Improved Magnetic Resonance Chemical Shift Imaging at 3 Tesla using a 32-channel Integrated RF-Shim Coil Array

by

Eren C. Kizildag

Submitted to the Department of Electrical Engineering and Computer Science
in partial fulfillment of the requirements for the degree of
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Abstract

In vivo chemical shift imaging is an imaging modality which uses the so-called chemical-shift phenomenon to quantitate brain metabolites spatially, therefore renders the study of brain metabolism and neurodegenerative diseases possible and eases diagnosis of tumors. However, the method is highly vulnerable to local main magnetic field ($B_0$) inhomogeneities arising from magnetic susceptibility differences which is predominantly present in air-tissue interfaces. Such magnetic field inhomogeneities result in number of imaging artifacts including chemical shift displacement of metabolites, spectral line broadening as well as complicated water and lipid suppression; which reduce spectral quality. The main goal of this work is to compensate $B_0$ imperfections and therefore mitigate aforementioned artifacts to earn enhanced spectral quality with the aid of a recently introduced, novel, 32-channel integrated RF-shim coil hardware. Experimental results indeed demonstrate sharper spectral lines with narrower line widths and improved water suppression performance in the regions with poor $B_0$ conditions with the application of the shim coil hardware.

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Acknowledgments

As I am finalizing my Master's thesis, the output of work that roughly spanned my past two years here at MIT, I have always been thinking that this section would be the easiest to write. It turns out that it is actually quite the opposite; especially due to non-visible societal pressures on the language that I should be using in this section—in the absence of which, this section would be much longer—.

I would like to start with Prof. Elfar Adalsteinsson, my thesis supervisor, to whom I am really grateful. The questions that he asked during our weekly individual meetings broadened my understanding of the problem quite a lot, and the suggestions he made really improved the quality of the work.

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Chapter 1

Outline and Bibliography

1.1 Outline

The outline of the thesis is as follows.

Chapter 2 will serve as a background and review chapter where a theoretical background for CSI, including the chemical shift phenomenon, acquisition details and signal equation (Fourier interpretation); sources of $B_0$ imperfections and discussion of several artifacts emerging from poor shimming will be provided. This chapter will be concluded with a review and summary of techniques employed for shimming. We will also provide brief historical notes about MR imaging in the beginning of Chapter 2. Historical notes and theoretical discussion on CSI can be accessed in a greater detail at [56], and we will be following that resource. For a more spectroscopy oriented discussion, in particular centered around shimming phenomenon, the reader is referred to [33], [32].

Chapter 3 of the thesis will introduce the aforementioned multi-coil shim hardware and will supply the all relevant details about the experimental protocol. In particular, details on the anthropomorphic head phantom that was imaged together with recipe of the metabolite solution that the phantom was filled with; details on acquisition, including both CSI and gradient-echo (GRE) field mapping sequence and the shimming protocol together with the optimization problem that was solved to recover shim currents will be provided. Generic protocol followed during the course
of experiments will be provided at the end of the chapter.

Experimental results will be presented in Chapter 4. The results will include the $B_0$ field maps before and after multi-coil shimming to assess the degree of improvement in the field homogeneity and will be followed by the representative spectra corresponding to field maps to gauge the improvement in the spectral quality. To quantify the degree of improvement in field homogeneity, standard deviations of field profiles within the whole region of interest (ROI) as well as per individual voxel will play a fundamental role. Spectral quality will be mainly judged using line widths, which are self-explanatory.
Chapter 5 will summarize the contribution of this work, discuss the possible drawbacks of the technique and supply possible future directions.
1.2 Bibliographical Notes

The work in this thesis was accepted as an oral presentation and received *Summa cum Laude* award at the 24th annual meeting of the International Society for Magnetic Resonance in Medicine (ISMRM) held in Singapore and can be reached under

Chapter 2

Theory and Background

2.1 Historical Notes

Nuclear magnetic resonance (NMR) is a phenomenon observed in atoms with an odd number of protons or neutrons and discovered independently by Edward Purcell [61] and Felix Bloch [8] in 1946, as a result of which they shared the Nobel Prize in Physics in 1952. NMR has been a key technique in chemistry and physics and used extensively to study molecular structure.

In 1973, the first MR image was generated by Paul Lauterbur [50] using linear gradients for spatial encoding. Lauterbur shared the Nobel Prize in Physiology or Medicine in 2003, together with another prominent MRI figure, Sir Peter Mansfield of Nottingham University, 'for their discoveries concerning magnetic resonance imaging' [57].

Since 1980’s, the research collaboration between academia and industry has yielded the commercial scanners that are being used in clinical routine currently.

This work falls within the scope of chemical shift imaging (CSI) and therefore the theoretical background will be particularly targeted towards CSI. Interested reader is referred to [56] and [4] for an elaborated view of MRI, starting from the historical notes, physical foundations and fundamental equations governing the behavior of spins, extending to signal processing view of imaging which couples magnetic phenomenon to the Fourier transform perspective through the signal equation derived
with the aid of Bloch's equation. [56] has an excellent treatment for fundamentals of MRI and in particular, most of the theoretical discussion below will follow [56]; whereas [4] serves as a rather encyclopedic reference where more recent techniques can be accessed.

2.2 Chemical Shift Imaging (CSI)

As mentioned previously, the NMR phenomenon is observed with atoms with an odd number of protons/neutrons and in particular, the main source of an MR signal is $^1H$ nuclei which is abundant in the body (roughly 50 M) due to the presence of water molecule. In contrast, the aim of the *in vivo* CSI is to study other chemical compounds present *in vivo* and therefore, the main source of CSI signal is those metabolites whose concentration is around 1-10 mM. The low concentration of metabolites that are desired to be studied inherently imposes SNR limitations on the CSI data.

Three main metabolites of utmost interest are N-acetylaspartate (NAA), creatine (Cr) and choline (Cho). Main functions of those metabolites can be summarized as follows [62, 64]. NAA is typically found in the neurons of the adult brain and functions as a marker of neuronal density and viability. Furthermore, NAA is also important during myelin formation and it controls osmosis. Cr plays a fundamental role in energy metabolism and in particular, PCr serves as an ATP reservoir. Cho is component that is soluble in water and is essential for functions such as memory and elevation of Cho is observed in developing brain. Other metabolites that are quantified during a CSI experiment but will not be discussed here include lactate, myo-inositol, glutamate and glutamine.

The metabolites explained above are highly linked with underlying biochemistry and can be used as an indicator of abnormalities. For instance, in adults, reduction in NAA level is associated with neuronal loss and therefore signaling neurodegenerative diseases such as X-linked adrenoleukodystrophy (X-ALD) [63], multiple sclerosis (MS) [2, 13]. Canavan disease is an instance where there is an increase in NAA level. Elevated Cho levels and Cho to Cr peak ratios have been observed in brain tumors.
Declined Cr levels are associated with gliomas, astrocytomas and meningiomas [72].

The potential of CSI spans, but not limited to adult brain. In fact, recent research revealed potentiality of CSI in fetal brain. For instance,

- In [59], ratios of NAA/Cr and NAA/Cho have been used to assess metabolic and cellular integrity in injured neonatal brain.

- Metabolites also mark normal brain development/maturation during pregnancy. For instance, signal from NAA increases significantly with progressing gestational age as shown in [47]. Also, Cho, being an important ingredient in short TE spectrum from 22 to 28 weeks and is involved in synthesis of acetylcholine and membrane phospholipids [49, 77] and high levels of Cho might indicate increased myelination.


- Even though not the focus of this work, other metabolites such as myo-inositol and lactate are also relevant in fetal domain.
  - In particular, [65, 24, 23] has shown elevated lactate in infants with severe perinatal asphyxia.
  - Myo-ino, on the other hand, is dominating signal in short TE spectra between 22-28 weeks of gestational age and dominance might reflect existence of high-density glial cells [18, 67].
  - [41] spectroscopic imaging is used to trace phosphatidylcholine, which is found in surfactant to diagnose respiratory distress syndrome, which is characterized by insufficient surfactant production in fetal lungs and is associated with high neonatal morbidity.

Accurate quantification of metabolites is essential for early diagnosis since the biochemical changes often times precede anatomical alterations. The main advantage of CSI over conventional MRI is the fact that CSI renders monitorization of in vivo chemical compounds possible with the assistance of chemical shift phenomenon.
2.2.1 Chemical Shift Phenomenon

The discussion below follows [56] and provides the most relevant parts therein for the purposes of our work.

Chemical shift is defined as a small displacement of the resonant frequency due to shielding created by the orbital motion of the surrounding electrons in response to the main $B_0$ field. The applied, external $B_0$ field induces a circulation in the electron cloud around the nucleus which results in a magnetic moment opposite to $B_0$. Therefore, the net magnetic field experienced is smaller than the applied field strength.

The effective field experienced by the nucleus is given by

$$B_{eff} = B_0 - B_{0\sigma} = B_0 (1 - \sigma)$$  \hspace{1cm} (2.1)

where the constant $\sigma$ is regarded as shielding constant and depends on the surrounding chemical environment. If we recall the Larmor relationship ($\omega = \gamma B_0$, where $\gamma$ is the gyromagnetic ratio and is equal to approximately 42 MHz/T) the effective resonance frequency turns out to be

$$\omega_{eff} = \gamma B_{eff}$$

$$= \gamma B_0 (1 - \sigma)$$  \hspace{1cm} (2.2)

$$= \omega_0 (1 - \sigma)$$

Therefore, the amount of displacement in the resonance frequency is precisely $\sigma \omega_0$ and proportional to the external field strength. Having discussed the shift in resonance frequency, the chemical shift is defined relative to a reference frequency, denoted as $\omega_R$ through the following formula

$$\delta = \frac{\omega_S - \omega_R}{\omega_R} \times 10^6$$

$$= \frac{\omega_S - \omega_R}{1 - \sigma_R} \times 10^6$$  \hspace{1cm} (2.3)

$$\approx (\sigma_R - \sigma_S) \times 10^6$$

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Figure 2-1: An illustrative schematic $^1$H NMR spectrum corresponding acetic acid (CH$_3$COOH), from [56].

where the last approximation is valid since $\sigma_R \ll 1$. The last equation above gives us the chemical shift in parts per million.

An NMR spectrum can be generated by exciting a specimen under uniform magnet, recording its free induction decay (FID) and finally taking the Fourier transform of FID. This would yield spectral lines at different frequencies, corresponding to different degrees of chemical shift. Figure 2-1 illustrates this effect on the NMR spectrum of acetic acid CH$_3$COOH.

