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REVIEW ARTICLE

Zero-TE MRI: principles and applications in the head and neck

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ABSTRACT

Zero echo-time (ZTE) MRI is a novel imaging technique that utilizes ultrafast readouts to capture signal from short-T2 tissues. Additional sequence advantages include rapid imaging times, silent scanning, and artifact resistance. A robust application of this technology is imaging of cortical bone without the use of ionizing radiation, thus representing a viable alternative to CT for both rapid screening and "one-stop-shop" MRI. Although ZTE is increasingly used in musculoskeletal and body imaging, neuroimaging applications have historically been limited by complex anatomy and pathology. In this article, we review the imaging physics of ZTE including pulse sequence options, practical limitations, and image reconstruction. We then discuss optimization of settings for ZTE bone neuroimaging including acquisition, processing, segmentation, synthetic CT generation, and artifacts. Finally, we examine clinical utility of ZTE in the head and neck with imaging examples including malformations, trauma, tumors, and interventional procedures.

INTRODUCTION

Zero echo-time (ZTE) MRI is a novel imaging technique that utilizes ultrafast readouts to capture signal from short-T2 tissues. Additional sequence advantages include rapid examination times, silent scanning, and artifact resistance. One robust application of this technology is imaging of cortical bone without ionizing radiation, which represents a viable alternative to CT for both rapid screening and "one-stop-shop" MRI. Although ZTE is increasingly used in musculoskeletal and body imaging, neuroimaging applications have been limited by the complex anatomy and pathology of the head and neck. In this article, we review the imaging physics of ZTE including pulse sequence options, practical limitations, and image reconstruction. We then discuss optimization of settings for bone imaging including acquisition, processing, segmentation, synthetic CT generation, and artifacts. Finally, we examine clinical utility in the head and neck with imaging examples including craniofacial malformations, trauma, chronic disorders, and interventional procedures.

ZTE IMAGING PHYSICS

ZTE is an MRI pulse sequence based on non-selective volume excitation and 3D radial center-out k-space encoding.¹ Distinct from conventional MRI pulse

sequences, ZTE uses a readout gradient amplitude that is kept constant throughout the scanning with only small directional updates in between repetitions. This approach yields unique properties in terms of silent scanning and nominal zero echo time (i.e. TE = 0). Like ultrashort TE (UTE) imaging, ZTE acquires free induction decay (FID) signal that does not rely on gradient echo or spin echo signal refocusing. The term ZTE was coined by Weiger et al,² and refers to a method invented and pioneered by Madio and Lowe in the 1990s that was originally known as RUFIS (Rotating Ultra-Fast Imaging Sequence). In this manuscript, we will summarize ZTE characteristics with respect to the pulse sequence, image reconstruction and contrast behavior, including specific considerations such as dead-time gap and flip angle limitations. For educational purposes, we will refer to a typical ZTE experiment with imaging bandwidth BW_{RX} = 62.5 kHz and 3D isotropic image matrix of $Nmtx^3 = 256^3$ points. For more in-depth discussion of ZTE physics, we refer the interested reader to excellent reviews by Weiger et al^{2,3} and Ljungberg et al.⁴ Table 1 provides an overview of the major physics considerations in ZTE.

Native pulse sequence

Among the vast array of existing MR pulse sequences, ZTE is arguably one of the simplest in terms of radiofrequency

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Table 1. Major physics considerations in ZTE

Characteristic	Description	
Pulse sequence	Constant readout gradient amplitude in combination with short block-pulse RF excitation enables nominal TE = 0 acquisition with 3D center-out radial k-space sampling. These characteristics permit rapid, silent, and artifact-resistant imaging of short-T2 tissues.	
Flip angle	Limited to maximum of ~4° in conventional MR imaging systems, in order for RF block pulses to achieve consistent excitation independent of the readout gradient.	
Image encoding	3D straight, center-out, radial spokes are scanned sequentially in a smooth spiral trajectory along the surface of spherical k-space. Enforcing Nyquist sampling at the edge of k-space requires a total of $p*N_{mtx}^2$ radial spokes, with p-fold undersampling resulting in $N_{spk} = N_{mtx}^2$ of required spokes.	
Image reconstruction	Non-Cartesian radial sampling requires 3D gridding image reconstruction. Advanced reconstruction methods include parallel imaging, total generalized variation regularization, compressed sensing, and deep learning.	
Steady-state response	Exceptionally short TR is primarily determined by the readout duration T _{read} . Compared to conventional pulse sequences, additional factors are of negligible duration. The steady-state signal response is of T1 and PD-weighted spoiled-gradient echo nature, with signal spoiling achieved via RF spoiling and the readout gradient.	
Image contrast	Magnetization-prepared ZTE has been implemented for a wide range of image contrasts including T1, T2, ASL-based MR angiography, magnetization transfer, diffusion, and quantitative parametric mapping. ZTE can be turned into a multiecho sequence via gradient refocusing, followed by equidistant gradient echoes that provide additional T2* information.	
Dead-time gap	Sampling the FID can begin only after RF hardware changes state from transmit to receive. This gap time is termed the transmit-receive switching time, dt_{TxRx} , and ranges from ~8 to 100 ms on conventional MRI systems. This center k-space gap can be addressed with minimal impact on scan time via algebraic image reconstruction, and/or single-point imaging, reacquisition of the gradient scaled original ZTE scan.	

FID, free induction decay; PD, proton density; RF, radiofrequency; TE, echo time; TR, repetition time; ZTE, zero echo-time.

(RF) and gradient waveform complexity. Conceptually, ZTE is based on the RUFIS pulse sequence, consisting of a constant readout gradient amplitude (not ramped down or up between repetitions) in combination with short block-pulse RF excitation. With the readout gradient kept constant, spatial signal encoding starts immediately at the time of RF excitation, resulting in nominal zero echo time (TE = 0) FID acquisition. This allows for capture of short-lived MRI signals from short-T2 tissues such as cortical bone. The direction (but not amplitude) of the x, y, z readout gradient is updated in between repetitions, resulting in 3D center-out radial k-space sampling. By arranging the 3D radial spokes such that their end points follow a smooth spiral trajectory along the surface of the 3D spherical k-space, gradient switching can be reduced to an inaudible level and enables silent imaging.⁵ Furthermore, this method also provides exceptionally short repetition times (TR) and resistance to MRI artifacts, such as eddy currents and motion. For the considered ZTE example with $BW_{Rx} = 62.5 \text{ kHz}$ (corresponding to a sampling time of Dt_{Rx} = $1/BW_{Rx}$ = 16 ms) and image matrix of N_{mtx} = 256³, the number of center-out readout points is $N_{read} = 256/2 = 128$, which results in an ultrafast readout of $T_{read} = N_{read}^*Dt_{Rx} = 128^*16ms =$ 2.048 ms (Figure 1),

