss is that it assumes that the discriminator being 1-Lipschitz continuous, meaning that the gradient of the discriminator function should not be greater than 1 at any points on the function [18]. To combat the limitation, many approaches have been proposed in the past (i.e., weight clipping, weight penalization) [19]. In this project, we will proceed with the weight penalization approach as it has shown better performance in the previous work [20] .

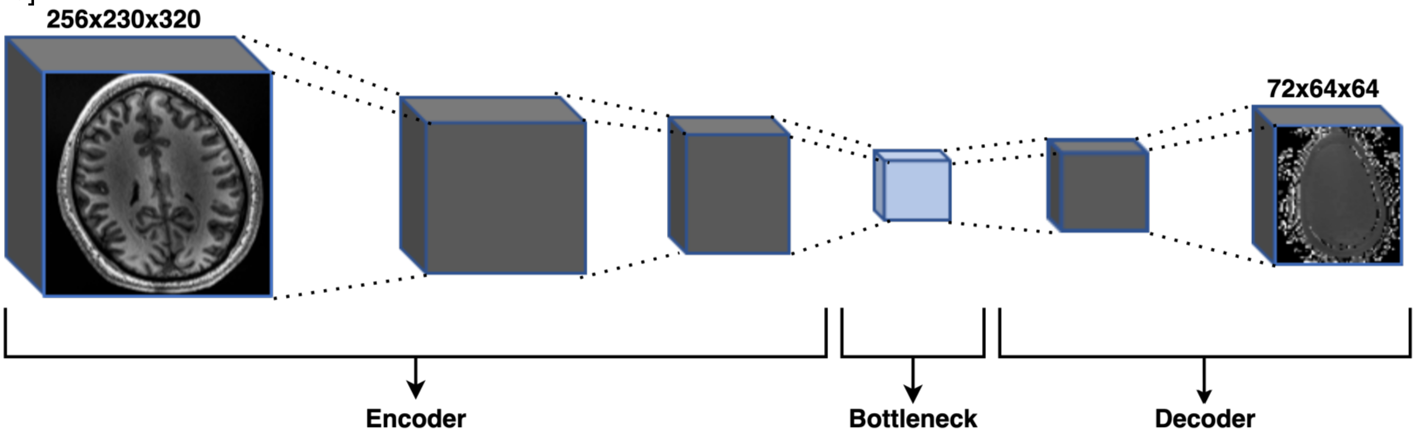

Figure 3 Pix2Pix GAN model architecture. This architecture illustrates that T1-w images are first encoded into the bottleneck of a much smaller dimension. Then the bottleneck information is passed on to the decoder to bring the compressed information into the desired B1 map dimension. The generated fake B1 maps will be compared against the real B1 maps using the Wasserstein loss function.

Aim1b: Learn the B1 map pattern translation via CycleGAN

GAN networks are notoriously difficult to train since it is intrinsically a mini-max game (i.e., discriminator and generator both desire different loss function outcome). To ensure the generalizability on unpaired images as well as minimum overfitting, a GAN model that incorporates cycle consistency loss was invented and is commonly referred to as CycleGAN [21]. CycleGAN is different than Pix2Pix GAN in that CycleGAN has two different generators while Pix2Pix GAN only has one. This model variation ensures robust translation between two different domains without the paired images as CycleGAN learns a two-way mapping between the domains simultaneously. For MR data harmonization problems, it is unrealistic to have coupled patient images across sites, which requires us adopting the GAN models that has similar properties as CycleGAN.

The proposed model architecture is illustrated below. The first generator maps the transmit field from the 16-channel head coil to the 60-channel head coil. The generated fake 60-channel B1 map is then passed into the second generator that maps the transmit field from the 60-channel domain back to the 16-channel domain. We will implement Wasserstein loss with weight penalty to train the two generators and the two discriminators.