Due to valency of the oxygen in COOH group, electron is attracted away from the proton and therefore there is less shielding for the proton of COOH group compared to the proton existing in CH$_3$ group. It is also worthy of noting that the area under CH$_3$ group is roughly three times the area under COOH group, consistent with the fact that the former has three times more protons than the latter. The unusual labeling of the frequency axis is due to historical reasons.

The reference frequency $\omega_R$ of tetramethylsilane, which is not found in vivo is selected to represent the 0 ppm reference point [3] due to its stability.
2.2.2 Signal Equation for CSI

Below, a derivation for the baseband signal equation, i.e. the signal obtained after demodulation for CSI will be given. The derivation is along the same lines as in [56].

Suppose the whole space is equipped with tiny magnetic oscillators of oscillation frequency $\omega(x, y, z) = \gamma B(x, y, z)$ where $B(x, y, z)$ is the field strength at $(x, y, z)$. The signal from an individual oscillator is therefore of the form $m(x, y, z)e^{-i\phi(x,y,z,t)}$ where we assume that the magnitude of the signal is time-invariant, whereas the phase is evolving over time. The received signal is therefore a volume integral expressed via

$$s(t) = \int_V m(x, y, z)e^{-i\phi(x,y,z,t)} dV$$  \hspace{1cm} (2.4)

where $dV = dx \, dy \, dz$ Recalling that $\frac{d\phi}{dt} = \omega$, we arrive at

$$\phi(t) = \int_0^t \omega(x, y, z, \tau)d\tau = \gamma \int_0^t B(x, y, z, \tau)d\tau$$  \hspace{1cm} (2.5)

Now, the field at $(x, y, z)$ has components from the main magnetic field ($B_0$) and the gradient contributions (ignoring field imperfections) and can be written as

$$B(x, y, z, t) = B_0 + G_x(t)x + G_y(t)y + G_z(t)z$$  \hspace{1cm} (2.6)

Therefore, the time evolution of the phase can be written as

$$\phi(t) = \gamma \int_0^t (B_0 + G_x(\tau)x + G_y(\tau)y + G_z(\tau)z)d\tau$$
$$= \omega_0 t + 2\pi k_x(t)x + 2\pi k_y(t)y + 2\pi k_z(t)z$$  \hspace{1cm} (2.7)

where $\omega_0 = \gamma B_0$, $k_x(t) = \frac{\gamma}{2\pi} \int_0^t G_x(\tau)d\tau$ and $k_y(t)$ and $k_z(t)$ are defined in an analogous way.

Inserting 2.7 into 2.4 above and after demodulation (i.e. removing $e^{-i\omega_0 t}$ term), we immediately obtain

$$s(t) = \int_V m(x, y, z)e^{-i2\pi(k_x(t)x+k_y(t)y+k_z(t)z)} dV$$  \hspace{1cm} (2.8)
The formula above provides a Fourier interpretation for the signal equation, since the expression above is precisely the Fourier transform of \( m(x, y, z) \) evaluated at \((k_x(t), k_y(t), k_z(t))\).

In order to take the chemical shift phenomenon into account, we need to modify the signal equation above. This is done by introducing a fourth dimension, denoted via \( k_f(t) = t \) and the modified expression is given by

\[
s(t) = \int_V \int m(x, y, z)e^{-i2\pi(k_x(t)x+k_y(t)y+k_z(t)z+k_f(t)f)}dVdf
\]

(2.9)

This possesses the signal equation for CSI as a four-dimensional Fourier transformation (more accurately, CSI reconstruction is a four-dimensional Fourier inversion problem). Before we conclude this section, it should be noted that the expression above does not take the \( T^*_2 \) decay into account, which is manifested via presence of an exponential term \( e^{-\frac{t}{T^*_2}} \) and causes an image blur along the phase encode direction since each individual k-space like is under a different weight. The mathematical formalism of the blur is simply due to the fact that multiplication with a decaying exponential in k-space corresponds to blurring the image with a Lorentzian kernel.

2.2.3 Acquisition Schemes for CSI

We will now explore the basics of two fundamental encoding (Cartesian and spiral) techniques used in CSI. More elaborate version of the material below can be accessed at [19, 20].

**Cartesian encoding**

Also known as phase-encoded CSI, this technique is the most fundamental and naive way to sample the k-space [10], [28] and commercially available as a stock sequence in most of the current scanners. The excitation waveforms and k-space coverage are provided in Figures 2-2 and 2-3, respectively.

This technique makes use of linear gradient fields to traverse through the k-space. If we recall, 3D CSI is naturally a 4-dimensional Fourier problem (with inclusion of
Figure 2-2: RF and gradient waveforms for conventional Cartesian CSI for one TR. At each TR, exactly one \((k_x, k_y, k_z)\) location is encoded with linear gradient fields and A/D-converter is turned on for data acquisition.

Figure 2-3: \(k\)-space coverage under Cartesian encoding technique. The lines parallel to \(k_f\) axis indicate data acquisition at the corresponding \((k_x, k_y, k_z)\) location.
time as fourth dimension). At each TR, a certain \((k_x, k_y, k_z)\) location is accessed and A/D-converter is turned on for FID signal acquisition in \(k_f\) dimension. This is repeated for entirety of the k-space to acquire voxels of interest.

Total imaging time is roughly equal to \(N_x \times N_y \times N_z \times TR\) where \(N_x\) is the number of \(k_x\) locations, \(N_y\) and \(N_z\) are defined analogously; and \(TR\) is the repetition time and therefore coupled to the resolution requirements. As a motivating example, a modest acquisition encoding \(16^3\) k-space locations through this manner with a \(TR = 2\) s would correspond to a total imaging time of approximately 2 hours and 16 minutes, which is highly impractical for clinical application.

Current advancements in A/D-converter hardware have rendered sampling rates of as low as 1\(\mu\)s possible, corresponding to a 1 MHz bandwidth. On the other hand, most of the metabolites of \(^1\)H brain spectra is spanned in a bandwidth of approximately 800 Hz, corresponding a sampling rate of 1.25 ms. Moreover, the gradient hardware has been improved tremendously and that time-varying gradients that are capable of traversing highly sophisticated trajectories are available. The lines above highlight the motivation behind the introduction of more effective spatial sampling strategies.

**Spiral encoding**

Proposed by Adalsteinsson et al. [1] this encoding technique utilizes time-varying gradient waveforms to trace a spiral trajectory in \((k_r, k_y)\) plane while \(k_z\) dimension remains to be phase-encoded. Unlike the Cartesian encoding where first a certain location in k-space is accessed, and then gradients are switched off for data acquisition, here the gradient waveforms are on during data acquisition interval. Corresponding RF waveforms are shown in Figure 2-4 and spiral-based k-space trajectory (from [1]) is shown in Figure 2-5.

Adjacent \(k_f\) samples acquired from a particular \((k_x, k_y, k_z)\) location should have a spacing of at most 1.25 ms in order not to violate Nyquist rate. As a motivating example, consider an object with a smaller FOV which allows utilization of sparse spiral trajectories that allows traversal of required \((k_x, k_y)\) extent as quick as 1.25 ms. For a matrix size of \(16 \times 16 \times 16\), total imaging time required for this object would
Figure 2-4: Gradient waveforms used for spiral spatial encoding. In contrast to Cartesian sequence, the gradient waveforms are active during data acquisition.

Figure 2-5: (a): Spiral based k-space trajectory as seen in \((k_x, k_y)\) plane. Trajectory is rewinded back to the origin. Dashed trajectory corresponds to interleaved version of the original trajectory shown in solid lines. (b): As the trajectories are played out during data acquisition, the traversed path in \((k_x, k_y, k_f)\) space is as shown. Additional temporal interleaves is necessitated in order to satisfy Nyquist requirement. (c): \(k_z\) direction remains to be phase encoded. The spatial k-space coverage is spherical or ellipsoid as shown. Reproduced from [1].
only be $16 \times TR$, as $k_z$ axis remains phase encoded [48].

However, the extent of the human brain which is roughly corresponding to a field-of-view (FOV) of 20 cm makes such rapid traversal nearly impossible with current gradient hardware. Suppose that the entirety of $(k_x, k_y)$ extent can be traversed in 2.5 ms. Same spiral encoding can be shifted and made to occur at 1.25 ms later during another $TR$. This enables fulfilling the Nyquist requirement in temporal dimension for any particular $(k_x, k_y, k_z)$ location and is termed as *temporal interleaving*.

Another approach is to divide the desired trajectory into sparser trajectories that can be traversed much rapidly while violating Nyquist criterion in spatial dimension (*i.e.* yielding spatial aliasing) individually. This is termed as *angular interleaving* and plays out rotated versions of a sparse trajectory in different $TR$s to increase sampling density and thereby removes aliasing in spatial domain.

For a more elaborated discussion of spiral trajectories, interested reader is referred to [19], [20].

### 2.2.4 Challenges

As we have mentioned previously, the metabolites that are desired to be imaged exist at relatively low concentrations (roughly 1-10mM) and thereby imposing a natural constraint on SNR. Problems with SNR can be overcome via increasing number of averages and/or increasing the voxel size, recalling the relation that

$$SNR \propto \sqrt{TAQV_{\text{voxel}}}$$  \hspace{1cm} (2.10)

where $TAQ$ is duration of acquisition and $V_{\text{voxel}}$ is the voxel size. However, the former results in prolonged scan times whereas latter reduces the resolution and increases intra-voxel dephasing.

Another challenge is abundant presence of water molecule whose signal might mask the underlying metabolites and therefore necessitates effective water suppression techniques. CHESS, which is an acronym for Chemical Shift Selective Imaging and WET which stands for Water Suppression Enhanced through $T_1$ effects are two
commonly used pulse sequences employed for water suppression.

The lipid signal from subcutaneous tissues of skull also contaminates metabolite signals by an effect known as signal bleeding through the side lobes of the point spread function (PSF). Techniques such as inversion recovery [17], [71]; outer-volume suppression (OVS) [51], [53] as well as techniques exploiting the orthogonality of lipid basis to metabolite basis [6] together with dual-density sampling are proposed to mitigate the artifacts sourcing from lipid contamination.

The main limitation that will be addressed and attempted to be nulled in this work is the $B_0$ inhomogeneity arising from susceptibility differences (especially near air-tissue boundaries) which is essentially manifested as line broadening through shortened $T_2^*$ parameter as well as drifted spectral peaks which altogether cause spectral peaks to merge become indistinguishable.

The presentation of the background material above is along similar lines in [12, 48, 20, 19] and interested reader is referred to those resources for other expositions of the background material focusing on various different aspects.