Flip angle limitations

Unlike conventional MR pulse sequences, in ZTE the RF excitation is entangled with the image encoding readout gradient. In order for the RF block pulses to achieve consistent excitation independent of the readout gradient, the RF excitation bandwidth has to encompass the full RF imaging bandwidth (*i.e.* $BW_{Tx} \ge BW_{Rx}$). This means that the RF pulse width must be shorter than the RF sampling time (*i.e.* $Dt_{Tx} \le Dt_{Rx}$), which in turn limits the maximum achievable flip angle. Otherwise, the readout gradient would result in a sinc-shape modulation of

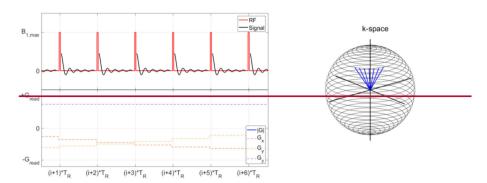
the RF excitation profile along the readout direction. Since the readout changes direction over the course of the sequence, this would result in blurring that scales with increasing distance from the center of the imaging field of view (FOV). For the considered ZTE example with $BW_{Rx}=62.5\,\mathrm{kHz}$ (and $Dt_{Rx}=1/BW_{Rx}=16\,\mathrm{ms}$), this limits the pulse width of the RF excitation block pulse to very short durations of $Dt_{Rx}{\leq}16\,\mathrm{ms}$, corresponding to a maximum flip angle of only ${\sim}4^{\circ}$ assuming a maximum RF amplitude of $B_{1,max}=16\,\mathrm{mT}$ (typical for whole-body human MRI systems). Using longer RF excitation pulses (i.e. $Dt_{Tx}{\geq}Dt_{Rx}$) would result in image blurring, especially towards the edge of the imaging FOV. Recently, Froidevaux et al developed pulse encoding for ZTE imaging that enables higher flip angle excitations by extending the RF pulse duration.

Image encoding and reconstruction

ZTE samples 3D k-space along straight, center-out, radial spokes that are scanned sequentially, such that their end points follow a smooth spiral trajectory along the surface of the spherical k-space. With equidistant spacing of samples acquired along each 3D center-out radial spoke, the resultant angular sampling is very high in the k-space center and lower toward the periphery. Enforcing Nyquist sampling at the edge of the k-space requires a total of $p^*N_{mtx}^2$ radial spokes. Practically, p-fold undersampling is considered acceptable and results in $N_{spk}=N_{mtx}^2$ of required spokes. Higher undersampling factors would result in streaking, a characteristic artifact for 3D radial scanning. Hence, for the considered ZTE example with $N_{mtx}=256$, a total of $N_{spk}=256^2\!=\!65,\!536$ spokes are required.

The non-Cartesian radial sampling requires 3D gridding image reconstruction. Advanced methods such as parallel imaging, total generalized variation (TGV) regularization, to

Figure 1. Schematic of the ZTE pulse sequence showing RF and gradient waveforms (left) and corresponding 3D radial center-out k-space sampling (right). For illustrative purposes, the RF pulse width is extended and a very small number of spokes (N_{spk} = 1024) are considered. ZTE, zero echo-time; RF, radiofrequency.



and compressed sensing16 are available for ZTE via the opensource RIESLING image reconstruction toolbox. 17 Recently, a novel deep learning (DL)-based image reconstruction method¹⁸ has been applied to ZTE for significant reduction in scan times and/or improved image quality. 19

Steady-state signal response

ZTE imaging allows rapid scanning with exceptionally short repetition times (TRs), which are primarily determined by the readout duration (T_{read}). Additional factors, such as RF pulse duration and gradient update time, are of negligible duration in comparison to T_{read}. Compared to conventional MRI pulse sequences, ZTE does not involve delays due to slice-rewinding, phase-encoding, frequency pre-winding, or gradient spoiling. For the considered ZTE example (i.e. $BW_{Rx} = 62.5 \text{ kHz}$, $N_{mtx} =$ 128), the repetition time TR ~2 ms. This results in a total scan time of N_{spk} *TR = 65536*2ms = 131 s, without acceleration techniques such as parallel imaging or compressed sensing.

The steady-state signal response of the ZTE pulse sequence is of a T1 and proton density (PD)-weighted spoiled-gradient echo (SPGR) nature, with signal spoiling achieved via RF spoiling and the readout gradient. More concretely, for zero nominal TE (i.e. TE = 0), small flip angle (i.e. $\alpha \ll 90^{\circ}$) and short TR (i.e. TR<<T1), the steady-state longitudinal magnetization (Mz,ss) can be stated as^{4,9}:

$$M_{z,SS} = \frac{PD.(1-E_1).E_2^*}{(1-E_1.\cos\alpha)} \cong \frac{PD}{1+\frac{T_1}{TR}\frac{\alpha^2}{2}}, \text{ with } E_1 = e^{-\frac{TR}{T_1}}, \text{ and } E_2^* = e^{-\frac{T^2}{T_1}}$$
[1]

with PD the proton density, T1 the longitudinal relaxation time, and T2* the effective transverse relaxation time. The corresponding signal to noise (SNR)-optimal Ernst (α_{Ernst}) can then be stated as:

$$\alpha_{Ernst} = a\cos\left(E_1\right) \cong \sqrt{\frac{2.T1}{TR}}$$
 [2]

Equation [1] demonstrates the ability of ZTE for rapid and silent 3D PD and T_1 weighted SGPR-type imaging with TE = 0. Because of the very short repetition times, the Ernst flip angle (α_{Ernst}) is also small and within the flip angle limitation discussed above. In our example, with longitudinal relaxation time of T1 = 1 s and TR = 2 ms, the Ernst flip angle becomes $\alpha_{Ernst} \sim 3.6^{\circ}$. With careful parameter adjustment, ZTE also allows variable flip angle PD and T1 mapping⁹ similar to DESPOT.

Magnetization preparation and multigradient echo Magnetization preparation in combination with segmented readout is a flexible and powerful concept for contrast enhancement of otherwise contrast-limited pulse sequences.²⁰ The best-known example is MP-RAGE, ²¹ which is based on inversionrecovery T1 preparation followed by segmented gradient echo (GRE) acquisition. The intrinsic characteristics of ZTE (rapid, silent, 3D image encoding with very short TR and TE = 0) are well suited for combination with magnetization preparation. Magnetization prepared ZTE has been implemented for a wide range of image contrasts including T1,5,9, T2,22 ASL-based MR angiography (MRA),²³ magnetization transfer (MT),²⁴ diffusion,²⁵ and quantitative parametric mapping.¹⁹

Analogous to multiecho GRE or UTE, ZTE can be turned into a multiecho sequence via gradient refocusing to acquire the original FID, followed by equidistant gradient echoes that provide additional T2* information. Multiecho ZTE has been used to generate positive bone contrast by subtracting a later in-phase $M_{z,SS} = \frac{PD.(1-E_1).E_2^*}{(1-E_1.\cos\alpha)} \cong \frac{PD}{1+\frac{T1}{TD}}\frac{\alpha^2}{\alpha^2}$, with $E_1 = e^{-\frac{TR}{T1}}$, and $E_2^* = e^{-\frac{T_2^*}{TE}}$ biplolar gradients results in loud acoustic noise. Quiet ZTE-based multigradient echo imaging can be achieved using the Looping Star sequence²⁷ where multiple FID signals are first excited and then sequentially gradient refocused in a looping, timemultiplexed manner.

