Shear shock formation and super-resolved shock focusing in the human head

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ABSTRACT

Even though Traumatic Brain Injuries (TBI) remain one of the leading causes of death and disability, the relationship between brain motion and injury is poorly understood, especially in the high strain and high rate regime. Recently, high frame-rate (10,000 images/second) quantitative ultrasound imaging has measured brain motion in a wide field of view (4 cm × 6 cm), with high displacement sensitivity (<1 µm). The direct quantification of brain motion in this previously unobserved viscoelastodynamic regime led to the discovery that shear waves develop into shear shocks deep inside the porcine brain. Here we study the formation of shear shocks in the human head. A high-order finite volume simulations that describe the nonlinearity and viscosity responsible for shear shock wave formation in the human head are used to determine the local acceleration, strain-rate, and strain for a range of frequency and impact amplitudes. Quantitative ultrasound imaging of motion in a human head phantom as well as fresh porcine brain are used to experimentally observe shock formation and to validate the simulation tool in this regime. It is shown that due to the highly nonlinear elastic behavior that shear shocks form deep inside the brain, that they are focused at the geometrical center, and that the acceleration and strain-rate foci are super-resolved. For a mild impact at 1.5 m/s, 24 g at 25 Hz at the brain surface, for example, the shear shocks deep in the brain in the focal zone have a Mach number of 1.14, a local acceleration 979 g, and a strain-rate of 927 1/s. The focal zone is super-resolved to a width of 1.34 mm, which is 56 times smaller than the initial impact wavelength of 75 mm. Compared to linear viscoelastic predictions the acceleration is 41.29 g, the strain-rate is 124.2 1/s. It is shown that even for broad range of moderate impacts that the nonlinear shear shock wave physics is a necessary and primary component of brain biomechanics which explosively amplifies the local biomechanical estimates. Local measurements and simulations of this shock wave behavior may fundamentally change the way we approach the design of protective equipment in transportation, sports, playground safety, falls and our understanding of the extreme biomechanical environment to which our brains can be subjected.

Introduction

Traumatic Brain Injuries (TBI) are a major cause of disability and mortality worldwide. Recent estimates indicate that each year in the United States 1.1 million are treated in emergency departments, 235,000 are hospitalized for nonfatal TBI, and 50,000 die1,2. According to a European survey, 51% of brain injuries are motor-vehicle related, which explains why globally the incidence of TBI’s is rising sharply as transportation becomes more widely available3–5. In children and young adults TBI produces long-lasting disability in 25% of cases6 and it is responsible for more years of disability than any other cause5. In addition to acute symptoms7–9, TBIs and in particular Diffuse Axonal Injuries (DAI’s) have been linked to progressive neurodegenerative diseases like Chronic Traumatic Encephalopathy (CTE), Parkinson’s, and Alzheimer’s10–12.

Despite the prevalence of TBI’s, the relationship between brain motion and injury remains poorly understood. Directly measuring local brain dynamics during impact has been a persistently challenging task. The lack of understanding of the basic mechanisms of traumatic brain injury remains an impediment to the rational design of protective measures in sports, military and automotive equipment, such as helmets, car restraint systems, airbags etc. If obtainable, such measurements would have a significant impact on our ability to understand, prevent, and treat brain injury by generating accurate relationships between impact, neuronal deformation, and injury. Head acceleration, although not the same as brain motion, can be easily measured with accelerometers, which is why in the past 50 years brain injury has been postulated principally in terms of head motion, typically using head, mouth, ear, skin based sensors and at times together with video-graphic data from the impact13–16. Current predictors of injury thus rely on measurements of the acceleration/time history of the impact. The motion can be aggregated, as in the head injury criterion (HIC), or the linear and rotational acceleration can be considered separately17,18. However these
injury metrics are often poor predictors of injury with errors as high as 500% and their link to mechanisms of injury has not been conclusively established. There is thus a clear motivation to increase the biofidelic accuracy of injury measurements, yet there have only been a few successful attempts to directly measure human brain deformation and its relationship to injury. Previous measurements of brain phantom motion have relied on optically transparent gels with a grid pattern that were filmed with a high speed camera, or with markers implanted ex vivo that were tracked with high speed biplanar X-ray imaging. More recently MRI has been used to non-invasively measure low-level brain motion using fast gradient-echo sequences to maximize the frame rate. MR imaging of the head is completely non-invasive and suitable for in vivo imaging in humans. However, due to fundamental limits imposed by the spin-relaxation time constants, MRI has acquisition that cannot far beyond approximately 167 images/second. Thus the field of brain injury biomechanics still suffers from “a dearth of large strain and high rate mechanical properties for brain tissue”.