2.3 $B_0$ Inhomogeneity

2.3.1 Origins of $B_0$ Inhomogeneity

Obtaining a homogeneous $B_0$ field distribution is one of the most crucial ingredients for success of various MR modalities as the techniques such as CSI and EPI could be very vulnerable to main field inhomogeneity. This section is intended to serve as a review material where we will first discuss the origins of such field variations together with electromagnetic equations governing field distribution and start uncovering artifacts emanating from $B_0$ inhomogeneity towards the end of the section. Some of those artifacts will be explored further in next section. Finally, a review of the state-of-art techniques that are employed to alleviate $B_0$ imperfections will be summarized in section 2.3.3.
Figure 2-6: A: 7 T magnetic field pattern (outer diameter of 100 cm) generated by a state-of-art 6-coil design. B: Across a 45 cm DSV, degree of magnetic field uniformity. C: Field pattern over the same DSV, under the situation that current in outermost right coil is 99.99% of its nominal value. Deterioration is more than 10 ppm. Figure source: [33].

The material below is essentially a summary of [33] and [32], focusing on the most relevant pieces of those resources. The reader is referred to [33] for a more detailed review centered around $B_0$ shimming. [32] offers a more spectroscopy oriented perspective.

Thanks to Ampere’s law, magnetic field generated by an infinitely long solenoid is perfectly homogeneous. Inside an MR scanner, the dominant magnetic field, or the so-called $B_0$ field -which is roughly 50,000 stronger than Earth’s magnetic field for a 3T platform- is generated via a solenoid coil that can be considered as a truncated version of infinitely long solenoid equipped with correction coils at either ends. The homogeneity of the $B_0$ field is the most important characteristic of an MR magnet and a good magnet is expected to exhibit uniform $B_0$ field distribution throughout the ROI.

Non-uniformities in $B_0$ can be attributed to number of sources one of which is manufacturing errors. While designing magnets, the field is optimized over a diameter-of-spherical-volume (DSV) on the order of 40-50 % of the magnet bore diameter. For a 6-ring magnet that is carefully designed, the generated field pattern is shown in Figure 2-6.
While with a carefully manufactured and tuned magnet, the field homogeneity is better than 1 ppm over a 45 cm DSV as shown in Figure 2-6 B, uniformity of field is highly sensitive to errors, where the effect of an error of only 0.01% in one of outer rings is shown in Figure 2-6 C and indicates a strong degree of field inhomogeneity over the same DSV.

Yet another source of field inhomogeneity is the presence of large metallic objects that perturb the field. This objects include laboratory equipment and structural beams that are placed near the magnet but also extend to those inside the magnet, even including the gradient and shim coils that are highly important components of an MR platform and patient bed. Inhomogeneity resulting from the sources above are often tuned during installation of the MR platform.

Even though there are field imperfections linked to sources explained above, the majority of the field inhomogeneity encountered in vivo is highly subject dependent and induced by the magnetic susceptibility differences, which is a parameter controlling magnetic permeability of the medium relative to that of vacuum.

The net magnetic field inside a continuous and homogeneous material within a perfectly uniform magnetic environment is given by

$$B_{net} = B_0 + \mu_0 M$$

where $$M = \chi \mu_0 B_0$$ is the induced magnetization, and $$B_0$$ is the magnetic field in vacuum. The parameter $$\chi$$ is called magnetic susceptibility and thereby controls the amount of magnetization that a presence of an external field can induce within the material.

According to the sign and magnitude of $$\chi$$, materials can be classified into one of the following three categories: diamagnetic, ferromagnetic and paramagnetic. Ferromagnetic materials possess a very large, positive $$\chi$$ and often MRI incompatible and therefore are out of the scope.

Diamagnetic materials are those with negative magnetic susceptibility and thereby possessing reduced field strength inside. Materials such as copper (which is used in
RF coil) and water ($\chi = -9.05 \times 10^{-6} = -9.05$ ppm) fall under this category. Due to the large presence of water molecule, most tissues have negative susceptibility, between -7 to -11 ppm [70] and therefore diamagnetic.

Paramagnetic materials possess a positive magnetic susceptibility and therefore increase the field strength inside. Air (with a $\chi$ of $0.36 \times 10^{-6} = 0.36$ ppm) is paramagnetic. The main difference between paramagnetic and ferromagnetic materials is that the magnetic properties of a paramagnetic material disappear in the absence of external field (same is also true for diamagnetic materials) whereas ferromagnetic materials retain magnetization even after removal of external field and possess a much larger $\chi$ value.

Magnetic field inhomogeneity is generated at transition boundaries where magnetic susceptibility is discontinuous. As an example, which is pronounced in vivo (e.g. in prefrontal cortex and temporal lobes) and which will also be apparent in this work, is air-tissue boundaries. Following equation provides $\Delta M$, change in induced magnetization as we move across the boundary

$$\Delta M = \frac{\chi_{\text{tissue}}}{\mu_0} B_0 - \frac{\chi_{\text{air}}}{\mu_0} B_0 = \frac{\Delta \chi}{\mu_0} B_0 \tag{2.12}$$

This magnetization difference creates a spatial field distribution that is given via the following formula [70] for a volume element $\Delta V$

$$\Delta B_z(r) = \Delta \chi \frac{B_0}{4\pi} \frac{3z^2 - r^2}{r^5} \Delta V \tag{2.13}$$

where $r^2 = x^2 + y^2 + z^2$. $B_0$ above is aligned with $z$-axis.

For a simplified human body, consisting solely of water and air, the magnetic susceptibility map is given in Figure 2-7 A and the field induced by this distribution is given in Figure 2-7 B.

A careful examination of Figure 2-7 reveals dropped magnetic field strength inside the diamagnetic water region and furthermore, highly perturbed field uniformity at the boundaries where magnetic susceptibility changes. As this figure suggests, the field variation is highly localized to the regions where susceptibility is discontinuous.
Figure 2-7: A: Simplified magnetic susceptibility map for an hypothetical human body consisting of water and air. B: Field pattern induced by the distribution shown in (A). Figure resource: [33].

In human brain, the most challenging regions are prefrontal cortex (PFC) area and temporal lobes where the field uniformity is perturbed due to nasal cavities and auditory passages, respectively.

Figure 2-8 shows the field perturbation induced by susceptibility changes for some simple geometries. (A) shows the field lines for a paramagnetic ellipsoid object of $\chi = 1$ ppm and indicates thickened field lines within a paramagnetic material. The induced field for this geometry is shown in (B) and manifests indicated field strength. Field lines for the same ellipsoidal geometry, but this time with a diamagnetic characteristics ($\chi = -1$ ppm) is shown in (C) and the induced field is given in (D). The field is homogeneous within the objects and highly perturbed outside.

The geometry of the object is also critical in determining field variation. Figure 2-8 E shows the induced field pattern inside a paramagnetic sphere with $\chi = 1$ ppm. Unlike the ellipsoidal geometry, the field inside the sphere is precisely equal to that in the vacuum, while the generic perturbations outside are still present.

Figure 2-8F is a simplified model to understand field perturbations in vivo. A small, air-filled paramagnetic sphere with $\chi = 0.36$ ppm is embedded into a large, diamagnetic, water-filled sphere of $\chi = -9.05$ ppm. The resultant field pattern displays highly perturbed and non-uniform field variation inside and corresponds to the situation induced in brain due to nasal and auditory cavities.
Figure 2-8: A: Magnetic field lines for a paramagnetic, ellipsoid object ($\chi = 1$ ppm). B: Field pattern induced within geometry shown in (A). C: Magnetic field lines for a diamagnetic, ellipsoid object ($\chi = -1$ ppm). D: Field pattern induced with geometry shown in (C). E: Induced magnetic field for a paramagnetic sphere ($\chi = 1$ ppm). F: Induced magnetic field of an air-filled sphere ($\chi = 0.36$ ppm) inside a larger, water-filled sphere ($\chi = -9.05$ ppm). Figure resource: [33].
[54] and [69] give a fast, Fourier based method to compute the field pattern generated by some susceptibility distribution according to the following formula:

\[
\Delta B_z = B_0 \mathcal{F}^{-1} \left\{ \left( \frac{1}{3} - \frac{k_z^2}{k^2} \right) \mathcal{F} \{ \Delta \chi(r) \} \right\}
\] (2.14)

where \( \mathcal{F} \) and \( \mathcal{F}^{-1} \) are forward and inverse Fourier operators, respectively and \( k^2 = k_x^2 + k_y^2 + k_z^2 \). [54, 69, 46, 52, 30] makes extensive use of this equation to characterize field inhomogeneity and [26] uses for quantitative susceptibility mapping (QSM).

Having discussed the origins of \( B_0 \) inhomogeneity, fundamental electromagnetic equations governing the behavior of the field as well as several simple geometries, we will now begin exploring the imaging artifacts caused by field imperfections. As mentioned previously, many of MR applications are highly vulnerable to the inhomogeneity of underlying \( B_0 \) field as field imperfections can be manifested as artifacts such as image distortion, signal loss, reduced spatial/spectral resolution and so on. Of particular interest among such applications and CSI and echo-planar imaging (EPI).

The idea behind \textit{in vivo} CSI, using NMR spectra to identify unknown compounds and investigate their characteristics, has been a fundamental technique in analytical chemistry. On the other hand, the main motivation of the \textit{in vivo} CSI is to extract the information embedded in the brain metabolites to make by accurately quantifying them. Reliable quantification of such metabolites is highly dependent on accurate separation, since most of the \textit{in vivo} metabolites are observed in 1-4 ppm range and have significant spectral overlaps. For instance, glutamate and glutamine have spectral overlap at around 2.4 ppm; creatine, phosphocreatine, \( \gamma \)-aminobutyric acid (GABA) and glutathione (GSH) at roughly 3 ppm and choline, taurine, phosphoethanolamine and alanine at 3.2 ppm.

Inhomogeneous \( B_0 \) field distribution causes metabolite peaks to broaden, merge and eventually become inseparable from each other, which is an effect that cannot be corrected via post-processing techniques and makes separation of strongly overlapping metabolites roughly impossible.
Broadened spectral peaks also corrupt SNR through declined signal amplitudes, as the integral of a peak should stay constant and therefore line broadening leads to decrease in height of the signal.

The effects of imperfect $B_0$ distribution are not limited to broadened spectral peaks. Techniques such as CHESS employ frequency-selective RF pulses to suppress water signal, whose presence masks the metabolites. Poor $B_0$ homogeneity results in insufficient water suppression if the variation in water frequency caused by $B_0$ inhomogeneity is meaningful compared to the bandwidth of such RF pulses. In the spectrum obtained from a voxel surrounded by a highly inhomogeneous $B_0$ pattern, a large, residual water signal from outside the voxel is observed, since the sidebands of RF pulses employed for spatial localization might extend beyond the voxel itself and thereby unsuppressed water signal can bleed into the voxel.

Spectral editing techniques such as J-difference editing for GABA quantification [68] also highly rely on the homogeneity of underlying $B_0$ field and altered under poor shim settings.