Dead-time gap

Even though ZTE starts image encoding immediately at the time of RF excitation, the MR system can start sampling the FID signal only after RF hardware changes state from transmit to receive. This gap time is termed the transmit-receive switching

Table 2. ZTE characteristics pertinent to bone neuroimaging

Characteristic	Explanation	
High bandwidth imaging	Rapid scanning and efficient capture of short-lived bone signal with minimal T2 decay. Limited flip angle yields proton density-weighted images with uniform bone appearance and low-contrast soft tissue.	
Bone enhancement	Bias correction, intensity normalization, and inverse linear scaling produce standardized signal response across the imaging field-of-view.	
Bone segmentation	In a typical histogram distribution of ZTE signal, there are clear peaks for air and soft tissue, with an intervening broader bone peak. Air, tissue, and bone segmentations can be obtained via intensity thresholding and morphologic operations to account for partial volume effects.	
Synthetic CT	Point-based operations (intensity thresholding and linear scaling) have been used to generate synthetic CT images for adult subjects with relatively normal bone anatomy. This can be used for basic applications such as MR-only radiation treatment planning and PET/MR attenuation correction. For more complex head and neck pathologies (poorly mineralized, thin, or irregular bone and variable soft tissues), DL-powered synthetic CT approaches show promise but are not fully optimized for anatomic delineation.	
Chemical shift artifacts	Due to 3D radial sampling, ZTE image quality can be severely affected by fat-water off-resonance. Chemical shift artifacts manifest with image blurring and signal interference at fat-water interfaces, which degrades the clarity of cortical bone depiction. These artifacts can be minimized by changing imaging parameters (increasing bandwidth, coarser spatial resolution, decreasing B ₀ field strength), and/or performing chemical shift decomposition-based in-phase reconstruction.	
Alternative techniques	Other options for bone imaging include UTE and GRE, which involve longer imaging times with darker and more pronounced bone signal due to additional susceptibility effects. However, this decreases the ability to distinguish cortical bone from medullary bone and other short-T2 tissues.	

GRE, gradient echo time; PET, positron emission tomography; UTE, ultrashort echo time; ZTE, zero echo-time.

time, dt_{TxRx} . Depending on the RF coil and system characteristics, dt_{TxRx} ranges from ~8 to 100 ms. Because of this finite transmit-receive switching delay, the first few data samples of the center-out 3D radial spokes are missed resulting in a spherical gap of samples at the center of k-space. Continuing with our example (*i.e.* BW_{RX} = 62.5 kHz, Dt_{Rx} = 16 ms) and assuming a transmit-receive switching time of dt_{TxRx} = 32 ms results in a spherical gap of five samples' diameter. This center k-space gap can be addressed with minimal impact on scan time via algebraic image reconstruction²⁸ or collection of the missed k-space samples using either single-point imaging,²⁹ reacquisition of the gradient scaled original ZTE scan,³⁰ or a combination thereof.³¹

ZTE for bone neuroimaging

MRI is well established for superior soft tissue contrast and multiple sequence weightings, but has not historically been utilized for structural bone assessment. This is because cortical bone is an extremely dry tissue with low proton density (~20% water) and short signal lifetimes (T2 ~390 ms at 3 T).³² Conventional MRI gradient echo or spin echo sequences with TEs in the millisecond range are generally too slow for meaningful bone signal detection. The following section explains ZTE bone imaging via PD-weighted ZTE and contrast-inversion as originally described by Wiesinger et al.^{33,34} Table 2 summarizes ZTE characteristics pertinent to bone neuroimaging.

High bandwidth PD-weighting

ZTE bone imaging exploits the natural strength of ZTE for high bandwidth, PD-weighted MRI.³³ More specifically, the zero echo time (TE = 0) characteristic in combination with high bandwidth imaging (*i.e.* fast sampling) assures rapid scanning and efficient capture of short-lived MRI bone signals with minimal T2 signal decay. High imaging bandwidth in turn limits the flip angle, leading to the desired PD-weighted contrast with minimal T1 saturation, ¹ producing a uniform bone appearance with

low-contrast soft tissue. In essence, high bandwidth PD-weighted ZTE enables excellent bone imaging by: (1) efficiently capturing weak short-lived MRI bone signals and (2) contrasting them against surrounding soft tissue and air. DL-based image reconstruction can further reduce noise and improve ringing artifacts. We show an example case (1.5 T, BW = $125\,\text{kHz}$, FA = 1° , FOV = $300\times300\times200\,\text{mm}^3$, res = $1\times1\times1\,\text{mm}^3$, 2 min 1 s scan time) using standard gridding (first row) and DL-based image reconstruction 18,19 with 75% denoising and 75% de-ringing (second row). A point-based synthetic CT reconstruction is demonstrated with logarithmic inversion of the grayscale (third row) to suppress soft tissue and enhance bone (Figure 2).

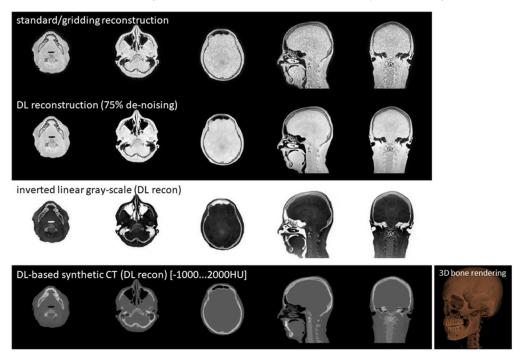
Image processing for bone enhancement

To enhance bone depiction, PD-weighted ZTE images undergo several image processing steps including bias correction, intensity normalization, and inverse linear scaling. ^{33,34} Bias correction eliminates smooth spatial signal intensity variations originating from the RF excitation and signal reception. This includes measured coil sensitivity maps obtained from dedicated fast calibration scans (similar to those used in parallel imaging) and/or post-processing methods such as polynomial fitting ^{33,34} or N4ITK bias correction. ³⁵ Together with z-score signal intensity normalization, this assures standardized ZTE signal response across the imaging FOV without RF shading effects.

