Full-waveform inversion of transmitted ultrasound to image the human brain

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Summary

We demonstrate that acoustic full-waveform inversion (FWI), using transmitted ultrasound, is able to reconstruct accurate high-resolution images of the human brain in three dimensions in a way that would be entirely familiar to most geophysicists. Imaging the brain through the bones of the skull has close analogies to imaging sedimentary sequences beneath complex salt bodies. Here we use adaptive waveform inversion to build the skull, and use conventional FWI to recover the brain, a similar approach to that used for sub-salt imaging. This new form of non-invasive neuroimaging has the potential for rapid diagnosis of stroke and head trauma, and for the routine monitoring of a wide range of neurological conditions.

Introduction

No universally applicable means of imaging the living human brain at high resolution exists. Magnetic resonance imaging (MRI), is contraindicated where the presence of magnetic foreign bodies cannot be excluded, and is impractical with claustrophobic, uncooperative, or severely obese patients. X-ray computed tomography (CT), involves exposure to harmful ionizing radiation. Both methods require large, expensive, immobile, high-power instruments that are near-impossible to deploy outside specialized environments. The clinical consequences of this are long symptom-to-image delays, and constraints on the range of patients that can be imaged successfully.

Here we show that the combination of 3D FWI, with observations of ultrasound transmitted across the human head, can produce brain images that are similar in resolution and tissue contrast to those produced by conventional MRI. But unlike MRI, ultrasound is compact, portable, fast, unconditionally safe, and universally applicable, allowing first responders to take neuroimaging straight to the patient, and allowing routine bedside monitoring of the brain on hospital wards.

The potential value of FWI imaging in neuro-medicine is three-fold. Most importantly it could improve outcomes in acute neurological disorders such as stroke and head trauma by enabling earlier intervention; the ultimate aim is diagnosis and treatment within minutes of first contact with paramedics. Second, the low cost, high safety, portability and high resolving power of the technology provides the ability to monitor the brains of patients continuously at the bedside allowing clinicians to intervene, for a range of pathologies, to prevent injury with the speed that the brain demands, acting in rapid response as if the brain image was a simple physiological variable such as blood pressure. And third, the technology can be deployed readily and safely, for prevention and diagnosis, in a wide range of situations where neuroimaging would be desirable but is currently unavailable – for example: within developing nations with limited health budgets, in remote locations, routinely at contact-sports events, within military deployments, or as part of disaster relief when local infrastructure is compromised.

Method

Figure 1 shows the ultrasound acquisition geometry. The head is surrounded in three dimensions by 1000 piezoelectric ultrasound transducers that act as both sources and sensors. We use a frequency range of 100 to 1000 kHz, equivalent to wavelengths in the brain of about 1.5 to 15 mm, giving FWI sub-millimeter resolution comparable to MRI in 2D and superior in 3D. The sensors, in water or sonographic gel, cover all parts of the cranium. Each source fires a short-duration broad-band pulse in turn which is received by all other transducers. Ultrasound takes about 200 μs to cross the head, so that a full 3D dataset can be acquired in less than a second.

Figure 2a, b & c shows sections through a 3D model of sound speed in the head that we used to generate synthetic data for subsequent inversion. This acoustic model was built using MRI and CT images, segmented by tissue type, and assigned acoustic properties on the basis of direct laboratory measurements where those exist, and on composition otherwise (Guasch et al., 2020).

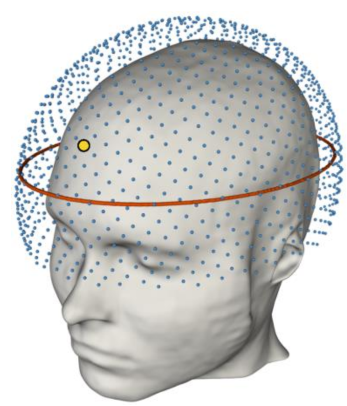

Figure 1: Schematic of the 3D acquisition geometry. Transducers surround the head, each acting as both source and receiver.

Results with a known skull model

We ran acoustic variable-density FWI on the synthetic data, beginning the inversion at 100 kHz, and extending the bandwidth by stages to a maximum frequency of 1 MHz To obtain the results shown in Figure 2 g-i, we began the inversion from a starting model that contained an exact model of the bones of the skull, Figure 2 d-f, but was homogeneous elsewhere. Using this idealized starting model, FWI is able to recover brain structure at a similar quality and resolution to MRI.

The method is able to differentiate grey and white matter clearly, and to recover features in the brain with a resolution of better than 1 mm. Similar inversions of data from perturbed models mimicking particular pathologies show that FWI can also differentiate hemorrhage and can identify blood clots in major vessels; both features are important in application to stroke. FWI loses resolution towards the base of the model where data coverage is incomplete. It has also proven difficult to recover fine structure immediately adjacent to the inner edge of the skull because of the large contrast in velocity between bone and brain.