Other possible consequences of non-uniform $B_0$ pattern include erroneous slice profile and position as a result of locally compromised effective gradient fields and geometric distortion in EPI images, which is a low-bandwidth MR modality heavily used. Some of aforementioned artifacts will be explored further in a more mathematical way in the next section.

### 2.3.2 A Detailed Look into Artifacts Emanating from $B_0$ Inhomogeneity

External magnetic field strength is coupled to the imaging modality through the signal equation and a severe inhomogeneity results in number of artifacts such as line broadening and chemical shift displacement of metabolite peaks in CSI; geometric distortion and image blurring in phase encode direction in EPI images. A closer look into those artifacts through a Fourier/signal equation point of view is provided below.
Line Broadening

The $T_2$ relaxation time constant is strongly affected by $B_0$ inhomogeneity and shortened under imperfect field distribution. The equation linking $\Delta B_0$ to $T_2$ relaxation is

$$\frac{1}{T_2^*} = \frac{1}{T_2} + \gamma \Delta B_0 \tag{2.15}$$

where $T_2^*$ is the effective time constant, reflecting signal loss due to intra-voxel dephasing caused by off-resonance. It is important to note that in equation 2.15; $\Delta B_0$ is actually a function of space, namely $\Delta B_0 = \Delta B_0(r)$; where the space of interest can be taken, e.g. a particular voxel that is being imaged.

An individual NMR line shape in time domain is expressed as

$$A e^{-i\Phi} e^{-i\omega_0 t} e^{-t/T_2^*} \tag{2.16}$$

where $A$ is the amplitude, $\Phi$ is the phase. $A e^{i\Phi}$ term is just a complex magnitude. Ignoring it for the time being, let $\mathcal{F}$ denote the Fourier operator. Multiplication in one domain corresponds to the convolution in the dual domain, and therefore,

$$\mathcal{F}\{e^{-i\omega_0 t} e^{-t/T_2^*}\} = \frac{1}{2\pi} \mathcal{F}\{e^{-i\omega_0 t}\} \ast \mathcal{F}\{e^{-t/T_2^*}\}$$

$$= \delta(\omega - \omega_0) \ast \frac{1}{i\omega + \frac{1}{T_2^*}} = \frac{1}{i(\omega - \omega_0) + \frac{1}{T_2^*}} \tag{2.17}$$

where $\delta$ is the Dirac delta function and $\ast$ denotes the convolution operator. Finally, after taking the real part of 2.17$^1$, we arrive at

$$\frac{1}{T_2^*} \left( \frac{1}{T_2^*} \right)^2 + (\omega - \omega_0)^2 \tag{2.18}$$

which is the profile of the real part of a spectral line as a function of $\omega$.

The full width at half maximum is therefore obtained as $2/T_2^*$ (proportionality

---

$^1$ Assuming a proper phasing has been performed; real part of a spectrum carries the same information as the imaginary part; while having narrower line width. Hence, it is a matter of convenience to work with real part of spectrum in clinical imaging setting.
with the inverse of $T_2^*$ is what we are interested in). Therefore, shortened $T_2^*$ causes spectral line broadening.

Figure 2-9 illustrates the aforementioned artifact on a poor and high quality spectra acquired from the same voxel location (indicated with a cross).

### Chemical shift displacement

The signal equation under off-resonance is modified (with an inclusion of field perturbation term) and prior to demodulation, a factor of $e^{-i(\omega_0 + \Delta \omega)t}$ term occurs (where $\Delta \omega = \gamma \Delta B_0$). After demodulation, we are left with a linear phase term, which corresponds to a shift in the dual domain.

### Geometric distortion in EPI

Discussion below follows that of [29] and a more elaborate discussion and a technique which employs $B_0$ field maps to unwarp the image can be found therein.

Off-resonance causes pixel shifts from actual pixel locations in an EPI experiment due to phase accrual as a result of field inhomogeneity. To analyze the geometric distortion artifact, let us recall that a signal from an individual point in space is given via

$$s(t) = m(x, y) e^{-i 2 \pi \gamma \int_0^t B(x, y, z, t) \, dt}$$

(2.19)

where $B(x, y, z, t)$ is the magnetic field at point $(x, y, z)$ at time $t$ and can be written
as $B(x, y, z, t) = B_0 + G_x(t)x + G_y(t)y + G_z(t)z + \Delta B_0(x, y, z)$, where the last term is to take field imperfection into account (assuming that the field inhomogeneity is time-invariant).

The exponential portion of the signal equation reduces to

$$e^{-i2\pi\gamma\left[\int_0^t G_x(\tau)d\tau + \int_0^t G_y(\tau)d\tau + \int_0^t G_z(\tau)d\tau + \int_0^t \Delta B_0(x, y, z)d\tau\right]}$$

(2.20)

Signal locations are recovered by extracting the information from signal phase. For a conventional 2DFT imaging, the phase evolution between adjacent points in readout direction is

$$\Delta \phi_r = 2\pi \gamma [G_x x \Delta t + \Delta B_0(x, y, z) \Delta t]$$

(2.21)

and in phase encode direction is

$$\Delta \phi_{pe} = 2\pi \gamma G_y y \tau_y$$

(2.22)

where $x$ direction is selected to be read-out and $y$ direction to be phase encode; $\Delta t$ is the dwell time of A/D-converter, $G_y$ is incremental gradient amplitude in phase encode direction and $\tau_y$ is the duration of phase encoding gradient.

From here, the effective $x$ location is obtained as

$$x_{eff} = x + \frac{\Delta B_0(x, y, z)}{G_x}$$

(2.23)

and corresponds to a shift of $N \times \frac{\Delta B_0(x, y, z)}{G_x} \times$ FOV pixels for an $N \times N$ image matrix. Typical values for pixel shift under 1.5 T field strength, as reported in [29], a mean inhomogeneity of $\gamma \Delta B_0(x, y, z) = 12$ Hz, sweep width of 32 kHz over a matrix size of $256 \times 256$ is $1/10$ of a pixel, which is hard to notice in the reconstructed image. Theoretically, field inhomogeneity should not cause any artifacts in the phase encoding direction as there is no contribution from field inhomogeneity into equation 2.22 above.

In an EPI experiment with trapezoidal gradients, the phase evolution in readout
direction remains intact, whereas the phase evolution during phase encode direction is no longer independent of field inhomogeneity and characterized by

\[
\Delta \phi_{pe} = 2\pi \gamma [G_{pe} y \tau_{ramp} + \Delta B_0(x, y, z)(2\tau_{ramp} + N\Delta t)] \tag{2.24}
\]

(where \(\tau_{ramp}\) is the ramp time for the switched, trapezoidal gradients used in EPI) and could be severe depending on the degree of field inhomogeneity.

### 2.3.3 Techniques for \(B_0\) Shimming

Derived from the word *shim*, small pieces of magnetic material used to improve the uniformity of field produced by pole magnets in the early days of NMR, shimming refers to the process of obtaining a homogeneous \(B_0\) field and arguably one of the most important steps of an MRI scan. The focus of this section is to give a review of various shimming approaches (which corresponds to alternative approaches to shimming strategy as suggested by us via multi-coil shimming), with an emphasis on spectroscopic imaging. The material here can be considered as a summary of [32] and interested reader is referred to that source for a more detailed treatment.

Figure 2-10 describes the ingredients universal to all shimming methodologies.
The first step that is central to all approaches is to accurately characterize the $B_0$ field pattern. Recall that the phase of the signal emanating from a voxel location $r$ at echo time $TE$ is given via

$$\phi = \phi_0 - \gamma \times \Delta B_0(r) \times TE$$

where $\gamma$ is the gyromagnetic ratio and $\phi_0$ is the phase offset. More than one $TE$ is required to eliminate the phase offset, and even more is recommended to improve the confidence of the procedure. This acquisition is followed by phase unwrapping which can be done e.g. by exploiting the fact that $B_0$ distribution is continuous and therefore, there should not be any phase jumps between adjacent locations [14]. This corresponds to Step I of Figure 2-10.

Step II of Figure 2-10 is to generate the ROI mask to eliminate the background which consists almost entirely of noise. During the course of generation of the mask, magnitude images of field maps play a key role.

Third step is to theoretically generate the correction field. Exploiting the fact that magnetic field obeys superposition principle, the goal is to tailor a field pattern which has opposite sign and approximately similar magnitude (theoretically, they should be the same) relative to the existing $B_0$ pattern, which will generate an almost perfectly homogeneous field pattern upon application.

Finally, the last step is to physically generate and apply those shim settings.

Different shimming methods are available and can be classified broadly under categories of passive and active shimming, based on how the correction fields are generated; and static or dynamic, depending on the way they are applied.

**Passive Shimming**

Passive shimming exploits the principle that the field is perturbed under presence of a magnetically susceptible object by carefully placing such objects within the scanner bore to homogenize the field pattern. Materials used for passive shimming include diamagnetic intra-oral shims used for human PFC [74, 75, 15] and external dia/para-
magnetic shims for whole brain shimming in mouse [44, 69]. Albeit simple in nature, passive shimming approaches are not versatile and cannot handle aforementioned subject varying $B_0$ imperfections and shim requirements.

**Active Shimming with Spherical Harmonic Shapes**

The phrase *active shimming* indicates that the correction terms are generated using electrical coils. The field pattern in free space is governed by Laplace equation and therefore can be captured via spherical harmonic basis functions, which is an orthogonal basis set. $2N + 1$ spherical harmonics exist per order $N$. Zeroth order refers to the global offset, three first order terms exactly correspond to $X,Y$ and $Z$ and therefore coincide with linear gradient fields. First order spherical harmonics are shown in Figure 2-11 and second order harmonics are provided in Figure 2-12.
Figure 2-11: Axial, sagittal, coronal and 3D views of first order spherical harmonic terms. Figure source: [32].
Figure 2-12: Axial, sagittal, coronal and 3D views of second order spherical harmonic terms. Figure source: [32].
Figure 2-13: Theoretical shimming of human PFC for an SVS application. Indeed, due to the fact that human PFC corresponds to a magnetic susceptibility boundary, the field variation is highly sophisticated. Inclusion of higher orders returns improved field uniformity as observed from field profile as well as the standard deviation of residual field distribution. Figure source: [32].

Addition of increased orders enables capturing more sophisticated field variations and therefore rendering their mitigation possible.

SH based shimming has been the dominant shimming approach for decades and in particular, most of scanners are equipped with spherical harmonics up to 2nd and 3rd order. This technique is highly flexible and can homogenize the magnetic field in a fully automated manner [25, 78]. Figure 2-13 shows theoretical $B_0$ shimming in human PFC for single voxel spectroscopy (SVS) application at 4 Tesla with an ROI size of $4 \times 4 \times 4 \text{ cm}^3$.