Bone segmentation and synthetic CT

The ZTE image quality obtained following bias correction and normalization is sufficient to enable bone segmentation. In a typical histogram distribution of ZTE signal, there are clear peaks for air and soft tissue, with an intervening broader bone peak. Air, tissue, and bone segmentations can be obtained via intensity thresholding (*i.e.* air < threshold_{air-bone}
bone<threshold_{bone-tissue}< tissue) and morphologic operations to account for partial volume effects. 33,34,36,37 Bone signal intensities in ZTE and

Figure 2. PD-weighted ZTE (FOV = 30 cm, res = 1mm, FA = 1deg, BW = ± 62.5 kHz, 2 min 11 s) acquired at 1.5 T using a head & neck coil array with standard/gridding reconstruction (top), DL-reconstruction (middle), inverted grayscale (bottom) and DL-derived synthetic CT and derived 3D bone rendering. BW, bandwidth; FOV, field of view; PD, proton density; ZTE, zero echo-time.



CT demonstrate a strong linear correction, such that robust segmentation and linear scaling (point-based operations) can generate synthetic CT images³⁴ for basic applications including MRI-only radiation treatment planning and PET/MRI attenuation correction 36,38-40 (Figure 3). With the advent of DL-based image segmentation and translation, more realistic synthetic CT images and 3D bone renderings can be created using convolutional neuronal networks (CNNs)⁴¹⁻⁴⁹ and generative adversarial networks (GAN). 50-53 For an excellent review on the subject of DL-based synthetic CT generation, we refer the interested reader to a recent ZTE review article. 44 So far, MRI-derived synthetic CTs have been used clinically in adult subjects with relatively normal bone anatomy. For more complex pathologies (poorly mineralized, thin, or irregular bone; variable soft tissues with similarly short-T2 properties), DL-powered synthetic CT approaches show promise but are not fully optimized for anatomic delineation given the current paucity of clinical training data.⁵⁴ Therefore, radiologists will benefit from routinely reviewing source ZTE images, which tend to be of higher quality and clinical diagnostic value in the head and neck (Figure 4).

Fat-water chemical shift artifacts

Due to 3D radial sampling, ZTE tissue uniformity and overall image quality can be severely affected by fat-water off-resonance. We illustrate examples of chemical shift artifacts in the pelvis at 3T in linear (top) and inverted (middle) grayscale. At the highest imaging bandwidth (BW = $250\,\mathrm{kHz}$, left), soft tissue appears uniform and contrasts well against bone and air. However, at the lowest imaging bandwidth (BW = $62.5\,\mathrm{kHz}$, right), there is severe chemical shift off-resonance artifact with signal interference at

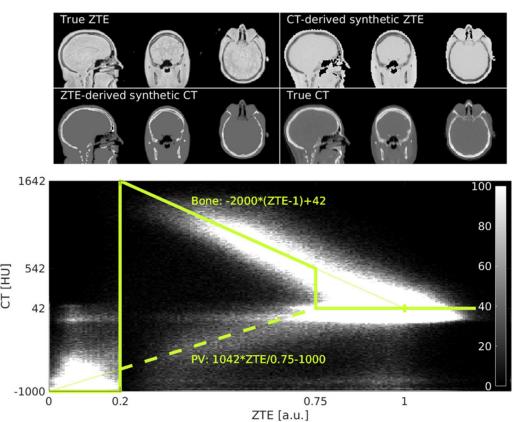
fat-water interfaces, severely degrading cortical bone depiction and overall image quality (Figure 5).

At 3T, the 3.5 ppm fat-water chemical shift translates into an off-resonance of Df ~440 Hz with an out-phase echo time of $TE_{OP}\sim 1.15$ ms (at 1.5T, Df ~ 220 Hz and $TE_{OP}\sim 2.3$ ms). This causes signal dephasing along the 3D radial center-out spoke readout. More concretely, fat and water resonances are aligned (i.e. in-phase) at the start of the 3D radial spoke in the center of k-space immediately following RF excitation. During the readout, the fat and water signals disperse and accumulate a phase difference of $\Delta \varphi = \Delta f * T_{Read} = \Delta f * N_{Read} * \Delta t_{RX}$ until the end of the readout. Off-resonance effects increase with increasing B₀ field strength, decreasing bandwidth, and finer spatial resolution; and become apparent when the readout duration ($T_{read} = N_{read}*Dt_{Rx}$) extends beyond the out-phase echo time $(TE_{OP} = 1/(2*Df)=1.15 \text{ ms at } 3T \text{ and } 2.3 \text{ ms at } 1.5T)$. The associated chemical shift artifacts manifest with image blurring (of the off-resonant species) and signal interference at fat-water tissue interfaces, which severely affects the clarity of cortical bone depiction. Fat-water chemical shift artifacts can be minimized by changing imaging parameters (bandwidth, spatial resolution and B₀ field strength), and/or performing chemical shift decomposition-based in-phase reconstruction. 55 While fat/ water suppression can be effective in eliminating off-resonance artifacts, it is less useful for ZTE bone imaging, due to the need for uniform soft-tissue signal.

Alternative bone imaging techniques

PD-weighted ZTE achieves excellent cortical bone depiction via: (1) efficient capture of short-lived bone signal and (2) uniform

Figure 3. Analytical ZTE to CT (and CT to ZTE) image translation (top). The 2D histogram distribution (bottom) illustrates a strong linear correlation between ZTE signal intensity and ZTE Hounsfield units. Reproduced with permission from reference.³⁴ ZTE, zero echo-time.



soft-tissue response. This method explores the unique strength of ZTE in terms of rapid, robust, 3D PD-weighted imaging.³³ ZTE can be combined with the traditional bone enhancement methods used in UTE imaging, including echo-subtraction²⁶ and magnetization prepared imaging.⁵⁶ These methods achieve selective bone depiction with true soft-tissue suppression, but involve significantly longer scan times and careful tuning of scan parameters and system performance (i.e. eddy current calibration). PD-weighted bone imaging can also be achieved with conventional gradient-echo (GRE) sequences, colloquially known as black bone MRI.⁵⁷ In this method, cortical bone appears dark (i.e. TE >> T2bone) and more pronounced due to additional susceptibility effects at longer echo times.⁵⁸ However, there is a decreased ability to distinguish cortical bone from medullary bone and other short-T2 tissues. As an example, we compare bone depiction with PDw ZTE (top) vs PDw GRE (bottom), where the latter uses Dixon-type fat-water separation⁵⁹ to provide additional soft-tissue differentiation (Figure 6).

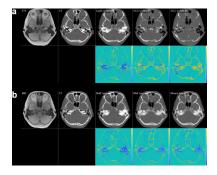
Clinical applications

Given its rapid, 3D, silent and artifact-resistant characteristics, ZTE is a viable alternative to CT for imaging cortical bone without ionizing radiation. In prior case series covering a variety of clinical applications, ZTE and CT show good diagnostic correlation among trained radiologists. 36,54,57,60-73 Current practical limitations of ZTE include inherently low SNR from weak bone signal, and limited spatial resolution of current MRI platforms

(0.8–1 mm, compared to 0.5–0.6 mm with CT). It is likely that continued advances in MRI hardware and software will address these technical barriers, especially given that ZTE shows correlation with μ CT for bone microstructure in *ex vivo* specimens. With regard to image post-processing, synthetic CT algorithms are not fully ready for clinical prime-time, therefore experience in interpreting source ZTE images is important. Especially in the head and neck, complex anatomy and pathology can result in false-positives (other short-T2 tissues such as fibrous tissue, cartilage, inspissated secretions), as well as false-negatives (thin, unmineralized, irregular bone).

