Comparative Analysis of Zero Echo-time MRI and CT for Pediatric Craniosynostosis

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Abstract

Zero echo-time (ZTE) MRI (K132376) is an emerging technique that has been shown to adequately image bone and will likely allow eventual widespread imaging of osseous structures. The opportunity to exchange standard CT evaluation for a radiation-free modality is desirable, particularly in the pediatric population. A promising clinical application is the use of ZTE for diagnosing craniosynostosis, potentially precluding the use of the standard volumetric head CT scan. We propose a comparative analysis between zero echo-time MRI and CT to assess their effectiveness in diagnosing this entity. Our hypothesis is that ZTE is concordant with CT for suture visualization and imaging diagnosis, permitting its use in the clinical setting for this purpose.

Research Plan

1. Specific Aims

To establish whether ZTE imaging of the infant calvarium can provide equivalent information to CT and allow for a reliable diagnosis of craniosynostosis in a child. This aim is based on the hypothesis that there will be 90% or greater concordance between ZTE and CT findings.

2. Background & Significance

Magnetic resonance imaging (MRI) has become the primary workhorse for pediatric neuroradiology, providing superior imaging of soft tissues in the brain, head, neck and spine, while offering the added benefit of having no ionizing radiation. Evaluating cortical bone, however, continues to be a limitation with conventional MRI sequences. The contents within cortical bone (inorganic minerals, collagen matrix and various water concentrations) and their tightly organized structure result in very short T2 values (T2 ~ 300-400 μs) and rapid magnetization decay which yield signal voids and insufficient image contrast.

Computed tomography (CT), therefore, continues to be the primary modality for evaluating osseous structures. This modality is not ideal in children who have increased sensitivity to the adverse effects of radiation. Developing a comparable MR sequence which can evaluate bone without radiation is critical and aligns with the ALARA ("as low as reasonably achievable") radiation safety principle to minimize radiation doses in children.

Three dimensional proton density-weighted zero echo-time (ZTE) is a developing technique that uses proton density differences rather than T2 relaxation time differences to achieve contrast. It has been used to better image bone structure within the calvarium, spine and extremities[1-5]and has been explored for use in attenuation correction for PET/MR studies[6-8]. The sequence is performed without preparation pulses or multiple echoes, rendering it time-efficient and (if performed alone), usually precluding the need for sedation[1]. Alternatively, it can easily be added to a more complete MR exam, providing an efficient “one stop” evaluation.

The diagnostic utility of ZTE is not yet established and a comparative validation study of ZTE with CT is needed before reliably using this in the clinical setting for preoperative purposes. If ZTE is shown to be non-inferior to CT for evaluation of craniosynostosis, clinical practice will be substantially improved; neurosurgeons as well as parents and children may be offered a radiation free imaging tool. This is particularly advantageous for this population of children which may require multiple follow-up exams after surgical correction. Moreover, this could serve as an initial study preceding evaluation of other osseous structures including facial bones and skull base. The findings in this study could also drive further technological advancements to include the creation of surface renderings based on ZTE data for anatomic modeling.

3. Study Design

3.1 Study population/Patient Enrollment

Eligibility criteria - Inclusion:

Pediatric patients 0-18 of age will be recruited by our surgical colleagues based on the clinical concern for craniosynostosis and possible need for calvarial reconstruction. Study Team will also review the surgical calendars and Mayo Clinic data base (MDE, i2b2) searching for potential pediatric patients. When a patient is found they will email the surgeons for a review and verification of qualification for the study. Patients must have gotten a clinically indicated CT within a 6 week time period from the ZTE MRI.

Eligibility criteria - Exclusion:

Exclusion criteria include lack of consent, clinical CT scan of the head, contraindication/inability to undergo both examinations within the designated time period and/or undiagnostic image quality. Pregnancy (women of childbearing age will be given a urine pregnancy test).

Patients will undergo ZTE within a 6 week time period from the CT scan (though attempting with each patient to schedule on the same day). ZTE MRI examinations will be added, when possible, to a patient’s already scheduled MRI or will take place as a standalone appointment without sedation.

Patient preparation

A Review Preparatory to Research will be conducted by the study coordinators to determine if the patient meets inclusion criteria including a pre-screen for MRI safety.