The optimization protocol usually tries to minimize the distance between baseline field profile and generated correction term in a least-squares sense. Even though the inclusion of higher order spherical harmonics theoretically enable correction of highly sophisticated field variations, the practical limitations prevent doing so as spherical harmonics are expensive to generate, consume space in the bore of magnet and also associated with challenges such as eddy currents and high inductance.
Dynamic Shimming with Spherical Harmonics

For any shimming technique, dynamic shimming refers to update of correction terms tailored to an individual sub volume immediately before the acquisition of MR signal from that particular volume as in interleaved multi-voxel MRS or multi-slice MRI. [7, 55] introduced dynamic shimming for multi-slice MRI with linear gradient terms and this was followed by demonstration of dynamic shimming using second-order SH terms [16, 45] and third-order SH terms [36].

The problem behind dynamic shimming using MRI platform’s own gradient coils and amplifier electronics is due to constraints imposed by slew rate limitations which prevents rapid update of shim currents. Therefore, dedicated gradient amplifiers are required for dynamic shimming. However, the challenge that is faced is the induced eddy currents triggered by rapid field switching and such eddy currents create artificial field terms throughout the scanner bore which should be characterized through a process called shim pre-emphasis. Commercial scanners generally do not have hardware enabling rapid current switching as well as shim pre-emphasis.

Static and Dynamic Multi-Coil Shimming

Having discussed the generic challenges in obtaining a near-perfect field homogeneity, it should be noted that highly sophisticated field variations (as in PFC and auditory cavities in temporal lobes) cannot be gauged adequately even with dynamic shimming utilizing all spherical harmonics up to 3rd order. Furthermore, spherical harmonics are also associated with aforementioned impairments, including high inductance, eddy current coupling in cryostat, expensive shim supplies as well as space limitation within the bore of magnet.

Spherical harmonics is one of the available basis sets that can be utilized to express and synthesize the desired field patterns and contains orthogonal terms. The earlier paradigm within MR community was that an orthogonal basis set is essential to accurately characterize the $B_0$ variation. However, it has recently been demonstrated in [38] that a non-orthogonal basis set corresponding to individually driven
electric coils can be used effectively to capture and model the inhomogeneous field patterns without suffering from the pronounced problems of SH shim supplies, i.e. eddy currents and cross-talks are no longer an issue and furthermore the hardware is much cheaper to manufacture. MC shim strategies have been demonstrated to outperform current shimming approaches in mouse brain [31, 34], the rat brain [35] and in human brain [39, 37]. In [38] RF array, however, constrains the placement of shim loops and this problem is addressed in [73] and a dedicated hardware which utilizes the same set of loops for both RF excitation and $B_0$ shimming is demonstrated to mitigate geometric distortion in EPI scans.

For spectroscopic imaging applications, the conventional shim strategies already provide an almost homogeneous $B_0$ field distribution for highly localized applications, such as single voxel spectroscopy where the shimmed volume is small and thereby rendering perfect mitigation of $B_0$ imperfections inside possible. However, the applications such as multi-slice CSI, and multi-voxel spectroscopy which require a homogeneous field pattern over a global ROI are expected to benefit multi-coil shim techniques, which is the main goal of this work and a first study is reported in [43].

### 2.4 Problem Description

In the light of the background above, CSI offers a glimpse into biochemical state of the brain, therefore gauges metabolic abnormalities which might indicate a pathology and also renders effective monitorization of treatments possible. However, a good spectral resolution and an effective water suppression are essential since most of the metabolites that are aimed to be quantified have significant spectral overlaps and water signal dominates and hides low-concentration metabolites. Therefore, mitigation of $B_0$ imperfections is of fundamental significance since field inhomogeneity causes broadened spectral peaks, which corrupts spectral resolution and diagnostic quality of spectral peaks; can damage the degree of water suppression, which is employing frequency-selective RF pulses and highly frequency-sensitive. This problem, however is not adequately compensated with the conventional strategies employing spherical
harmonic basis sets to gauge and correct field variations, without suffering from afore-
mentioned drawbacks. The main goal of this work is to make use of a state-of-art
multi-coil shim strategy which uses a dedicated 32-channel integrated RF-shim coil
hardware [73] to homogenize $B_0$ field pattern and correspondingly improve the quality
of the CSI experiment.
Chapter 3

Experimental Methodology

In this chapter, all the relevant details about the experimental procedure will be supplied. As mentioned previously, the key hardware at the core of this work is the 32-channel integrated RF-shim coil developed by Stockmann et al. [73] at MGH. The same hardware is utilized for both $B_0$ shimming and RF reception. The experiments were conducted on a Siemens Skyra 3 Tesla platform (Siemens Healthcare, Erlangen, Germany) using an anthropomorphic head phantom which is 3D printed in ABS plastic shells. The procedure is roughly as follows. CSI data is acquired without multi-coil shims are on and is followed by GRE field mapping. Field maps are then exported to MATLAB (MathWorks, Natick, MA) to minimize an objective function on the norm of the residual field subject to current constraints. This procedure will yield the optimal shim currents and experimental procedure is repeated in the presence of those shim currents.

3.1 32-channel Integrated RF-Shim Coil Array

As we have already discussed in the previous chapters, in vivo $B_0$ inhomogeneity possesses a significant challenge for many MRI applications. The uneven distribution of main magnetic field shortens the $T_2^*$ and therefore broadens and distorts the line shapes in CSI, creates chemical shift artifacts as a first order Fourier effect, reduces the effectiveness of RF pulses [76] and complicates lipid suppression and water-lipid
separation. The artifacts are not limited to those mentioned above. In techniques such as EPI, poor shimming leads Lorentzian blur in the phase encode direction and generates geometric distortion in EPI during echo spacing period.

The conventional approach to mitigate higher order field variation is to use spherical harmonic shim coils up to second order [66] which can be driven statically [40] or dynamically [55, 16]. However, due to the highly complicated nature of field distribution, it is very hard to capture this field variation and mitigate it with spherical harmonics up to second order. Therefore, one has to extend the basis set to a higher order.

Even though the spherical harmonics of higher orders stand as a satisfactory option [58] the problems associated with spherical harmonic shim supplies impede their practicality. The spherical harmonics are associated with high inductance, expensive shim drivers, decreased efficiency at higher orders as well as they induce eddy currents and therefore require pre-emphasis for dynamic shimming.

The challenges discussed above resulted in recent introduction of alternative single-coil [5] and multi-coil [31, 37] shimming systems. The idea of such systems are as follows.

Those systems consist of loops arrayed close to body, where each loop is driven independently with appropriate amount of current to generate a designated field profile within the ROI. In this setting, each loop generates its own field pattern; hence the entire set of loops can be considered as an alternative basis set which is not necessarily orthogonal.

The advantages of such systems include improved shimming quality, compared to 3\textsuperscript{rd} order spherical harmonics as demonstrated in mouse brain [31] and in human brain [37] while not suffering from the problems apparent in SH shim supplies. In particular, MC shim systems have low inductance, low-cost shim current supplies, little coupling to cryostat or gradient coils hence do not need pre-emphasis and they are more efficient at generating higher-order fields.

The lines above highlight the motivation in using the MC shim hardware. However, in the earlier realization by Juchem \textit{et al.} [37] the shim coils compete for the
space with RF receive arrays and may interfere with RF reception; and therefore performances of both systems might be compromised.

In this work, a 32-channel integrated RF-shim coil hardware which was developed by Stockmann et al. [73] at MGH is employed. This hardware uses the same close-fitting array of loops for both RF reception and $B_0$ shimming, while maintaining the performances of both systems.

The hardware is shown in Figure 3-1 and have previously been utilized to reduce geometric distortion in EPI experiment, as shown in Figure 3-2. The main goal of this work is to demonstrate the effectiveness of this hardware within the realm of CSI, since an improved shim quality should yield an improved spectral quality due to the fact that the spectrum is highly dependent on the underlying field profile.

A more detailed discussion of the points made earlier in this section, details related to construction of shim-supply circuit boards, field simulations, SNR studies as well as in vivo results on EPI geometric distortion correction can be found at [73].

Figure 3-1: 32-channel integrated RF-shim coil, reproduced from [73] and also in [43].
Figure 3-2: Top: $B_0$ profile with and without multi-coil shimming. Evidently, the field distribution is more homogeneous under multi-coil shims. **Bottom:** Reduced geometric distortion in EPI scans (1 mm in-plane, 1.11 ms echo spacing, GRAPPA R=1). Reproduced from [73] and also in [43].
3.2 Phantom

The phantom that was imaged is an anthropomorphic head phantom generated based on the automatic segmentation of a human subject. The phantom involves two nested compartments, where the inner compartment is skull which is 3D printed as two matching parts. The material used for inner compartment was plastic and was motivated by the low conductivity of bone. The front half of the skull contains many fine details.

The skull compartment has an inner volume which is filled with the liquid Braino solution (GE Medical Systems, Milwaukee, WI, USA). It is worthwhile to note that the brain compartment is uniform, i.e. it does not mimic structures such as gray, white matter and ventricles. However, it does have an air cavity that mimics the $B_0$ hot spot encountered in frontal lobes.

In this work, our main goal is to demonstrate proof-of-concept, by illustrating the feasibility of the aforementioned novel, 32-channel integrated RF-shim hardware for the purposes of spectroscopic imaging. Since the spectra can be viewed as a product of field maps (where, roughly speaking, the mean of field variation represents the amount of chemical shift and the standard deviation within a voxel simply dictates the line widths within that voxel), improving field profile is expected to yield improved spectral quality. Hence, it is very important to mimic realistic $B_0$ distributions in the phantom.

The main feature of the phantom that makes it very well-tailored for this work is the associated air cavity (which resembles the frontal lobe hot spot), that gives rise to realistic $B_0$ field patterns as encountered in vivo.

The phantom is shown together with an axial field map in Figure 3-3 to illustrate the point.

More details on phantom, including STL and Inventor files and construction tips can be found at [60] and interested reader is referred to paper by Graedel et al. [22].
Figure 3-3: Left: 3D-printed, anthropomorphic head phantom. Right: An axial \( B_0 \) field map taken at 7T. The GRE experiment indeed depicts a hot spot at frontal lobe around 200 Hz and realistic \( B_0 \) profile. Reproduced from [43].