Based on the rapidity of ZTE, there is potential clinical utility for initial screening in the setting of acute trauma (evaluate for fractures and intracranial injury), abnormal head shape or size (evaluate for craniosynostosis and increased intracranial pressure), or bone abnormality (rule-out pathology). For more comprehensive examinations, ZTE can also be utilized to acquire bone information as part of a "one-stop-shop" MRI. This approach is particularly attractive in scenarios that would normally require both MRI and CT—e.g. craniofacial malformations, trauma, tumors, and interventional procedures. The advantages of a single MRI examination with ZTE—permitting combined soft tissue and bone characterization—could supersede the current workflow of sequential CT and MRI. The opportunity for longitudinal follow-up MRIs with ZTE are especially valuable to patients that require minimization or elimination of radiation exposure:

Figure 4. Synthetic CT generation using deep learning with encoder-decoder CNN architectures. (a) Example ZTE and CT images with synthetic CT generated using light U-Net (2,161,361 parameters), VGG-16 U-Net (28,845,505 parameters), and VGG-16 U-Net with TL from the ImageNet database. Bottom row shows color-coded subtraction maps of pixellevel differences between CT and synthetic CT. (b) Example ZTE and CT images with light U-Net using loss functions of MAE, MSE, and a weighted mixture of MAE and MSE. Models trained on MAE loss produce sharper-appearing synthetic CT images with fewer overall white pixels, resulting in better precision or positive predictive value for bone. Models trained on MSE loss produce smoother-appearing images with more overall white pixels, enabling better bone sensitivity or recall. The mixture loss provides a weighted average of the two contributions, balancing bone precision and recall. Courtesy of Sven Bambach, PhD. CNN, convolutional neural network; MAE, mean absolute error; MSE, mean squared error; TL, transfer learning; ZTE, zero echo-time.



children, pregnant females, patients with cancer predisposition and related genetic syndromes, and chronic bone conditions requiring extended imaging surveillance.^{37,60} Table 3 provides an overview of ZTE potential applications in the head and neck, organized by examination type, anatomic region, and disease process.

Craniofacial malformations

ZTE is useful for assessing craniofacial bony anatomy in the setting of abnormal head size, head shape, or dysmorphic facies suggestive of a genetic syndrome. The newborn skull consists of multiple flat bones separated by open sutures and fontanelles. Sutures are bridges of tough fibrous connective tissue that separate pairs of flat bones, while fontanelles are soft membrane-covered gaps located at the junctions of multiple cranial bones. These structures allow for plasticity of the cranial vault and enable passage through the birth canal. In the majority of infants, transient birth-related skull deformities will naturally correct over time. However, if a consistent external force is applied—usually from a stereotyped sleeping position—deformational or positional plagiocephaly results with asymmetric flattening of the skull. If the sutures remain open, there will be a compensatory asymmetric shift of the skull assuming a parallelogram morphology. 76-78 ZTE is a rapid, safe, and effective method to screen such infants, confirming the diagnosis of plagiocephaly with open sutures and normal intracranial pressures.⁶⁰

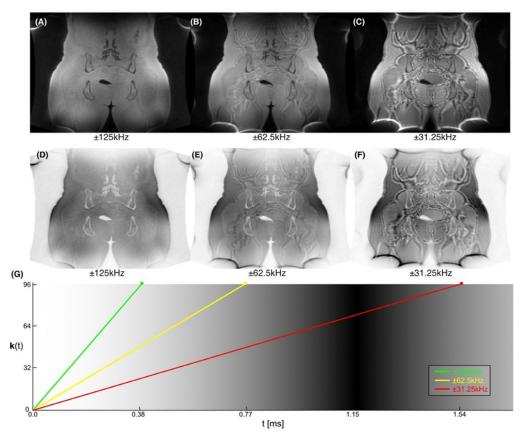
Brain growth during childhood expands the cranial vault, keeps sutures open, and triggers additional osteogenesis. Monitoring head

shape and circumference relative to age can aid in early diagnosis of pathology. Typical ages for fontanelle closure are: posterior 2-3 months, sphenoid 6 months, mastoid 6-18 months, anterior 9-18 months. Other than the metopic suture, which closes around 3-9 months of age, the remaining sutures (sagittal, coronal, lambdoid) normally stay open until brain growth ceases in the second decade. Premature closure of a suture is known as synostosis and can result from genetic or acquired (trauma, surgery, infection, malnutrition, brain injury) causes. The membranous bones actively remodel via central resorption and deposition of new bone along the periphery (suture edges). Therefore, the earliest manifestation of pathology will be narrowing of the involved suture (craniostenosis), followed by eventual closure (craniosynostosis).^{79–82} On MRI, the fibrocartilaginous tissue within fontanelles and sutures has transverse relaxation time that is short, but slightly longer than ossified bone. Therefore on ZTE, the process of cranial ossification manifests with evolving PD signal, such that the relatively brighter fibrous gap gradually decreases in size and is ultimately replaced by a frank bony bridge. 37,79

Isolated or single-suture synostosis accounts for the majority (at least 80%) of craniosynostosis cases. There is characteristic restriction of skull expansion perpendicular to the suture, with compensatory bone growth parallel and distal to the involved suture. This results in characteristic abnormal head shapes based on the affected sutures. Metopic synostosis presents with a "beak and notch" appearance (ectocranial ridging and endocranial notching), trigonocephaly (Greek for "triangle head"), and "quizzical eye" with elevation of the medial orbital rims. Sagittal synostosis is associated with dolichocephaly ("long head") or scaphocephaly ("boat head") when an overlying bony ridge is present. Coronal synostosis presents with anterior plagiocephaly, brachycephaly ("short head"), and a "harlequin eye" appearance with elevation of the superolateral orbit. Lambdoid synostosis presents with downward tilting of the back of head and a mastoid bulge behind the ear. ^{80,81}

Multisuture synostosis is far rarer, and usually genetic in etiology.⁸¹ Turricephaly ("tower head") is seen with bilateral coronal and lambdoid synostosis; acrocephaly or oxycephaly ("point/sharp head") with coronal and sagittal synostosis; and Kleeblattschädel (German for "cloverleaf skull") with diffuse pancraniosynostosis. Additional craniofacial dysmorphisms can be characterized including frontal bossing, orbital changes, midface anomalies, skull base malformations, segmentation failures, facial clefts, micrognathia, and dental abnormalities. These abnormalities can be quantified using various metrics such as craniofacial and jaw ratios, orbital distances, and skull base measurements. Other craniofacial stigmata can also be assessed by ZTE, e.g. Luckenschädel ("lacunar") skull in Chiari II malformation; "bare orbit" and "asterion" signs in neurofibromatosis Type 1; "beaten brass" skull with increased intracranial pressure; dermal sinus tracts and inclusion cysts; and encephaloceles in various locations.⁸² Finally, the brain develops concurrently with the face and is located in the same embryologic field, subject to similar molecular patterning and environmental influences—*i.e.* "the face predicts the brain."66 Therefore, the use of MRI with ZTE is an excellent approach for comprehensively evaluating craniofacial and skeletal abnormalities—particularly if radiation needs to be avoided due to patient age (fetus, neonate, child) and/or status (pregnancy, cancer, radiation sensitivity). 37,61–66,79,83,84 (Figure 7)

Figure 5. ZTE fat-water chemical shift artifacts. Reproduced with permission from reference.⁵⁵ ZTE, zero echo-time.