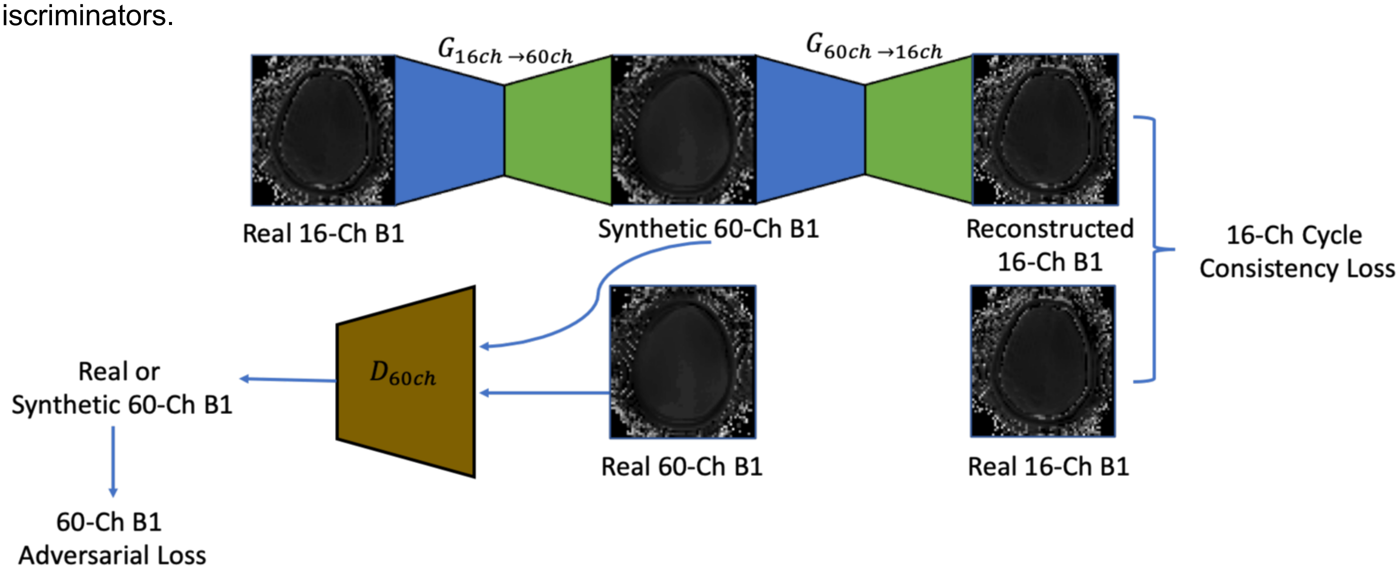

Figure 4 CycleGAN model architecture for translating unpaired B1 maps from the 16-channel head coil to the 60-channel head coil. With the incorporated cycle consistency loss, the two generators and the two discriminators will learn the two-way mapping between the two domains simultaneously.

Aim2: Implementation and evaluation of the proposed method for data harmonization across structural modalities

Aim2a: Implementing structural image translation via CycleGAN

For the actual image translation, we decide to implement similar architecture to the B1 map translation, as it is extremely rare to have patient images in a paired-wise fashion. The key distinction in this model is that the latent images in the two generators will be first passed on to the trained networks that specializes in the B1 map conversion. Then they will be further processed by the decoder models. To prevent the catastrophic forgetting, the learned B1 map translation generators will be frozen during training.

In our previous work on semantic segmentation, we discovered that even with multi-domain images, the model was able to achieve convergence provided with the correct labels. Inspired by this result, we will incorporate multi-modal MR images during training (e.g., T1-w, T2-w, FLAIR etc.). This interleaves fashion training will help improve the model's generalizability across MR image modalities.

The translation model structure is illustrated below (Figure 5). Similar to that of the B1 map translation, this model has two losses: the cycle consistency loss and the adversarial loss. However, what makes this proposed model unique is the usage of the pretrained B1 map generators. We will freeze these B1 map generators during the actual image translation during the training process to prevent catastrophic forgetting. We believe that there exist similar differences in these latent images to that of the B1 maps. Therefore, applying these pretrained generators on the image latent space will translate the underlying differences between images across RF coils.