### 3.2.1 Metabolite Solution

The skull compartment of the phantom is filled with the liquid Braino (GE Medical Systems, Milwaukee, WI, USA) metabolite solution containing NAA, Cr, Cho, Glutamate, GABA and Myo-Inositol using the following recipe:

The recipe above provides the amounts required to make the phantom at 5× typical \textit{in vivo} concentrations, which is desired to avoid multiple averaging during acquisition, therefore accelerating the scan time; due to the fact that SNR is propor-

Table 3.1: Recipe for liquid Braino phantom (GE Medical Systems, Milwaukee, WI, USA)

<table>
<thead>
<tr>
<th>Metabolite</th>
<th>Physiological Concentration (mM)</th>
<th>Amount (g/1L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAA</td>
<td>12.5</td>
<td>2.1892</td>
</tr>
<tr>
<td>Cr anhydrous</td>
<td>10</td>
<td>1.3113</td>
</tr>
<tr>
<td>Choline Chloride</td>
<td>3</td>
<td>0.4819</td>
</tr>
<tr>
<td>Myo-Inositol</td>
<td>7.5</td>
<td>1.3512</td>
</tr>
<tr>
<td>GABA</td>
<td>1.6</td>
<td>0.6430</td>
</tr>
<tr>
<td>L Glutamic Acid</td>
<td>12.5</td>
<td>1.8391</td>
</tr>
</tbody>
</table>

58
tional with the amount of signal source.

The safety instructions for the metabolites above are as follows. All metabolites should be stored in a cool place, the container should be tightly closed in a dry and well-ventilated environment. Furthermore, Cho is hygroscopic and therefore should be stored with dessicant and the container should be opened and closed quickly. L Glutamic acid should also be opened and closed quickly.

The required amounts for each metabolite should be calculated based on the volume of basis solution. In this work, the brain compartment has a volume of approximately 1.2L and therefore the numbers required for 1 L are adjusted accordingly.

Finally, the phantom also includes a very small amount of sodium azide (approximately 1 g per liter of water) which is a highly toxic substance employed to prevent fungal growth within the phantom. It is very important to note that sodium azide should never contact with skin, should be disposed very carefully following the hazardous waste disposal procedures in comply with federal regulations.

Metabolites were ordered from a vendor (Sigma-Aldrich, St.Louis); and can be accessed under the following index codes: NAA (Sigma-Aldrich, St.Louis, 00920-25G); Cr anhydrous (Sigma-Aldrich, St.Louis, C0780-50G); Choline Chloride (Sigma-Aldrich, St.Louis, C7527-100G); Myo-Inositol (Sigma-Aldrich, St.Louis, 57570-25G); GABA (Sigma-Aldrich, St.Louis, A2129-25G); L Glutamic Acid (Sigma-Aldrich, St.Louis, 49449-100G) and Sodium azide (Sigma-Aldrich, St.Louis, S2002-25G).

3.3 Acquisition

During the course of this work, the earlier experiments that were submitted as a conference abstract to the 24th annual meeting of the International Society for Magnetic Resonance in Medicine (ISMRM) were performed using spiral CSI acquisition -which is a very effective spatial encoding technique and accelerates the scan time- and the those results were enriched using Cartesian CSI acquisition during the preparation of oral presentation. It should be noted that the multi-coil shimming technique employed is decoupled from the particular acquisition scheme selected and provides the
similar improvements under both acquisition settings and the switching from spiral to Cartesian was because of the facts that most of the commercial CSI scans use Cartesian sequence and a discrepancy encountered after evaluation of spiral data on the voxels near excitation boundary, which has nothing to do with the shimming procedure and totally related to the excitation. The second point will be elaborated more during the last chapter where a detailed discussion of the experimental results will be provided.

3.3.1 Spiral CSI

Constant density, spiral-based k-space trajectories were appended to conventional PRESS\(^1\)-box excitation for single-slice, time-efficient spectral-spatial encoding [1]. Three TRs encoded a Cartesian matrix of \((x, y, f) = (12, 12, 460)\) points, (which is zero-padded to \(16 \times 16 \times 512\) for FFT purposes) over a 24 cm field-of-view (FOV) and spectral bandwidth of 1450 Hz. This scheme yielded an overall voxel size of 16 cc (2 x 2 cm in-plane and 4 cm slice). The PRESS-box excited VOI was \([80 \times 140 \times 40]\) mm\(^3\) and inscribed wholly within the brain.

Ten averages yielded an NAA SNR of approximately 25, under a 90 s of total imaging time, where \(TR = 2\) s and \(TE = 30\) ms.

3.3.2 Cartesian CSI

The Cartesian CSI acquisition consists of an acquisition with total duration 3:30, with a TR of 1400 ms and a \(TE\) of 144 ms. These numbers were adjusted to stay as much loyal to the usual clinical routine as possible. The voxel size was approximately 2 cc (12.5 x 12.5 x 12 mm) and the LASER excited VOI was \([80 \times 80]\) mm. The overall FOV was 20 cm with a matrix size of \(16 \times 16 \times 512\).

\(^1\)Introduced by Bottomley [9], PRESS stands as an acronym for Point RESolved Spectroscopy and is a broadly used spectroscopy sequence consisting of \(90^\circ\)-180\(^\circ\)-180\(^\circ\) pulses.
3.3.3 GRE Field Mapping

The GRE acquisition consisted of a 2-minute scan 2.4 mm in-plane ([240 × 240] mm over 100 × 100 matrix size) and 2 mm slice resolution parameters.

3.4 Shimming

During the experiments, the GRE acquisition is executed under scanner spherical harmonic shims up to 2\textsuperscript{nd} order. The field maps obtained are then exported to MATLAB (MathWorks, Natick, MA) and the optimization procedure was executed. Figure 3-4 depicts the graphical user interface of the software which recovers optimal shim currents to be applied through a number of steps, which will be explained below.

The software has several features. In particular, it enables both global shim (in which case we consider the entire volume) or slice optimal shim (which is localized to region being studied, hence is expected to benefit more); incorporation of different objective functions (in particular, penalizing standard deviation of field map profile, penalizing gradients of field map on top of norm of residual which is default) and also has number of features to adjust $B_0$ offset, which is a zeroth order effect that is corrected by scanner.

After uploading the field map magnitudes and field map phase, the brain extraction tool was called. This tool generates the mask corresponding to the region corresponding to brain. After the phase unwrapping, optimal shim currents are computed using the optimization problem in equation 3.1, which involves a convex objective function with a convex constraint set.
Figure 3-4: The GUI of the software that was employed during the optimization procedure.

\[
\begin{align*}
\min_x \|B_0 - Ax\|_2^2 \\
\text{s.t. } |x_i| &\leq I_{\text{max,loop}} \\
\sum_i |x_i| &\leq I_{\text{max,total}}
\end{align*}
\] (3.1)

In equation 3.1, \(B_0\) is the baseline field map, which is obtained under spherical harmonic shims. \(A\) is a matrix which corresponds to field profile obtained from each coil under 1 A of current\(^2\). It should also be noted that \(A\) has spatial dependency as well, since the field strength diminishes as we move away from the source. \(x\) is variable that we optimize over and it is the vector storing the optimal shim currents; and the two constraints denote the maximum current per loop (typically around 1.5 A) and total current in the whole array (around 35 A), respectively. Those constraints can be adjusted in software in order to deliver less or more current, if necessary. Moreover, the region that we consider is a masked region; \textit{i.e.} the objective is actually of form

\(^2\)Therefore, \(A\) constitutes our basis set, as explained previously.
where \( M \) is a binary mask; corresponding to brain region.

The interpretation of the problem is to match the inhomogeneous, baseline profile with a previously mapped basis set via minimization of an \( l_2 \) norm objective on the residual field, subject to the current constraints\(^3\). The problem was solved using \textit{fmincon} function of MATLAB (MathWorks, Natick, MA), the predicted field profile is generated and the optimal currents are ready to be applied with reverse signs to mitigate the inhomogeneity. The empirical shim data can be loaded to assess the accuracy of prediction to the GUI.

It is worth mentioning that even though the array is capable of handling such high current values, the numbers are restricted in order to avoid from heating related instability problems.

The only drawback of this procedure is an online-offline jump between the scanner and the computing terminal that requires active user interaction. Nevertheless, the whole procedure is very quick, around 2 minutes, and is not prohibiting for in vivo scans.

### 3.5 Methodology

The individual ingredients of the protocol have already been discussed in previous sections. The lines below is to tidy up the protocol.

- The phantom and metabolite solution are built using the corresponding concentrations provided earlier, tailored to 1.2 L.

- The scan is initiated with a CSI acquisition, under scanner spherical harmonic shims, using any of the desired spatial encoding technique (in this work, spiral and Cartesian acquisitions were followed). For the sake of consistency, the same scheme should be employed during one scan session.

- CSI acquisition is followed by a GRE field mapping acquisition, again under scanner spherical harmonic shims.

\(^3\)As we have mentioned previously, one can incorporate extra terms into objective function; but the \( l_2 \) norm objective on the residual field is the widely accepted methodology up to date.
• The field maps are exported, brain extraction tool and phase unwrapping were called and the optimal shim currents are evaluated by solving the optimization problem of equation 3.1. Optimization covers slices that are excited. Furthermore, in this step, optimization zone was restricted to an ROI mask covering the LASER/PRESS-excited region. The reason is for the sake of the fairness of comparison since the scanner attempts to shim over the region that is excited.

• The optimal currents are then applied with reverted signs, and the CSI and GRE acquisitions are repeated under multi-coil shims.

• The purpose of repeating the GRE acquisition is to judge whether the prediction of the field profile under the application of multi-coil shims is accurate or not.

• The results are compared with the aid of several metrics to assess the degree of improvement.

In order to establish experimental protocol, we have experimented with different acquisition parameters (in particular, different TR, TE, voxel size, number of averages) and the values utilized in this work is a compromise between this experimentation and the widely accepted clinical standards.

For the fairness of comparison, it is recommended to perform manual shimming, under scanner’s manual adjustment menu before CSI acquisitions. This allows user interaction to manually tune the spherical harmonic shims and is found to render more optimal spherical harmonic shim currents than those evaluated by the scanner.
Chapter 4

Results

As we recall, despite all the advantages offered by the CSI, the inherent limitations such as SNR and $B_0$ inhomogeneity severely obstructs the practicality of CSI in usual diagnostic imaging. The main goal of this work was to overcome with the artifacts emerging from severe $B_0$ inhomogeneity by nulling the uneven field distribution via a recently introduced, novel multi-coil shim hardware which allows generation of a target field distribution within the ROI without suffering from the handicaps of the conventional, spherical harmonic shim hardware. Once the imperfect field pattern is corrected, the profile of line shapes should be enhanced as the spectra is highly dictated by the field profile.\footnote{As a rule of thumb, the standard deviation within each voxel is a crucial factor that controls spectral line widths and the mean of the field profile roughly corresponds to amount of chemical shift.}

In this chapter, the results from the experiments will be presented. The chapter will begin with the quantification metrics that are utilized to assess the degree of improvement in both spectral quality and field distribution. Following section will present the experimental data. Since the spectra is a product of field distribution, the natural flow in this chapter will be to first present the representative field maps from an experiment, provide the quantitative information and conclude with the representative spectra corresponding to this particular experiment.
4.1 Quantification Metrics

Even though most of the results that will be presented in this chapter are pretty self-explanatory, the quantification metrics are employed with a purpose of making a more concrete comparison.

