Specialty Area: ***UTE: Applications & Advances***

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Highlights

- Ultrashort echo time (UTE) and zero echo time (ZTE) methods can image ultrashort-T2 components (T2 < 1 ms)
- Myelin has an ultrashort-T2 component associated with myelin membranes
- Imaging cortical bone in the skull with UTE and ZTE is valuable for PET/MR, radiation therapy planning, and MR-guided focused ultrasound applications

Neurological Applications of UTE

TARGET AUDIENCE: MR scientists/engineers and physicians with interests in new neurological imaging methods.

OUTCOME/OBJECTIVES: The goal of this talk is to describe the progress and rationale for applying ultrashort echo time (UTE) and zero echo time (ZTE) MRI pulse sequences in the brain. Current neurological applications include imaging ultrashort-T2 components (T2 < 1 ms) in myelin and cortical bone, which are invisible with conventional pulse sequences that have longer minimum TEs. Participants will be able to understand the technical considerations of UTE/ZTE pulse sequences and the imaging targets for neurological applications.

PURPOSE: Ultrashort echo time (UTE) and zero echo time (ZTE) pulse sequences allow for visualization of fast-relaxing components with submillisecond T2 relaxation times. These components are effectively invisible in conventional gradient-echo pulse sequences due to limitations on the minimum echo time (TE) from the RF pulse and Cartesian readout gradient. These fast-relaxing, "ultrashort-T2" components are typically semi-solid in structure, and are found in tendons, cortical bone, myelin, liagments, menisci, falx cerebri, nerves, and more.

There are two primary neurological applications of UTE and ZTE being explored: (1) Myelin – Recent Ex vivo studies [1, 2] have validated the presence of ultrashort-T2 components in myelin, arising from bound protons in the membranes and macromolecules. Imaging this component has the potential to provide information about formation, degeneration and regeneration of myelin, and maybe a more direct marker that previous methods. (2) Skull imaging – Cortical bone in the skull has a T2 ~ 400 μs, and mapping bone is crucial for PET/MR systems, MR-guided Focused Ultrasound (MRgFUS), and radiation therapy planning. This is because bone significantly perturbs ultrasound and high-energy radiation. Providing accurate bone maps enables precise therapy localization and accurate PET reconstructions.

METHODS: UTE and ZTE pulse sequences have specialized features for depicting fast relaxing components:

1) *Excitation*: RF excitation pulses must be short compared to the ultrashort-T2 values of interest. (Equivalently, they must have large bandwidths compared to the broad ultrashort-T2 linewidths.) 2D UTE is enabled by the use of half-pulse excitations [3]. In ZTE, short pulses must be used to eliminate RF shading artifacts.

2) *Readout*: After switching RF hardware from transmit to receive modes, center-out k-space trajectories are typically used to capture the fast relaxing signals. Most common are radial trajectories, although spirals [4] and 3D cones [5] have also been used. The total readout duration should be on the order of the ultrashort-T2 values of interest [6]. Non-Cartesian methods are used for reconstruction, such as gridding [7] and the Non-Uniform Fast Fourier Transform [8].

3) *Image contrast*: The inherent contrast (e.g. T1 or PD) of ultrashort-T2 components is typically poor due to low proton density and/or high signals from longer T2 components. This is particularly challenging in neurological applications, where there are much larger long T2 components in the brain itself, as well as large signals from fat in the bone marrow. The following methods have demonstrated improvements in ultrashort-T2 component contrast [9, 10]: subtraction of a later TE image; inversion recovery (IR) to null based on T1 [11]; and saturation pulses of either the long-T2 [12, 13] or short-T2 [14] components.

Artifacts: The center-out readout trajectories are sensitive to off-resonance, which results in blurring and ringing artifacts. These trajectories are also sensitive to gradient infidelities, such as eddy currents. ZTE is much less sensitive to eddy currents because the gradient is changed in small increments.

See References [15, 16] for additional methodological discussions.

RESULTS:

Myelin Imaging: Two recent *ex vivo* nuclear magnetic resonance (NMR) studies have characterized a potential new MRI myelin biomarker associated with methylene protons in myelin membranes [1, 2]. These studies measure a wide range of ultrashort-T2 values between 50 μs and 1 ms at 4.7 and 9.4 T. Horch et al. estimated that this was primarily arising from the methylene protons in the myelin membranes [1]. Wilhelm et al. further demonstrated a strong correlation between myelin content and the ultrashort-T2 signal as well as 3D UTE images of this component using IR and dual-echo subtraction in the rat spinal cord [2].

Several in vivo studies have also measured a submillisecond T2 component in the brain, with T2* values of 100-350 μs (1.5T) [17], 600-900 μs (1.5T) [18], and 420 ± 80 μs (3T) [19]. Recently, 2D UTE imaging with inversion recovery and dual-echo subtraction (3T) has demonstrated the most reliable and consistent detection, measuring average values in normal volunteers of T2* = 320 and 420 μs, T1 = 226 ms, and a relative proton density of 4.05% [19, 20]. The key challenge in this application is to suppress the much larger long T2 components and imaging within reasonable scan times.

Skull: Cortical bone has a T2 ~ 400 μs, and it is a well-established imaging target of UTE and ZTE [12, 21, 22, 23, 24, 25, 26]. Mapping cortical bone in the brain is of critical importance for PET reconstruction on PET/MR systems [27, 28, 29, 30, 31], as well as planning in radiation therapy planning [28] and MR guided focused ultrasound [32] because bone significantly perturbs the positrons, high-energy radiation, and ultrasound waves that are being generated and/or observed.

Dual-echo or R2* methods – subtraction of a later TE – are a simple method for mapping cortical bone in the skull [27, 28, 30, 31]. These work well for cortical bone becaue there is no overlapping spins (unlike myelin ultrashort-T2), but suffer from susceptibility artifacts (creates short-T2*) and blurring artifacts from marrow fat. Fat separation can be corrected with Dixon-type methods [29]. There are also magnitude-based separation methods, segmenting based on the much lower signal of cortical bone [33].

Other Applications: Several other potential neurological applications of UTE include calcifications, gliosis in and around gliomas, scar tissue resulting from meningioma surgery, cavernomas, and melanoma metastases [34]. While promising, none of these applications has been more extensively explored.

DISCUSSION & CONCLUSION: The primary neurological applications of UTE and ZTE are myelin and skull imaging. Imaging of the ultrashort-T2 component in myelin is relatively new, and improvements need to be made in image contrast and exploration of clinical pathologies. Skull imaging is becoming increasingly widespread, particularly of PET/MR attenuation

correction mapping. Improvements in spatial accuracy will be important and it would be ideal if UTE/ZTE MRI can provide quantitative measurements of bone density.

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