Trauma and stroke

Currently, CT is the accepted first-line modality for imaging of suspected stroke, trauma, and other acute neurologic conditions. This is a broadly utilized technique thanks to its rapid and accessible nature, with scanners available and easily operated

at a variety of centers. Additionally, high-spatial resolution and attenuation-based technique are useful for evaluating hyperdense bone and hemorrhage. Nevertheless, MRI is becoming increasingly available and utilizes non-ionizing magnetic fields with multiple sequences providing high-contrast resolution.

Figure 6. Comparison of proton density-weighted ZTE (top) vs LAVA-Flex (bottom) bone depiction in the pelvis at 3T. ZTE, zero echo-time.

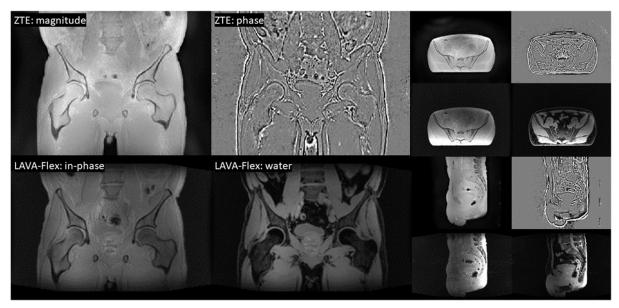
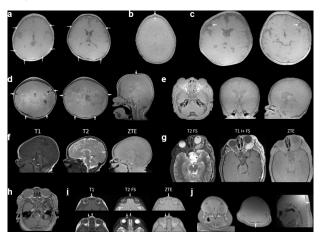


Table 3. ZTE clinical applications in the head and neck organized by examination type, anatomic region, and disease process

Examination type	Applications
Initial screening	Acute trauma Abnormal head shape or size Suspected bone abnormality
One-stop-shop MRI	Craniofacial malformations Stroke Trauma Tumors Infection and inflammation Follow-up examinations in patients with radiation sensitivity
Follow-up MRI	Children Pregnant females Genetic syndromes including cancer predisposition Chronic bone conditions
PET/MRI	Attenuation correction for PET Fully integrated imaging
Radiation therapy	Attenuation correction for dosimetry Multiparametric tissue mapping
Interventional radiology	Interventional planning Bone correction for ablation Intraoperative navigation and monitoring
Surgery	3D visualization and printing Surgical education and planning Intraoperative navigation Postoperative follow-up
Anatomic region	Utility
Cranial vault	Head shape Sutures and fontanelles Calvarial remodeling Encephaloceles
Skull base	Neurovascular canals and foramina Tumor, infection, inflammation
Face	Facial bones and orbit Dermal sinus tracts Sinonasal inflammation Tumors
Jaw	Jaw morphology and dentition Dental hardware Jaw tumors Osteomyelitis, osteonecrosis Temporomandibular joint
Disease process	Diagnostic value
Malformations	Plagiocephaly, single-suture, and multisuture craniosynostosis Congenital and acquired abnormalities of cranial vault, facial bones, skull base, and jaw
Trauma	Acute, healing, and chronic fractures Brain and soft tissue injury
Stroke	Intracranial calcification and hemorrhage Acute, subacute, and chronic infarcts
Tumor, infection, inflammation	Soft tissue components Marrow infiltration Cortical remodeling and breakthrough Periosteal reaction Pathologic fractures
Bone disorders	Mineralization status Joint inflammation, erosion, degeneration Bone morphology Pathologic fractures

PET, positron emission tomography: ZTE, zero echo-time.

Figure 7. Craniofacial malformations. (a) Left and right positional plagiocephaly. There is posterior flattening of the cranial vault with a parallelogram morphology. The coronal, squamosal, and lambdoid sutures are patent (arrows), demonstrating brighter signal than the ossified bone on proton density-weighted ZTE. In addition to bone, ZTE demonstrates brain parenchyma, ventricles, and subarachnoid spaces, and is a viable alternative to CT for rapid screening. (b) Metopic synostosis with triangular appearance of the anterior skull, ectocranial ridging (thick arrow) and endocranial notching (thin arrow) reflecting premature sutural fusion. (c) Right and left coronal synostosis (arrows) with anterior plagiocephaly and brachycephaly. (d) Apert syndrome with multisuture synostosis, turribrachycephaly, frontal bossing, midface hypoplasia, and skull base hypoplasia. The bilateral coronal, lambdoid, and sagittal sutures are prematurely fused (arrows). Mild ventriculomegaly is present with effaced peripheral subarachnoid spaces and gyral remodeling of the inner table ("beaten brass" appearance), suggesting increased intracranial pressure. (e) Achondroplasia with frontal bossing, macrocephaly, midface hypoplasia, J-shaped sella, narrow skull base, superiorly rotated petrous apices, medialized carotid canals, and foramen magnum stenosis. (f) Ecchordosis physaliphora (notochordal remnant) with T1-hypointense, T2-hyperintense and well-corticated osseous defect in the dorsal clivus (arrows). (g) Neurofibromatosis Type 1 with transspatial plexiform neurofibroma involving the left orbit, periorbital soft tissues, and temporal scalp. There is associated left buphthalmos and proptosis. ZTE shows expansion of the bony orbit and sphenoid wing dysplasia ("bare orbit" appearance). (h) Congenital midnasal stenosis with inward bowing of the nasal bones in the mid-nasal cavity (arrows), halfway between the pyriform apertures and choanae. (i) Congenital dermoid inclusion cysts overlying the frontonasal suture and right orbit (arrows). ZTE shows smooth subjacent osseous remodeling, without communicating intracranial tract. (j) Post-mortem imaging of infant with Meckel-Gruber syndrome showing microcephaly, overlapping sutures with occipital cephalocele (thick arrow), midface hypoplasia, and cleft palate (thin arrows). ZTE, zero echo-time.