To gauge the improvement in the homogeneity of the field, we will use $\sigma^{GLOBAL}$ and $\sigma^{LOCAL}$, where the former metric corresponds to the standard deviation of $B_0$ maps within the ROI, therefore aiming to quantify the global degree of improvement over the whole slice and the second metric targets to capture the standard deviation within each particular voxel to relate the degree of improvement in the line widths to the degree of improvement in standard deviation of field distribution, recalling the earlier fact about the relationship between spectral quality and underlying field variation.

The first metric was computed via

- Calling `roipoly` function of MATLAB (MathWorks, Natick, MA) and drawing a mask that matches with the excitation boundary

- Computing the standard deviation of field map voxels contained within the mask.

In the sequel, global might correspond to entire slice or entire slab (with multiple slices); and the one being referred to will be stated explicitly.

The second metric is a bit more tedious to compute. As mentioned in the methodology chapter the resolution of the field maps exported was $100 \times 100$ whereas the resolution of the CSI was $16 \times 16$ voxels. Hence, the field map resolution is not an integer multiple of CSI resolution and should be first interpolated to a resolution that is evenly divisible by 16, e.g. to a resolution of $128 \times 128$. After this, the field maps are simply divided into grids and `std` function was called to obtain the numerical values.

The degree of enhancement in the line shapes is pretty self-explanatory, hence we will only provide a numerical excerpt for the Cartesian CSI experiment. The line
widths are extracted from the scanner by maintaining the standard post-processing tools that take place and verified manually. The line widths are measured in Hz.

4.2 Results from the Spiral CSI Experiment

To recall, the spiral CSI experiment was conducted under TR/TE: 2000 ms/30 ms with a voxel size of 16 cc ($[2 \times 2 \times 4]$ cm) under a total acquisition time of 1:30. The PRESS-box excited volume was of size $[80 \times 140]$ mm.

CSI acquisition is followed by a high-resolution, 2-minute GRE field mapping acquisition which has 2.4 mm in-plane and 2 mm slice resolution.

The position of the encoded and PRESS-excited volume in axial view, together with the position of the CSI slab in sagittal view are shown in Figure 4-1.

The representative field maps corresponding to the experiment are provided in Figure 4-2. This set corresponds to four slices separated 1 cm apart within a CSI slab of thickness 4 cm. The column entitled $2^{nd}$ order shim corresponds to the baseline profile which is acquired under SH shims. The columns under multi-coil shim display
the field profile obtained after pushing the corresponding shim currents that are evaluated through the optimization procedure. The rightmost column corresponds to the empirical profile and to assess the accuracy of prediction, the field maps predicted by the software are also attached as an individual column.

In Figure 4-2, $\sigma_{B_0}$ under each slice is the standard deviation within the black excitation box (selected via roipoly function to match with the PRESS-excited volume). $\sigma_{B_0}^{GLOBAL}$ corresponds to the standard deviation of the field distribution within the whole slab rather than individual slices.

The results indeed indicate more homogeneous field distribution under multi-coil shimming. The overall $\sigma_{B_0}^{GLOBAL}$ parameters is improved around 50% and similar improvements have been observed per individual slice. It is also worthwhile to note that the prediction is indeed of high accuracy, which can be verified by comparing the columns labeled predicted and acquired.

Within the PRESS-excited volume, there were 24 target CSI voxels. An ensemble containing 12 voxels was selected and provided in Figure 4-3 above to demonstrate the experimental results.

For each individual voxel, the red spectrum is acquired under spherical harmonics (up to and including 2nd order) and the blue spectrum is obtained under MC shims. A comparison indeed reveals enhanced spectral quality and sharper spectral lines, in particular in the posterior area of the phantom where 2nd order shims are compromised due to the attempt of cancelling severe $B_0$ hotspot existing in the frontal lobe.

In this ensemble, spectral line widths are improved to a great extent in particular for the voxels F, G, I, J, K and L; remained comparable for voxels such as C and D; got slight declined for voxels such as A and B. In total, of the 24 voxels, 13 got improved; 8 remained highly untouched and 3 got declined modestly.

It is worthwhile to discuss the trend in $\sigma_{B_0}^{LOCAL}$. As mentioned previously, $\sigma_{B_0}^{LOCAL}$ within a particular voxel can be thought of as a measure of amount of dephasing present in the spins within that voxel and therefore is expected to be correlated with $T_2^*$ and therefore with spectral line widths. In the voxels such as F, G, I, J, K and L; this parameter is improved and this improvement is also reflected as an improvement.
**Figure 4-2:** Four representative CSI slices spaced 1 cm apart. The black rectangle corresponds to the excited region. $\sigma_{B_0}$ values correspond to the standard deviation of the field distribution.
Comparison of spectra showing voxel-wise $\sigma B_0$

<table>
<thead>
<tr>
<th>Location</th>
<th>$\sigma B_0^{LOCAL}$</th>
<th>$\sigma B_0^{GLOBAL}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>14.7 Hz</td>
<td>8.8 Hz</td>
</tr>
<tr>
<td>B</td>
<td>5.9 Hz</td>
<td>8.5 Hz</td>
</tr>
<tr>
<td>C</td>
<td>4.4 Hz</td>
<td>4.0 Hz</td>
</tr>
<tr>
<td>D</td>
<td>3.8 Hz</td>
<td>2.4 Hz</td>
</tr>
<tr>
<td>E</td>
<td>1.7 Hz</td>
<td>2.5 Hz</td>
</tr>
<tr>
<td>F</td>
<td>3.0 Hz</td>
<td>1.4 Hz</td>
</tr>
<tr>
<td>G</td>
<td>3.7 Hz</td>
<td>1.6 Hz</td>
</tr>
<tr>
<td>H</td>
<td>1.2 Hz</td>
<td>1.2 Hz</td>
</tr>
<tr>
<td>I</td>
<td>1.8 Hz</td>
<td>1.0 Hz</td>
</tr>
<tr>
<td>J</td>
<td>2.9 Hz</td>
<td>1.9 Hz</td>
</tr>
<tr>
<td>K</td>
<td>3.5 Hz</td>
<td>1.1 Hz</td>
</tr>
<tr>
<td>L</td>
<td>5.3 Hz</td>
<td>1.0 Hz</td>
</tr>
</tbody>
</table>

**Figure 4-3:** Left: Locations of the CSI voxels inside the phantom. Right: Spectra obtained from corresponding voxels under 2nd order and MC shim settings. The numbers indicate the aforementioned $\sigma B_0^{LOCAL}$ parameters within that particular voxel.

in line widths. For voxels such as C, this number remained comparable and indeed the spectra look very alike. Voxel B is an example of a voxel where $\sigma B_0^{LOCAL}$ increased and the spectral quality also got worsened, in particular for the NAA peak. However, a discrepancy exists, especially for voxel A where $\sigma B_0^{LOCAL}$ is improved significantly while spectral quality got slightly worsened.

A mismatch between $\sigma B_0^{LOCAL}$ and line width trend exists in e.g. voxel A, which is located at the intersection of PRESS-excitation boundary and frontal lobe. The possible reasons for this mismatch include shifts in the acquired voxel location as a result of highly inhomogeneous $B_0$ profile in the corresponding position; big voxel size (which causes too much intra-voxel dephasing) as well as the frequency sensitivity of particular excitation scheme. Therefore, the proposed method would benefit from swapping the PRESS-box excitation module with a technique that has sharper spatial localization as well as less sensitivity to chemical shift, e.g. LASER, which is an acronym for Localized Adiabatic Selective Refocusing [21].

To summarize the results, MC shims provided up to 50% improvement in $\sigma B_0^{GLOBAL}$.
over the whole CSI slab and similar improvements per individual CSI slice, produced a much homogeneous $B_0$ distribution and reduced the peak $\Delta B_0$, compared to 2nd order SH shimming. Furthermore, as a result of improved field homogeneity, the spectral quality is enhanced within the majority of CSI voxels, in particular in the posterior area of the phantom. Field variations within individual CSI voxels as measured via $\sigma_{B_0}^{\text{LOCAL}}$ are also improved. For the voxels that are away from the $B_0$ hotspot, $\sigma_{B_0}^{\text{LOCAL}}$ stands as an efficient predictor of the amount of improvement/worsening in the spectral line widths. However, for voxels located near intersection of $B_0$ hotspot and excitation boundary, the prediction accuracy is slightly declined. This would benefit by swapping the excitation module to a one with better-defined excitation boundaries, such as aforementioned LASER module. The Cartesian CSI sequence that was run after the spiral CSI experiments use LASER for RF-excitation and indeed exhibits an improved correlation between $\sigma_{B_0}^{\text{LOCAL}}$ and spectral line widths. This point will be elaborated more on the next section.

### 4.3 Results from the Cartesian CSI Experiment

As mentioned previously, Cartesian CSI experiments have been conducted during the course of preparation for oral presentation in Singapore, and work below is delivered as a talk in the conference. Most of the figures below are reproduced from there and can be accessed at [42].

The Cartesian sequence that was employed has a TR/TE of 1400/144 ms with a voxel size of $[12.5 \times 12.5 \times 12]$ mm (roughly 2 cc) under a total imaging time of 03:30. The LASER-excited volume is of size $[80 \times 80]$ mm and the corresponding TR/TE values are selected as such to follow the clinical routine.

As in the earlier spiral CSI section, the Cartesian acquisition is followed by 2 minute, GRE acquisition which has 2.4 mm in-plane and 2 mm slice resolution. After pushing the appropriate amount of currents for the MC shimming, the CSI and GRE acquisitions were repeated.

Position of the spatially encoded and LASER-excited volumes in axial view to-
Figure 4-4: **Left:** The positioning under sagittal view. **Right:** The position of the spatially encoded and LASER-excited volumes. The white box corresponds to LASER-excitation boundaries.

Together with the positioning in sagittal view are shown in Figure 4-4.

Within 12 mm thick region, there were 6 field map slices. Two representative slices corresponding to second and second-to-last in this ensemble are provided in Figure 4-5.

The black rectangle corresponds to the LASER-excited volume. $\sigma_{B_0}$ values correspond the standard deviation taken within the black rectangle for the corresponding slice. The pronounced degree of improvement for these two slices is $\% 41$ and $\% 58$, respectively. Furthermore, $\sigma_{B_0}^{GLOBAL}$ value over the whole CSI slab, within the black box was reported as 15.8 Hz under 2nd order shims; 8 Hz under multi-coil shims and predicted as 8.8 Hz, corresponding to an improvement of 50%. The prediction is also highly accurate as in the spiral CSI experiment.