The results shown here ignore the effects of attenuation and elasticity, and treat acoustic velocity and density as coupled parameters as is common in geophysics. Guasch et al. (2020) show that pure-acoustic inversion of models generated with realistic attenuation and density produces results little different to those shown here. We have not yet tested elastic effects for the head. For the brain and other soft tissues, shear velocities are low, and elastic effects unimportant; for bone however, elasticity is potentially important. Unlike geophysics, shear velocities in bone are similar to acoustic velocities in soft tissue, so that practical elastic FWI for the head can use a coarse mesh and is only moderately more expensive than acoustic FWI.

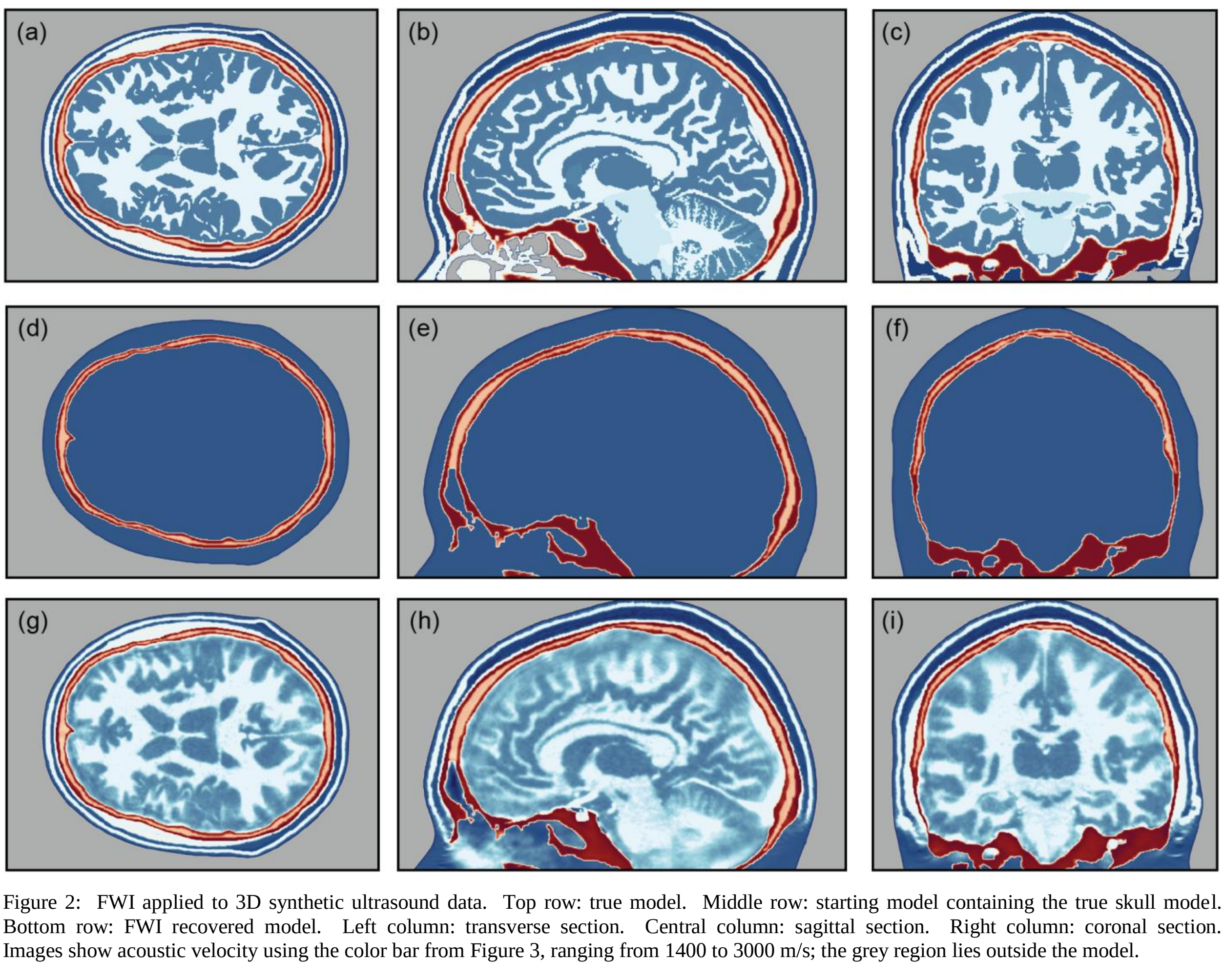

Figure 2: FWI applied to 3D synthetic ultrasound data. Top row: true model. Middle row: starting model containing the true skull model. Bottom row: FWI recovered model. Left column: transverse section. Central column: sagittal section. Right column: coronal section. Images show acoustic velocity using the color bar from Figure 3, ranging from 1400 to 3000 m/s; the grey region lies outside the model.

