Evaluating Echo Planar Spectroscopic Imaging with a Columnar Excitation for "Virtual Biopsies"

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Synopsis

The acquisition of high-resolution quantitative measurements is of particular interest in studying the laminar structure and layer-specific pathology in the cerebral cortex. In this work, we propose a method to address this need by acquiring 1-D echo planar spectroscopic imaging (EPSI) as a "virtual biopsy" with 200 µm resolution along the readout direction. Our sequence yields expected spectra for common compounds and produces high-quality quantitative T_2* and off-resonance measurements in ex vivo brain tissue. Our goal is to use this quantitative virtual biopsy to discriminate laminar variations in cortical iron deposition in diseases such as frontotemporal lobar degeneration (FTLD).

Introduction

Recent advancements in neuroimaging have demonstrated the use of columnar excitations and high-resolution 1-D readouts to encode cortical laminar features[1]. In particular, prior work has focused on columnar diffusion-weighted imaging (DWI), which is strongly sensitive to the laminar features of the cortical myeloarchitecture. However, neurodegenerative diseases—in particular Alzheimer's Disease (AD)[2], Amyotrophic lateral sclerosis (ALS)[3], and frontotemporal lobar degeneration (FTLD)[4]—also produce notable iron deposition within the cortical laminae. The layer-specific resonance frequency shift that results from the cortical distribution of laminar iron has previously been imaged using 2-D T_2*-weighted[3,5] and 2-D phase-contrast methods[6]. Combing these concepts, we explored the use of columnar excitations and high-resolution 1-D echo planar spectroscopic imaging (EPSI) readouts[7] to produce a "virtual biopsy" with depth-resolved quantification of the water signal's off-resonance shift, towards the goal of resolving the pathologic iron distributions associated with different neurodegenerative diseases that can be difficult to distinguish in vivo[2-4].

Methods

A spin-echo EPI sequence was modified to achieve columnar excitation and 1-D EPSI readout (Fig. 1). The refocusing RF pulse was adjusted to be applied in the phase-encoding (PE) direction orthogonal to the excitation pulse used for slice-selection. In this way, coherent signal is only acquired from a 1-D columnar segment at the intersection of the excitation and refocusing slice-selection planes. Removing the PE blips from the EPI readout train and centering the first readout of the train at the spin echo produces a 1-D EPSI, which we use to acquire multiple sequential echoes from this "virtual biopsy" column. To achieve sufficient SNR, the experiment is then repeated to acquire multiple averages.

To demonstrate our proposed technique, we imaged a phantom constructed using four 50-mL conical tubes individually filled with methanol (MeOH), ethanol (EtOH), olive oil, and water on a 3T scanner (Prisma, Siemens Healthineers, Erlangen, Germany) using the vendor's 64-channel head coil (with 52 channels active). We collected 32 averages of the virtual biopsy scan with 200 µm resolution and 150 mm FOV along the readout dimension, and 3.0 mm thickness for both the excitation and refocusing pulses. Additional parameters were 16 ms TE, 1000 ms TR, 304 Hz/px bandwidth, 3.92 ms echo-spacing, and 36 sec total scan time.

To explore whether our EPSI sequence could interrogate clinical pathology, we also imaged a formalin-fixed ex vivo cerebral human hemisphere specimen. The sample donor had pathologically confirmed progressive supranuclear palsy (PSP), which we have previously shown to have focal cortical iron deposition observable in the motor cortex on T_2*-weighted ex vivo scans[4,8]. We used the same 3T imaging setup with similar imaging parameters, collecting 32 averages using 48 active channels with 200 µm resolution; 140 mm readout FOV; 3.0 mm slice thickness; 15 ms, 30 ms, and 45 ms TE; 1000 ms TR; 388 Hz/px bandwidth; 3.22 ms echo-spacing; and 36 sec total scan time.

We phase-corrected for EPI even-odd readout coherence by computing the all-pass delay filter that optimally aligns even- and odd-polarity readouts[9], and combined individual coil data using the approach described by Hu et al (2021)[10]. To analyze our ex vivo data, we calculated the spatially dependent peak off-resonance and both T_2* and T_2 relaxation time using methods described by Funai et al (2008)[11] and Bonny et al (1996)[12], respectively. The code and data for our work is available at https://www.github.com/michael-s-yao/VirtualBiopsy and is licensed under the MIT License.