Nevertheless, the high strain and high strain-rate regime, which is relatively unexplored, is where injuries are most likely to occur. Recently, high frame-rate (up to 10,000 images/second) 2D ultrasound techniques have quantified brain motion in a wide field of view (4 cm \( \times \) 6 cm), with a high displacement sensitivity (< 1 \( \mu \)m). This temporal and spatial resolution has been enabled by advances in high-speed computing and programmable high frame-rate ultrasound scanners, in combination with beamforming methods and algorithms which operate on raw echo data to track motion with sub-micron resolution. With these techniques, which operate in the large strain and high rate regime, a previously unknown biomechanical phenomenon was discovered. Smooth shear waves develop into destructive shock waves deep inside the brain. In porcine brain, for example, a mild 35g shear wave at the brain surface develops into a destructive 320g shock wave as it propagates deep into the brain. These planar shock waves are governed by cubically nonlinear viscoelastic behavior and they can be simulated using custom methods developed for this purpose. We hypothesize that the violent gradients in these recently discovered shear shock waves are the primary biomechanical origin for neuronal damage deep inside the brain, ranging from diffuse axonal injuries to chronic traumatic encephalopathy.

Shear shocks are fundamentally unlike acoustic shocks which have been studied extensively including within the context of traumatic brain injuries. The soft tissue in the brain has nonlinear shear properties that are several orders of magnitude larger than its compressional properties. A typical Mach number (particle-velocity/wave-speed) for compressional waves in soft tissue is on the order of \( 10^{-4} \), and for shear waves it is on the order of one. This is due to the very low value of the shear wave velocity (typically 2 m/s) which in the case of a violent impact is the same magnitude as the particle velocity (typically 2 m/s or higher). Consequently these extremely nonlinear shear waves can generate shock fronts within a single propagation wavelength. I.e. areas with smooth shear waves can be adjacent to areas with violent shear shocks. There are few reports of shear shock wave modeling in soft tissue. Models for wave propagation in nonlinear soft solids have been developed based on Landau’s description of nonlinear elasticity, other shear shock descriptions have also been proposed. There are also models that are specific to soft-tissue which, in addition to the shear wave nonlinearity, include the non-classical viscous or attenuating behavior soft tissue. Describing the non-classical viscous behavior is of fundamental importance because its effect on the wave dynamics is just as significant as nonlinearity when estimating injury-relevant metrics such as the local acceleration or strain-rate.

Solutions to these models, especially in configurations that describe injuries in humans, require numerical solvers. Experiments with cadaveric heads are infeasible for shear shock waves because neural tissue liquefies quickly, after about 24 hours, destroying its ability to support shear stress and obtaining specimens in less than a day is nearly impossible. Furthermore, in the absence of direct experimental measurements of brain motion, simulation tools must rely on material properties measured by mechanical testing of brain samples, where even fundamental measurements of linear elastic constants vary by three orders of magnitude depending on the method used. Generally, biomechanical experiments with human specimens are challenging which is why simulation tools have been used extensively to understand brain deformation based on measurements of head motion. Commercial finite element (FE) tools such as LS-DYNA (Livermore, CA) or ABAQUS (Johnston, RI) are widely used in the study of TBI’s because they contain well-developed contact algorithms for efficient modeling of impacts ranging from closed skull to controlled cortical impacts. They are also capable of describing brain anatomy in detail using unstructured meshes and sophisticated nonlinear viscoelastic material models. However, these finite element tools have not been used to model the brain biomechanics of shear shock formation.