Building the skull model

Imaging the brain at high-resolution within the skull is not currently possible for all existing non-FWI ultrasound modalities, so this result is exciting to clinicians. But to be useful we must also be able to generate FWI neurological images without assuming a known structure for the bones of the skull. For the head, soft-tissue velocities lie between about 1400 ms^{-1} for fat and 1600 ms^{-1} for muscle and cartilage. At 100 kHz, these relatively small perturbations are readily retrievable starting from a homogeneous model having a wave speed around 1500 ms^{-1}. This is the reason why FWI applied, for example, to breast imaging has been immediately successful (Pratt et al., 2007). In contrast, the wave speed for the bones of the skull varies between about 2100 and 2800 ms^{-1}. These high values are far removed from those of water. Consequently, recovery of the full model of the head requires a more-sophisticated approach.

Figure 3 demonstrates that this problem can be solved by adaptive waveform inversion (AWI) (Warner & Guasch, 2016). Figure 3a shows a homogeneous starting model, and Figure 3b shows the failure of conventional FWI, beginning from 100 kHz, to recover the true model from this simple starting model. The reason for the failure of this attempt is that the starting model is cycle skipped. AWI is a modification of FWI that is less sensitive to the quality of the starting model, and it is able to move towards the true model even when the data are initially cycle skipped. Figure 3c shows the result of applying AWI, using the same data and starting from the same homogeneous model as was used to generate Figure 3b. AWI here was run only at 100 kHz.

Now the attempt to recover a model of both the skull and the brain has been reasonably successful, and no *a-priori* model of the skull has been assumed. The low-frequency AWI model though is not the final result. Figure 3d shows the result subsequently obtained by conventional FWI beginning from a smoothed version of the model recovered by AWI. The final model generated by this combination of methods is now accurate and compares well to the model in Fig 2g that was recovered using a perfect model of the skull. AWI and FWI together then can fully solve the problem of building a well-resolved accurate model of the brain within the skull purely from ultrasound data without any *a-priori* knowledge of the properties of the skull.

Practical implementation

As well as demonstrating proof of principle that FWI and AWI applied to transcranial ultrasound can recover a highly resolved 3D image of the brain, proof of clinical applicability requires that we also demonstrate that ultra-sound of the required bandwidth can cross the skull and be

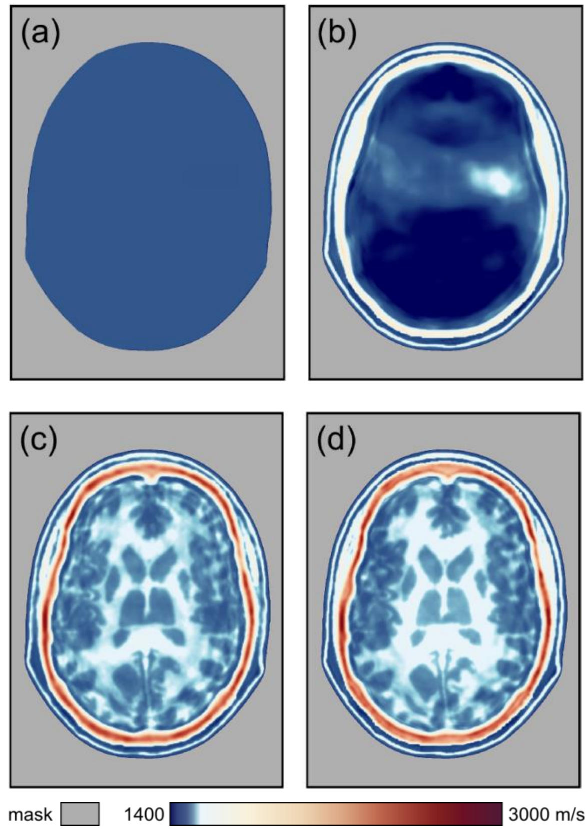

Figure 3: Recovering the brain without *a priori* knowledge of the skull. (a) Homogeneous starting model. (b) FWI-recovered model. (c) AWI-recovered model. (d) AWI followed by FWI.

recorded with adequate signal-to-noise ratio, and that FWI can deliver results sufficiently rapidly.