Results and Discussion

Figure 2 illustrates our proposed EPSI method using a phantom consisting of methanol, ethanol, olive oil, and water. Our imaging bandwidth was approximately 2 ppm, which lead to aliasing of resonance peaks such as the hydroxyl group contribution in the alcohol spectra that fall outside of our limited bandwidth. However, for practical clinical applications, resolving T_2* and off-resonance shifts in human tissue are well-known to be resolvable within our 2 ppm bandwidth[2-4].

To validate this claim, we imaged the motor cortex of an ex vivo specimen demonstrating the pathophysiology of PSP to explore laminar cortical iron deposition using our EPSI approach (Fig. 3). As expected, the white matter regions at approximately 65 and 72 mm along the biopsy dimension immediately surrounding the central sulcus are characterized by shorter T_2* and T_2 relaxation times due to myelin and co-located iron in the white matter. A "dip" in the T_2* within the cortex at roughly 67.5 mm is likely due to pathologic iron deposits in the middle layers of the cortex, as previously described for this disease[4]. Detecting variations in relaxation times, peak off-resonances, and other features that vary with cortical anatomy is made possible by our high spatial resolution of 200 µm along the biopsy direction.

Conclusion

We have presented a method for efficient virtual biopsy acquisition via EPSI imaging for high-resolution tissue resonance spectra. Our proposed technique trades a second spatial dimension for frequency information along the readout dimension, which may enable future studies on early detection of FTLD and other neuropathological diseases through noninvasive cortical iron analysis[4]. Further work remains to be done to achieve this goal, such as in motion correction and phase stabilization that are necessary for real-world in vivo applications.

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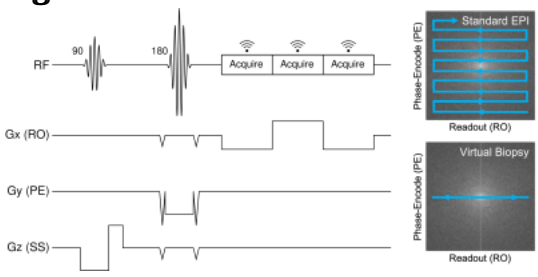
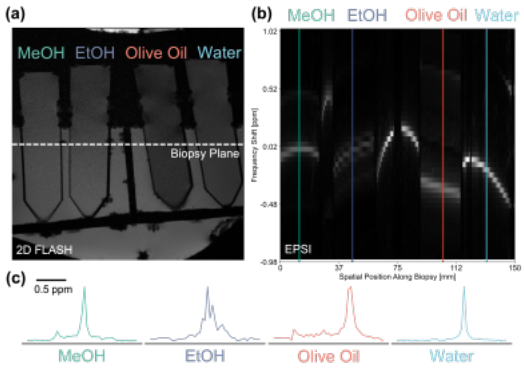
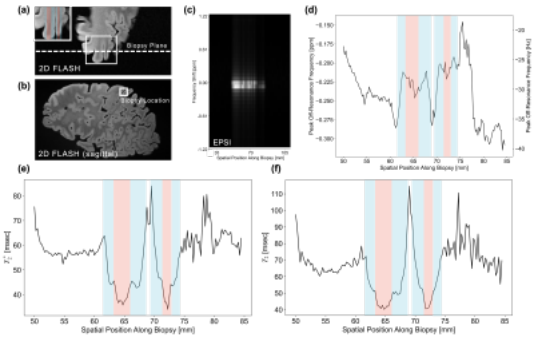
Figures



(Left) MR pulse sequence diagram for our EPSI-like virtual biopsy sequence. (Right) Visual illustration of our virtual biopsy *k*-space trajectory compared to that of typical EPI imaging approaches.



EPSI spectroscopic analysis of a phantom containing four chemical samples: methanol (MeOH), ethanol (EtOH), olive oil, and water. (a) Reference 2-D FLASH scan of the phantom setup indicating the virtual biopsy readout axis. (b) EPSI virtual biopsy T_2-weighted spectrum. (c) Plotting the 1-D MR spectra at the four indicated locations demonstrate the expected peaks for each of the imaged compounds.



EPSI imaging of an ex vivo specimen of a cortical hemisphere from a patient with PSP. Reference (a) 2-D FLASH scan co-planar with our 1-D EPSI (approximately coronal/sagittal) and (b) sagittal 2-D FLASH scans demonstrate the virtual biopsy readout axis and biopsy location, respectively. (c) EPSI virtual biopsy T_2-weighted spectrum using a TE of 15 ms. (d) Peak off-resonance frequency, (e) T_2*, and (f) T_2 relaxation times as a function of spatial position in the virtual biopsy. Cortical regions are highlighted in blue and white matter are highlighted in red.