This has motivated the development of custom simulation tools designed specifically for shear shock wave generation and propagation that are validated by direct measurements of the nonlinear viscoelastic brain properties in the large strain and high rate regime. Here we model the shear shock wave formation in human brain using a high-order finite volume simulation tool. Ultrasonic imaging of the nonlinear elastodynamics during shock wave generation deep in a human head phantom, and in fresh porcine brain are used to validate a the shear shock wave simulation tool based on direct quantitative imaging of velocity, strain, and strain rate. This validation is performed across a range of frequencies, between 12.5 to 200 Hz, that are representative of the spectral content in injurious impacts. Once validated, the simulation tool is used to simulate impacts in a head model that has the nonlinear properties of neural tissue. It is shown that there is a dramatic amplification of the local acceleration and
strain-rates from the highly nonlinear propagation of these waves and that there is a focusing of shear waves that propagate in the brain, which occurs naturally due to the spherical geometry of the skull. Specifically, three distinct regimes appear 1) at low frequencies shear shock waves develop at the geometric focus of the head 2) at intermediate frequencies shocks form near the brain surface and at the focus 3) at high frequencies shock form only near the brain surface. It is shown that these three regimes arise from the interplay of attenuation and nonlinearity both of which are frequency-dependent and only one of which is amplitude-dependent. Finally it is shown that super-resolution occurs in the focal regime when the highly nonlinear harmonics generate acceleration and strain-rate focal zones that are much smaller than the impact wavelength. Together these simulations and experiments demonstrate the existence and determine the extent of the regimes where this previously unappreciated shear shock wave physics plays the leading-order role in brain biomechanics.

Results

Shear wave propagation and its formation into shock waves was directly imaged at depth using custom high frame-rate ultrasound imaging sequences implemented on a programmable research scanner (Verasonics Vantage 256, Kirkland, WA, USA) and adaptive quality-weighted shock wave tracking algorithms. This quantitative ultrasound imaging technique was performed here in a human head phantom based on a 3D printed skull and brain-mimicking gelatin. The acoustic and linear elastic properties of the gelatin in the head phantom were tuned to be consistent with the properties of neural tissue. Direct quantitative imaging of velocity, acceleration, and strain rates generated by the shear wave dynamics at depth were used to validate a recently developed nonlinear viscoelastodynamic model and simulation tool to establish their ability to describe shock wave formation and focusing deep within the human head. The model, which describes the propagation of linearly-polarized nonlinear shear waves in soft solids in a 2D plane orthogonal to the axis of particle displacement, is numerically simulated using a custom piecewise parabolic method designed for the purpose of shock wave formation in soft tissue. Tissue mimicking gelatin has lower nonlinearity, attenuation, and dispersion compared to neural tissue. Previous ultrasound-based measurements of these properties in fresh brain were then used in the validated simulation tool and to estimate the local velocity, acceleration, and strain rates within the human head due to shear shock wave formation for a range of amplitudes and frequencies that are representative of injurious impacts.
Figure 2. (a): Snapshot of the experimental setup showing the human head phantom clamped from three sides filled with a gelatin phantom submerged in water with an ultrasound probe over it. (b): the RMS average in time calculated for all space points using the experimental data. (c): the RMS average in time calculated for the simulated data using the physical parameters obtained from the planar experiments: $\beta = 3.5$, $c(75\text{ Hz}) = 1.9\text{ m/s}$, $\alpha(\omega) = 0.012\omega^{1.12}$. Second, third, and fourth row show velocity, acceleration, strain-rate at 4 different spatial location (black), shown in the legend in (c) plot, along with the experimental reference (grey). Note the steepening of the waveform with increase in amplitude, and spike in the local acceleration and strain-rate at in the vicinity of the steep profile. Propagation movie for both the experiment and simulation is provided in the supplementary material.
Figure 3. Maximum acceleration ($g$) for frequencies 12.5, 25, 75, 200 Hz with amplitude 1.5 m/s inside human head is shown in subplots (a)-(d), respectively. Three focal regimes were observed: 1) focusing at the geometric foci (12.5, 25 Hz) 2) focusing at the geometric foci and at just under the surface as a ring (50, 75 Hz) 3) focusing only under the surface (75-200 Hz). Insets show the rice grain sized focal region inside the brain with the contour of the area corresponding to FWHM. Propagation movies for 25, 75, 200 Hz showing the three regimes are provided in the supplementary material.