At the sub-MHz frequencies that were used in our numerical experiments, transmission losses in the brain are small, but scattering and anelastic losses in the bones of the skull can be important. To test the significance of these losses, and to measure signal-to-noise ratios in real transcranial ultrasound, we made *in-vivo* observations using one of the authors as a subject. In this laboratory experiment, the transducer bandwidth and the source waveform were identical to that used in the synthetic simulations. Ultrasound intensities employed were below the limits recommended by the British Medical Ultrasound Society for continuous adult diagnostic ultrasound. Source and receiver transducers were held against the scalp, and coupled to the subject using sonographic gel.

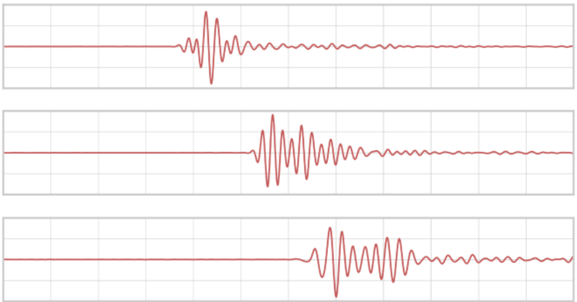

Figure 4: Single-channel direct measurements of transcranial ultrasound made through the skull of one of the authors in three orientations. Signal duration shown is from 60 to 180 μs. At all orientations the signal-to-noise ratio is excellent, and is better than noise levels in typical analogous geophysical seismograms.

Figure 4 shows the subsequent transcranial *in-vivo* waveforms acquired at three orientations. The data are single-channel, un-stacked and un-processed. These observations demonstrate unequivocally that transcranial ultrasound can be recorded for the *in-vivo* adult human head, with good signal-to-noise ratios, for the 100 – 1000 kHz bandwidth that we have used for FWI, employing even the simplest of ultrasound acquisition systems.

The computational effort required for FWI is considerable. The results shown in Figure 2 required about 32 hours elapsed time to complete, running on a conventional cluster of 128, CPU-based, 24-core, compute nodes. Our target is to reduce this elapsed time to below ten minutes; this requires a speed up of about two-hundred times. The simple hardware that we used has a peak performance of about 60 teraFLOPS, so achieving the desired speed up requires hardware capable of operating usefully at a peak of about 12 petaFLOPS. Individual high-performance GPU-based servers are currently able to achieve speeds in excess of 1 petaFLOPS, so that a small array of these is in principle capable of producing a final model in 10 minutes.

In the 3D FWI runs described, we inverted about 100 sources simultaneously, and required less than 64 Gbytes of RAM per source. It is possible currently to buy a high-performance 2-PetaFLOPS GPU server containing 16 GPUs, each with 32 Gbytes of GPU memory, for about USD100,000. It is feasible to invert one source across two GPUs on these machines, so that an array of 12 such servers could invert 96 sources simultaneously. Assuming 2020 prices, amortization over three years, and full utilization of the hardware, the capital cost of the GPU-server hardware required to invert a transcranial dataset on the 500-μm mesh that we used here represents a few tens of dollars. So, while the computational cost of FWI is high, the cost per patient to achieve a ten-minute turnaround is not high under appropriate circumstances. In practice, the provision of on-demand high-intensity compute for many hundreds of thousands of neurological images a year is most likely to be provisioned by the commercial cloud.

Conclusions

Both X-ray CT and MRI revolutionized medical imaging when they first appeared; 3D trans-cranial full-waveform inversion to recover high-resolution brain images has the same potential for impact across multiple disciplines, and has especial relevance for rapid diagnosis and treatment of stroke. FWI is robust against the levels of noise that we observe in realistic *in-vivo* measurements, and transcranial ultrasound signals have large amplitudes at the relatively low, sub-MHz, frequencies that are sufficient for successful sub-millimeter resolution. FWI overcomes the well-known limitations of conventional pulse-echo ultrasound imaging of the adult human brain, and the related limitations of conventional time-of-flight ultrasound tomography.

It is necessary either to include some prior model of the skull within the starting model before attempting to recover the brain, or to use an advanced form of FWI such as adaptive waveform inversion that can converge towards the correct answer from a simple starting model. In order to account correctly for and remove the distorting effects of the skull, it is essential to acquire and invert the data in three-dimensions, and unlike many other medical imaging techniques, it is not possible to reduce three-dimensional imaging merely to the sum total of a sequence of two-dimensional slices. It does not appear necessary to include density or anelastic absorption explicitly in the inversion in order to recover a good image, but it may be desirable to do so, both to improve the accuracy of the final image, and to obtain additional independent parameters to aid diagnosis.

Medical imaging using FWI is already a reality in soft-tissue imaging, particularly for tumor detection in breast. Leveraging several decades of investment and experience in the oil and gas industry in both FWI and in sub-salt imaging, seems likely to lead to the next major breakthrough in neurological imaging with significant worldwide consequences for human health and wellbeing.

Acknowledgements

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