3.2 Patient Scanning Protocol

CT examinations will include age-appropriate protocols for radiation dose minimization, with three-dimensional reconstruction, per the cranisynostosis protocol. MR imaging will be performed on a 3T scanner capable of ZTE imaging. The pediatric whole-head ZTE protocol is set up to acquire volumetric proton density-weighted images with the following acquisition parameters: TE 0.016ms, field-of-view 18×18 cm, readout matrix 180×180, number of slices 180, slice thickness 1 mm, bandwidth 31.25kHz, flip angle 2°. The image resolution is 1-mm isotropic and therefore can be reformatted in any plane. The acquisition time for each acquisition is approximately 2 minutes. The acquisition is repeated to achieve better SNR by averaging the two acquisitions during post-processing offline after rigid body registration. In case significant motion is observed in one of the acquisitions, only the acquisition with less motion will be used during post-processing to generate the bright-bone images. An adjunct 3D GRE sequence will be made available to aid with differentiating between cortical bone and soft tissue. The acquisition parameters for the axial 3D GRE sequence are: TR 6.8ms, TE 2.3ms ("in phase"), flip angle 5-degree, field-of-view: 18X18 cm, acquisition matrix 256 X 256, slice thickness 1mm. The scan time for the 3D GRE sequence is ~6 minutes.

3.3 MRI and CT evaluation

Four CAQ certified neuroradiologists will independently evaluate CT and ZTE images in separate sessions. There will be at least a two-week time window between readings of CT and ZTE to diminish recall bias. ZTE data will be presented in three display formats: (1) raw magnitude image with multiplanar reformats, (2) bright-bone reconstructions, (3) 3D volume renderings. CT data will be presented in two display formats: (1) source images with multiplanar reformats and (2) 3D volume renderings. The images will be reviewed in a blinded fashion during separate interpretation sessions to prevent recall bias.

3.4 Data Collection:

Each observer will provide ordinal ratings with regard to (a) visibility of each major cranial suture and fontanelles [1 = poorly seen, 2 = partially seen, 3 = fully seen] and (b) confirmation of diagnosis based on the clinical question [+1 = pathologic abnormality present, 0 = unable to tell, -1 = pathologic abnormality absent].

3.5 Data Analysis

Sample size estimation for this interobserver agreement study was based on a confidence interval approach[9]. Using 4 raters and 3 levels of rating for their assessment, with type I error (alpha) fixed at 0.05 and an expected 80/20 probability of the absence or presence of craniosynostosis, respectively, we will have 80% power to claim the interobserver kappa statistics is greater than 0.7 when the true kappa is 0.95 with a sample size of 37 patients. Interobserver agreement will be summarized by the kappa coefficient statistic and corresponding 95% confidence intervals.

3.6 Associated staff

A research coordinator (Suson Walsh) will work with the ordering staff from the plastic surgery or neurosurgery group and the radiology schedulers to arrange for scheduling the CT and MRI exams for the patient. The research coordinator will also be contacting or meeting patient before the scans to obtain consent. Biomedical Imaging Resource (BIR) will create a viewing platform that will be used to evaluate the de-identified images presented in a randomized and blinded fashion. Statistics support will be used for data analysis.

3.7 Budget and Research Category B Time

Funding will go to research coordinators, statistics, and BIR for their contributions as detailed above. Statistics has used approximately 4 hours for study planning and anticipates an additional 40 hours for performing statistical analysis, preparation of publication tables and figures, as well as abstract and manuscript support. Research category B days are requested for the neuroradiologists who will be involved with project management/organization for MRI and the time intensive process of evaluating both ZTE and CT images for the multiple criteria detailed above. Time will also be used for data interpretation, manuscript drafting, editing and submission.

3.8 Project Timeline

It is expected that patient recruitment will be readily achievable drawing from the plastic surgery and neuroradiology practices with the first half of patients recruited and tested by 6 months. Data will be available for analysis as soon as ZTE and CT evaluation has been performed. It is expected that the data accrual will be completed 1 year from the start of the project. As a continuation of this project, comparing anatomic modeling and operative planning based on the 3D datasets from these ZTE and CT studies could be a subsequent endeavor.

4. Innovation

The zero-echo time MR sequence is an exciting tool that certainly challenges our current clinical paradigms, offering a radiation free method for assessing osseous structures. These comparative analyses will likely lead to additional analyses of other osseous pathologies and open the door for further application of this MRI technique.

5. References

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