The trend in $\sigma_{B_0}^{LOCAL}$ for each particular voxel are provided in Figure 4-6 and pronounces an improvement in majority of CSI voxels.

The set of spectra corresponding to $6 \times 6$ grid of voxels within the LASER-excited region under the 2nd order shims is shown in Figure 4-7 and that acquired under MC shims is provided in Figure 4-8. These images are generated under the spectroscopy toolbox of the Siemens platform while keeping all the present post-processing tools
Figure 4-5: \( B_0 \) profiles for two representative GRE slices under 2\(^{nd}\) order spherical harmonic shims and under multi-coil shims.

Figure 4-6: Local standard deviation of the field variation per individual CSI voxel under SH and MC shims together with the prediction.
except curve fitting.

These results indicate highly improved spectral quality within a dominating majority of CSI voxels. Spectral lines are much sharper and higher (since the integral of each peak, which measures amount of a certain metabolite, is constant) under MC shim settings. Furthermore, one may also observe that a better water saturation is observed especially in the frontal lobe area where poor shimming highly reduces the effectiveness of pulses employed for water saturation.

The comparison of the $\sigma_{B0}^{LOCAL}$ trend together with the line widths observed provides a plausible evidence for the earlier hypothesis made about the discrepancy observed in spiral CSI experiment.

The shimming performance is highly improved in the areas other than frontal lobes where the shims got slightly worsened and this is consistent with the trend in $\sigma_{B0}^{LOCAL}$. The improved spectral quality within the frontal lobes is possibly due to improved water suppression and slice profile.

It should be highlighted that this slice is located in a very deep region and highly challenging, which is evident from the field maps. Several individual spectra are provided to illustrate this point and provide a closer look into degree of improvement in spectral line shapes.

For the two voxels shown in Figures 4-9 and 4-10, the spectra under $2^{nd}$ order shims has such insufficient quality that the metabolite peaks are highly corrupted/almost indistinguishable. Furthermore for the voxel in Figure 4-10, the water saturation seems to be corrupted, as well. For the voxel shown in Figure 4-11, Cr and Cho peaks are not resolved under $2^{nd}$ order shims and well-separated under MC shims.

The spectra in Figure 4-12 is also an example where the peaks are totally corrupted and has zero diagnostic quality under $2^{nd}$ order shims and are improved significantly with the presence of MC shims.

Voxels in Figures 4-13, 4-14, 4-15 and 4-16 correspond to a set of spectra where the peaks are visible and almost distinguishable but are of low quality and broadened under $2^{nd}$ order shims and enhanced to a great extend under MC shims.

We will conclude the results by providing two representative spectra extracted
Figure 4-7: Spectra corresponding to $6 \times 6$ grid within LASER-excited region under spherical harmonic shims.
Figure 4-8: Spectra corresponding to $6 \times 6$ grid within LASER-excited region under multi-coil shims.
Figure 4-9: Left: Spectrum under $2^{nd}$ order shims. Middle: Spectrum under multi-coil shims. The voxel location is denoted with a (x) in anatomical view

Figure 4-10: Left: Spectrum under $2^{nd}$ order shims. Middle: Spectrum under multi-coil shims. The voxel location is denoted with a (x) in anatomical view
Figure 4-11: **Left:** Spectrum under 2nd order shims. **Middle:** Spectrum under multi-coil shims. The voxel location is denoted with a (x) in anatomical view.

Figure 4-12: **Left:** Spectrum under 2nd order shims. **Middle:** Spectrum under multi-coil shims. The voxel location is denoted with a (x) in anatomical view.
Figure 4-13: **Left:** Spectrum under 2\textsuperscript{nd} order shims. **Middle:** Spectrum under multi-coil shims. The voxel location is denoted with a (x) in anatomical view

Figure 4-14: **Left:** Spectrum under 2\textsuperscript{nd} order shims. **Middle:** Spectrum under multi-coil shims. The voxel location is denoted with a (x) in anatomical view

Figure 4-15: **Left:** Spectrum under 2\textsuperscript{nd} order shims. **Middle:** Spectrum under multi-coil shims. The voxel location is denoted with a (x) in anatomical view
from voxels located at severe \( B_0 \) hotspot zone.

The example spectral pairs in Figures 4-17 and 4-18 illustrate the fact that the CSI slab that was imaged was indeed a highly challenging region, had very poor spectral quality as a result of associated \( B_0 \) inhomogeneity. Spherical harmonics up to 2\(^{nd}\) order performed poorly and could not capture such higher order field variation, whereas the prescribed multi-coil shims improved line widths substantially within the whole phantom, provided better-resolved peaks as well as improved water suppression, which was an aforesaid challenge originating from field inhomogeneity.

Figure 4-19 depicts the trend between \( \sigma_{B_0}^{\text{LOCAL}} \) versus spectral line shapes. \( \sigma_{B_0}^{\text{LOCAL}} \)
Figure 4-18: **Left:** Spectrum under $2^{nd}$ order shims. **Middle:** Spectrum under multi-coil shims. The voxel location is denoted with a (x) in anatomical view.

is plotted in a range of $[0, 10]$ Hz, the $6 \times 6$ grid of voxels are overlaid with the $\sigma_{B_0}^{LOCAL}$ map under both $2^{nd}$ order and multi-coil shim settings.

The correlation between $\sigma_{B_0}^{LOCAL}$ and line widths are much more noticeable compared to the earlier experiment. Except a very small number of frontal lobe voxels, for which the improvement is possibly due to improved slice profile as well improved water suppression, the improvement in $\sigma_{B_0}^{LOCAL}$ is indeed manifested as enhanced line quality which justifies the earlier hypothesis made about the importance of having a well-defined excitation boundary as in LASER.

To sum up, the multi-coil shims reduced $\sigma_{B_0}^{GLOBAL}$ for the overall slab up to 50%, provided similar enhancements per individual slices, improved $\sigma_{B_0}^{LOCAL}$ for a majority of CSI voxels. As a result of improved field homogeneity, the spectral quality is improved for a dominating majority of the voxels, returned sharper spectral line shapes in almost entire phantom and provided much better water saturation throughout.

This collection of data is presented at the 24$^{th}$ annual meeting of the International Society for Magnetic Resonance in Medicine (ISMRM) held in Singapore in May 2016 as an oral presentation and the full version of the talk can be accessed at [42].
Figure 4-19: Left: $6 \times 6$ grid of spectra overlaid with corresponding $\sigma_{B_0}^{\text{LOCAL}}$ map under $2^{nd}$ order shims. Right: Same grid overlaid with corresponding standard deviation map, under multi-coil shims.
Chapter 5

Conclusion and Future Work

5.1 Summary of the Contribution

In this work, an improved way of performing chemical shift imaging, with the focus on multi-voxel approach\(^1\), has been demonstrated. The technique takes advantage of recently introduced novel 32-channel integrated RF-shim coil array to mitigate higher order \(B_0\) inhomogeneity while not suffering from the aforementioned drawbacks of conventional, spherical harmonic shimming approach. Studies are conducted on an anthropomorphic head phantom using a Siemens Skyra 3T platform (Siemens Healthcare, Erlangen, Germany) under spiral CSI sequence with PRESS excitation and conventional, Cartesian stock CSI sequence under LASER excitation.

As a result of improved field distribution, the artifacts (including, chemical shift displacement of metabolites as a first order effect; line broadening and diminished water suppression) sourcing from uneven field distribution are corrected to a high extend, the spectral quality is enhanced under both spiral and Cartesian acquisition schemes, sharper and better-resolved line shapes are earned and likewise the water suppression performance is improved.

The technique requires exporting field maps to a computing platform to execute an optimization protocol that returns the prescribed shim currents. Nevertheless, this

\(^1\)The alternative technique is single voxel spectroscopy (SVS), where, obtaining a good shim is not a challenging problem, since the region being studied in SVS is small and easier to shim.
step takes only around 2 minutes and is not prohibitive for clinical studies.

5.2 Discussion and Future Work

The experimental results indicate improved field homogeneity and as a result, improved spectral profile. The predicted and acquired field maps are consistent and prediction is indeed of high accuracy.

Some relevant points that might arise and worth discussing are as follows. The purpose of using a phantom was to demonstrate a proof-of-concept for the in vivo studies. In fact, the $B_0$ profile observed in the phantom highly matches with that observed in vivo and therefore phantom studies established a strong ground for in vivo studies.

As noted earlier, the slight discrepancy in spiral CSI experiment is addressed via switching to an excitation module with sharper spatial localization and excitation boundary -which is LASER in our case- and indeed yielded much better correlation between local standard deviation parameter and spectral line width.

During the Cartesian CSI experiment, even though the field distribution is improved within the majority of brain compartment, frontal lobe region got slightly worse. This is possibly related to the shapes of spherical harmonic basis functions and we expected to outperform spherical harmonic approach in frontal lobe, if we solely focus on frontal lobes. Indeed, an experimentation with a localized shimming focusing entirely on frontal lobes revealed tremendous improvement in the spectra extracted from frontal lobes.

The techniques might benefit significantly from switching to a hardware that is capable of dynamical shimming. If we recall, the current technique uses the field maps and runs the optimization protocol restricted to the excited slices to evaluate the shim currents. An improved way is to compute shim currents individually per slice -as the field pattern of adjacent slices are not completely the same, and therefore requires different currents if we treat each slice individually- and dynamically update them on the fly, which is precisely dynamical shimming. To be able to do so, the
hardware should be able to update shim currents as early as 500 µs. As of now, despite the fact that the current hardware that phantom experiments are conducted is not capable of handling so, the forthcoming version shim drivers are going to be suited to update shim currents tailored to individual slices.

During the experimental protocol, heating related stability issues with the hardware have been observed. If the shim currents stay active for a long time, the resultant spectra was highly corrupted. This issue is going to be addressed and improved again in the next generation shim hardware, which will be capable of supplying much higher current values for much longer times.

Unlike the spherical harmonics, the basis set used for optimization purposes is non-orthogonal and furthermore, the optimization problem does not have a closed form solution and requires to switch to a different platform during the protocol. Nonetheless, MATLAB’s (MathWorks, Natick, MA) fmincon performs pretty well for evaluating shim currents and the whole process takes about 2 minutes, which is not a significant limitation.

To summarize, the experiments conducted illustrated proof-of-concept, established a working protocol on the shim array and therefore formed a strong backbone to push studies forward. The ultimate goal is to make the technique routinely available to the clinicians.
Bibliography


[64] Eva M. Ratai. personal communication.


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