Rapid MRI protocols are being introduced in the acute neurologic setting, and can be even more sensitive than CT for specific applications, such as hyperacute stroke (with diffusionweighted imaging), microhemorrhage and microcalcification

Figure 8. Trauma. (a) Comminuted and depressed right parieto-occipital skull fractures (arrows) with overlying subgaleal hematoma, underlying extra-axial hemorrhage, and brain hemorrhagic contusions. (b) Abusive head trauma with right greater than left subdural hematohygromas and bridging venous injury. ZTE shows diastatic sutures and bulging anterior fontanelle (arrow). (c) Right and left parietal growing fractures (leptomeningeal cysts), caused by dural injury with continued cerebrospinal fluid pulsations causing diastasis of the original skull fracture (arrows). (d) Organizing right parietal cephalohematoma with complex internal signal. On ZTE, there is early peripheral ossification (arrows) abutting the outer table. ZTE, zero echo-time.

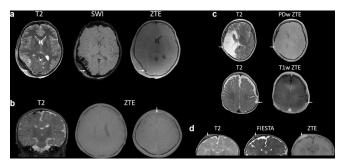
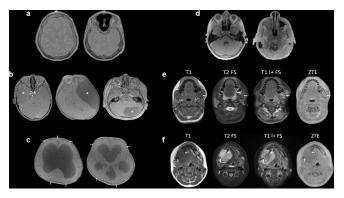


Figure 9. Chronic disorders. (a) Diffuse calvarial hyperostosis and pneumosinus dilatans in patient with chronic epilepsy on anticonvulsant therapy. (b) Arachnoid cysts (asterisks) of the right middle cranial fossa, left middle cranial fossa, and posterior fossa with associated parenchymal mass effect and smooth calvarial remodeling on ZTE. (c) Communicating hydrocephalus with severe tetraventricular enlargement, crowded subarachnoid spaces, and diastatic cranial sutures (arrows) on ZTE. (d) Chronic sinusitis with mucosal thickening, retention cysts, and maxillary sinus hyperostosis. (e) Giant cell lesion of the left mandibular angle (arrows). ZTE shows a multilobular expansile appearance with multiple curvilinear septations, cortical and alveolar erosions. (f) Desmoplastic fibroma arising from the right mandibular angle with heterogeneous exophytic soft tissue (arrows). ZTE demonstrates marrow expansion with alveolar erosions, lateral endosteal scalloping, medial cortical breakthrough, and aggressive periosteal reaction (sunburst and Codman triangle patterns). ZTE, zero echo-time.



(using susceptibility-weighted imaging), and brain/soft tissue evaluation. $^{85-90}$

In the setting of acute trauma, CT of the head and cervical spine are routinely ordered for rapid triage of fractures and hemorrhage. When CT findings, injury mechanism, and/or neurologic examination are concerning for brain or soft tissue injury, patients proceed to MRI. In hospitals with 24/7 MRI coverage, screening protocols are available for high-probability cases. As MRI becomes increasingly available in emergency departments, it is conceivable that a rapid MRI with ZTE could become an alternative first-line approach to imaging major trauma. Assuming no contraindications to MRI, the rapid readouts of ZTE also minimize susceptibility artifacts related to air and nonferromagnetic foreign bodies. For patients with complex findings, such as traumatic brain injury or ligamentous injury, the rapid MRI could then be directly upgraded to a comprehensive "one-stop-shop" MRI at the radiologist's discretion.

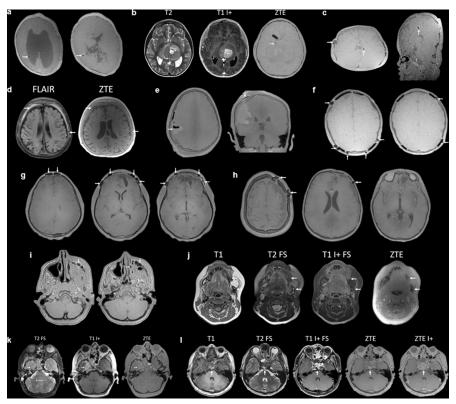
In case series of acute trauma, ZTE successfully characterizes fractures of the cranial vault, facial bones, jaw, and spine. ^{68–73,79,90–92} As previously noted, standard MRI platforms provide slightly lower spatial resolution than CT, meaning that a non-displaced fracture or microfracture <1 mm could theoretically be missed using ZTE alone. However, most such fractures do not require intervention unless there is related brain or soft tissue injury, for which MRI is far more sensitive. With ongoing improvements in MRI hardware and software, ZTE will likely become able to delineate bone microstructure, based on *ex vivo* and animal studies with biomechanical and histopathological correlation. ^{74,75,93–97} In the subacute to chronic stage, MRI with ZTE is useful for evaluating healing *vs* non-healing fractures, organizing hematomas, and ossification ^{98,99} (Figure 8).

Tumors, infection, and inflammation

Bone is a dynamic organ that undergoes constant remodeling by osteoblasts, osteocytes, and osteoclasts. ¹⁰⁰ Various pathologic conditions such as neoplasia, infection, and inflammation can yield characteristic patterns of bone remodeling visible on ZTE. ^{37,79,101} These patterns are related to the rate of progression, rather than histology. Aggressive bone lesions (*e.g.* osteomyelitis, fast-growing tumors) rapidly increase in size with imaging features including permeative bone destruction, soft tissue components, cortical breakthrough, florid periosteal reaction, and pathologic fractures. Non-aggressive lesions (*e.g.* slow-growing tumors) are indolent and produce well-defined geographic abnormalities with chronic bone remodeling and minimal smooth periostitis. ¹⁰²

ZTE provides excellent bony detail of the cranial vault and jaw. Cranial vault imaging is useful for evaluating calvarial remodeling secondary to various conditions including tumors, hydrocephalus, idiopathic intracranial hypertension, or chronic shunting. Te is routinely utilized in dentistry for evaluating tooth structure, jaw landmarks, and osseous remodeling. Given the superior soft tissue contrast and non-ionizing technique of MRI, this approach has clear advantages over CT in evaluating osteomyelitis, osteonecrosis, arthropathies. and suspected jaw tumors with associated marrow, pulp, and mucosal findings. Te, 103,104 Due to the ultrafast readout of ZTE, dental amalgam and hardware demonstrate