Aim2b: Evaluation on paired images

To assess the proposed model performance, some evaluation criteria should be determined beforehand. Although, loss functions implemented during training give some preliminary evaluation on the training process, it does not offer qualitive assessment on the generated images. For example, a low loss during training only indicates that the models are no longer learning and may experience mode collapse [22]. Additional metrics will be used to achieve impartial assessment after training. In our previous work on 3T to 7T MR image translation, we discovered that there are significant changes in the different tissue voxel counts. Therefore, we will use the mean and the standard deviation of the number of voxels of specific tissues on paired patient images to evaluate the image translation performance. Specifically, we will examinate the differences in white matter, grey matter, and cerebral spinal fluid. Additionally, we will evaluate our model translation using all commonly acquired structural MR scans (e.g., T1-w, T2-w, and FLAIR images).

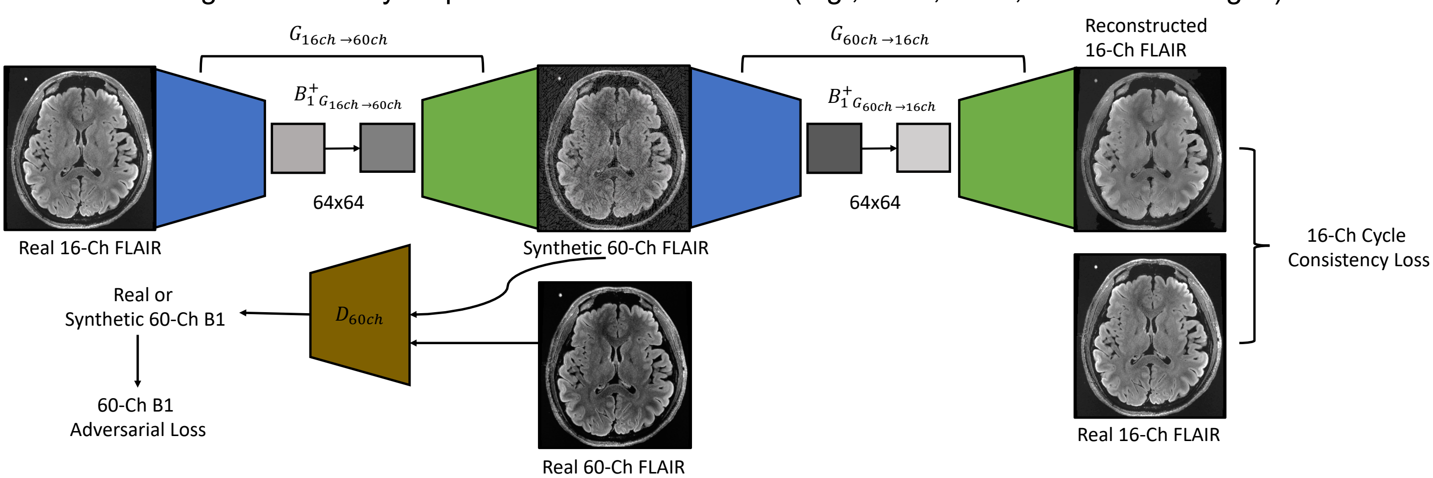

Figure 5 CycleGAN model architecture for translating unpaired images from the 16-channel head coil to the 60-channel head coil. With the incorporated cycle consistency loss, the two generators and the two discriminators will learn the two-way mapping between the two domains simultaneously.

Expected Results

Within one imaging modality, we expect that our translated images will have significant lower variance and closer means to that of the real 60 channel images in voxel counts across tissue types than the generated images from the CycleGAN without using the pretrained B1 map generators. Lastly, leveraging these RF coil differences will aid the generators' training in the GAN model, thus enabling more efficient training.

Anticipated Problems and Alternative Strategies

While it is ideal to generate B1 maps from structural images via a 3D fashion, this approach may face computer hardware issues due to limited GPU memories. One way to bypass the expensive 3D computations is to conduct electromagnetic simulations to calculate the transmit field pattern via an in-house finite difference time domain simulation algorithm. To get the simulation loading geometry, we will use FreeSurfer to segment the patient head geometry. Although, electromagnetic simulation will be relatively time consuming, it will give us the most accurate B1 maps.

REFERENCE:

1. Santini, T., et al., *In-vivo and numerical analysis of the eigenmodes produced by a multi-level Tic-Tac-Toe head transmit array for 7 Tesla MRI.* PLoS One, 2018. **13**(11): p. e0206127.
2. Santini, T., et al., *Improved 7 Tesla transmit field homogeneity with reduced electromagnetic power deposition using coupled Tic Tac Toe antennas.* Sci Rep, 2021. **11**(1): p. 3370.
3. Kim, J., et al., *Experimental and numerical analysis of B1(+) field and SAR with a new transmit array design for 7T breast MRI.* J Magn Reson, 2016. **269**: p. 55-64.
4. Krishnamurthy, N., et al., *Computational and experimental evaluation of the Tic-Tac-Toe RF coil for 7 Tesla MRI.* PLoS One, 2019. **14**(1): p. e0209663.
5. Haast, R.A.M., et al., *Effects of MP2RAGE B1(+) sensitivity on inter-site T1 reproducibility and hippocampal morphometry at 7T.* Neuroimage, 2021. **224**: p. 117373.
6. Vaidya, M.V., et al., *Dependence of B1+ and B1- Field Patterns of Surface Coils on the Electrical Properties of the Sample and the MR Operating Frequency.* Concepts Magn Reson Part B Magn Reson Eng, 2016. **46**(1): p. 25-40.
7. Tustison, N.J., et al., *N4ITK: improved N3 bias correction.* IEEE Trans Med Imaging, 2010. **29**(6): p. 1310-20.
8. Ibrahim, T., et al., *Tic Tac Toe: Highly-Coupled, Load Insensitive Tx/Rx Array and a Quadrature Coil Without Lumped Capacitors.* 2008.
9. Isola, P., et al. *Image-to-Image Translation with Conditional Adversarial Networks*. 2016. arXiv:1611.07004.
10. Keenan, K.E., et al., *Multi-site, multi-platform comparison of MRI T1 measurement using the system phantom.* PLoS One, 2021. **16**(6): p. e0252966.
11. Chalela, J.A., et al., *Magnetic resonance imaging and computed tomography in emergency assessment of patients with suspected acute stroke: a prospective comparison.* Lancet, 2007. **369**(9558): p. 293-8.
12. Kraff, O. and H.H. Quick, *Radiofrequency Coils for 7 Tesla MRI.* Top Magn Reson Imaging, 2019. **28**(3): p. 145-158.
13. Tales Santini, et al. *64-channel Double-Octagon Tx Head Coil for 7T Imaging*. in *ISMRM*. 2017. Honolulu.
14. Eduardo Diniz, et al. *Image-to-image translation of 3T to 7T MRI using Generative Adversarial Networks: A step towards longitudinal harmonization*. in *ISMRM*. 2021. Vancouver.
15. Christ, A., et al., *The Virtual Family--development of surface-based anatomical models of two adults and two children for dosimetric simulations.* Phys Med Biol, 2010. **55**(2): p. N23-38.
16. Zuo, L., et al., *Unsupervised MR harmonization by learning disentangled representations using information bottleneck theory.* Neuroimage, 2021. **243**: p. 118569.
17. Bokhtia, R.M., et al., *Synthesis, Antibacterial Evaluation, and Computational Studies of a Diverse Set of Linezolid Conjugates.* Pharmaceuticals (Basel), 2022. **15**(2).
18. Frogner, C., et al. *Learning with a Wasserstein Loss*. 2015. arXiv:1506.05439.
19. Arjovsky, M., S. Chintala, and L. Bottou *Wasserstein GAN*. 2017. arXiv:1701.07875.
20. Gulrajani, I., et al. *Improved Training of Wasserstein GANs*. 2017. arXiv:1704.00028.
21. Zhu, J.-Y., et al. *Unpaired Image-to-Image Translation using Cycle-Consistent Adversarial Networks*. 2017. arXiv:1703.10593.
22. Thanh-Tung, H. and T. Tran *On Catastrophic Forgetting and Mode Collapse in Generative Adversarial Networks*. 2018. arXiv:1807.04015.