Figure 10. Interventional procedures. (a) Shunted Chiari II with right plagiocephaly. ZTE shows the shunt catheter (arrows) with minimal susceptibility artifact. The ventricular system is mildly dilated with colpocephaly. The gyri are interdigitating due to hypoplasia of the interhemispheric falx. There is a Luckenschädel (lacunar) appearance of the skull. (b) Bithalamic high-grade glioma with enhancing and necrotic components, causing biventricular hydrocephalus and crowding of subarachnoid spaces. Postoperative ZTE shows nondependent pneumocephalus in the right frontal horn and shunt catheter in the third ventricle (arrow). (c) Post-surgical Shprintzen-Goldberg syndrome with pancraniosynostosis, turribrachycephaly, midface hypoplasia, and platybasia. ZTE shows surgical hardware, shunt reservoir (thick arrow), and catheter (thin arrows) with minimal susceptibility artifact. There is effacement of peripheral subarachnoid spaces and a "beaten brass" skull compatible with increased intracranial pressure. (d) Remote abusive head trauma with global parenchymal volume loss and chronic bilateral subdural hematomas with indwelling subdural shunts (arrows). Overshunting produces an "armored brain" appearance with diffuse calvarial hyperostosis. (e) Postcraniotomy for right parietal glioma resection (arrows). ZTE effectively distinguishes postoperative bone, metallic hardware, air, serous fluid, and hemorrhage, with minimal susceptibility artifacts. (f) Follow-up cranioplasty. ZTE shows polyetheretherketone implants and metal screws (arrows) with minimal susceptibility artifact. (g) Anterior cranial fossa reconstruction. Fixation plates and screws (arrows) show minimal susceptibility on ZTE. There is cystic encephalomalacia in both inferior frontal lobes. (h) Follow-up comminuted and depressed bifrontal calvarial fractures. Left frontal fixation plate and screws (arrows) show minimal susceptibility on ZTE. There is a left subdural hematoma and cystic encephalomalacia in the left greater than right inferior frontal lobes. (a) Repaired left zygomaticomaxillary fracture. Fixation plate and screws (arrows) show minimal susceptibility on ZTE. (i) Left segmental mandibulectomy follow-up. Residual mandibular bone (arrows) is well corticated, without concerning irregularity. The resection bed is filled with fat packing and there is no enhancing soft tissue to suggest recurrence. (j) Radiation therapy planning study for right skull base rhabdomyosarcoma (arrows) with infiltration of sphenoid bone and petrous apex, direct extension into middle cranial fossa, and perineural spread into pterygopalatine fossa, foramen rotundum, vidian canal, and foramen lacerum. ZTE demonstrates neoplastic bone erosions and osseous landmarks for radiation dosimetry. (k) Post-operative skull base chordoma. The resection bed is filled with fat packing material (arrows) and there is no enhancing soft tissue to suggest recurrence. ZTE demonstrates the transoral osseous resection defect. Pre- and post-contrast sequences depict cortical bone equally well, with enhancing marrow and vascular structures visible on the contrast study. ZTE, zero echo-time.



minimal susceptibility artifacts compared to conventional MRI sequences. $^{105-107}$

ZTE of face and neck structures (orbits, sinonasal cavity, skull base, airway) is far more challenging than in the cranium and jaw. Factors that can degrade image quality include multiple bone-air interfaces, variable mucosal secretions, and complex soft tissue/fascial anatomy.

These practical issues can be addressed by a combination of radiologist experience, improved sequence and post-processing tools. In patients requiring surveillance imaging examinations, "one-stop-shop" MRI with ZTE is a promising option tool for diagnosis, treatment planning, and longitudinal follow-up, offering higher contrast resolution and marginally lower spatial resolution than CT. This approach allows for integrated evaluation of cortical bone, bone marrow, and

soft tissues—ideal for complex pathologies that can demonstrate infiltrative involvement and perineural spread ^{37,54,79,108,109} (Figure 9).

Interventional procedures

Many medical interventions require perioperative image guidance prior to, during, and/or after the treatment session. Stereotactic approaches require precise 3D localization based on rigid nondeformable bony landmarks to perform various interventions such as biopsy, injection, stimulation, implantation, radiosurgery, ablation, or resection. In most clinical scenarios, CT and MRI examinations are acquired separately, then mathematically superimposed using various software packages. This approach leverages the bone detail and high spatial resolution of CT, along with the soft tissue contrast of MRI. However, patient motion during or between examinations can disrupt the image registration process and lead to incorrect spatial targeting. "One-stop-shop" MRI with ZTE—in which soft tissue and bone information are acquired in a single imaging session—offers several practical advantages for image-guided therapy. ZTE algorithms with computational corrections based on synthetic CT have been trialed for PET/MRI with attenuation correction, radiation therapy planning with dosimetry correction, and interventional ablation with skull correction. 34-53,110-113

Perioperative surgical applications of ZTE are manifold. Many surgeons request 3D reconstruction, visualization, and/or printing to aid preoperative planning and intraoperative navigation. ZTE offers high-resolution, isotropic data sets with crisp bone detail and soft tissue contrast background suppression. However, typical 3D printing workflows are based on CT with intensity thresholding. This conventional pipeline is not well suited to identifying dark bone signal of ZTE, coexisting with multiple other short-T2 tissues against a brighter-intensity background. Therefore, ZTE bone segmentation in the head and neck can be fairly labor-intensive and requires knowledge of the underlying anatomy and pathology. In clinical patients, bone MRI with parameter optimization has been utilized to generate both physical 3D prints and virtual/augmented/mixed reality models .37,54-57,64-66,68,108,109 Preliminary cadaver and surgical studies suggest that ZTE can be successfully used to plan operations on the cranium, jaw, face, skull base, and spine, with accuracy and outcomes comparable to CT. 114-119 Continued improvements in synthetic CT reconstruction approaches, as well as MRI hardware and software, should aid in greater adoption.

Within the surgical suite, intraoperative MRI units allow real-time image guidance and confirmation of procedural success without ionizing radiation exposure or follow-up imaging. During post-operative follow-up, hardware susceptibility is greatly reduced due to the ultrafast readout. ZTE incurs less artifacts when evaluating MRI-compatible needles, catheters, dental amalgam, ablation zones, and

surgical hardware. The paramagnetic relaxivity effects of gadolinium are also minimized, such that ZTE can be performed both preand post-contrast with negligible effects on bone detail. Treatment changes can be assessed similar to or better than CT, with distinction of air, edema, hemorrhage, and calcification. $^{120-123}$

Existing barriers to widespread implementation of ZTE include patient awareness and access; radiologist understanding; clinician perception of added value; inherent MRI hardware/software limitations; and synthetic CT post-processing algorithms. ^{37,54,79,108} As ZTE technology continues to improve, large-scale comparative effectiveness studies will help quantify the relative diagnostic value, therapeutic outcomes, and cost-effectiveness relative to CT (Figure 10).

CONCLUSION

ZTE MRI is a robust alternative to CT for imaging of cortical bone without the use of ionizing radiation. This technology offers the advantages of rapid examination times, silent scanning, and artifact resistance. Applications of ZTE in the head and neck have historically been limited by complex anatomy and pathology. In this article, we discuss the imaging physics of ZTE with optimal settings for bone imaging including acquisition, processing, segmentation, synthetic CT generation, and artifacts. We also review clinical utility in the head and neck with imaging examples including malformations, trauma, tumors, and interventional procedures. Widespread clinical adoption will be accelerated by technical and post-processing improvements, cost-effectiveness analysis, physician education, and patient advocacy.

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CONFLICTS OF INTEREST

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