Figure 4. Particle velocity (a) and its spectrum (b) at the initial and the point of maximum acceleration for the amplitude 1.5 m/s and frequency 25 Hz. A strong shark-fin shaped shock is formed at the geometrical foci of the head. The cubic nonlinearity responsible for this peculiar shape is expressed by the generation of odd harmonics in the Fourier space.

Figure 5. Maximum strain-rate (1/s) for frequencies 12.5, 25, 75, 200 Hz with amplitude 1.5 m/s inside human head is shown in subplots (a)-(d), respectively. Like the maximum acceleration, here also three different regimes of shock focusing can be observed. A zoom of the focal region shows the minute region of peak strain-rate which could be damaging.
Figure 6. Maximum strain for frequencies 12.5, 25, 75, 200 Hz with amplitude 1.5 m/s inside the human head is shown in subplots (a)-(d), respectively. Note the strain does not follow the same trend as that of the strain-rate. In fact, it is lower in regions with high strain-rate, this is probably due to the lower amplitude at the shock front (versus smooth regions) due to higher dissipation of higher frequencies responsible for the shock formation.

Head Phantom Experiments and Simulations
To validate the 2D shear shock wave simulation tool, experiments and simulations were based on the same CT measurements of an adult male human skull (Fig. 1). A 2D section of the skull in the transverse plane was extruded in the third dimension to fabricate a cylindrical fiberglass composite skull that was subsequently filled with graphite-gelatin calibrated to have the same linear elastic (shear speed $c_0 = 1.90$ m/s) and ultrasonic ($c = 1480$ m/s) properties as brain tissue. The nonlinear elastic parameter of the tissue-mimicking gelatin were measured to be $\beta = 3.5 \pm 0.4$ and the attenuation was measured to be $\alpha(\omega) = 0.012\omega^{1.12}$ Np/m, which differ from fresh brain properties. By attaching the skull to an electromechanical shaker (Fig. 2a) a broad range of impacts were repeatably generated in the phantom. For the purposes of validation, a 75 Hz shear wave input with an 8-cycle -80 dB Chebychev window was used as an input to the shaker. The direction of brain motion is in the same direction as the ultrasound imaging wave i.e. along the axial axis and the direction of shear wave propagation is orthogonal to this axis, i.e. in the axial or transverse plane. An ultrasound probe (ATL L7–4, Philips, Bothell, WA, USA) attached to a six degree of freedom robotic arm (IRB 120, ABB Ltd, Zurich, Switzerland) had access to the surface at the top of the head phantom to obtain measurements at depth (up to 8 cm) within its entire volume. Custom high frame-rate (6000 images/second) imaging sequences were acquired and the beamformed RF data was processed with adaptive and tracking algorithms to detect displacements smaller than 1 micron. By scanning the robot arm and subsequently stitching together the 2D movies, the displacement estimates where obtained within the approximately 130 x 110 x 100 mm volume at 6000 volumes/second.

Shear wave focusing within the head, in the middle of anterior region, can be seen in the measured time-averaged RMS velocity averaged over a depth range of 60 to 100 mm (Fig. 2b). In addition to the prominent focal spot with a maximum RMS = 0.44 m/s at $x=1.04$ mm, $y=28.2$ mm, a number of other regions also give rise to local maxima in RMS velocity. The velocity measurements at the outer brain boundary, just inside of the skull surface, and the linear, nonlinear, and viscous parameters of the brain-mimicking gelatin phantom were used as an input to the simulation tool. With these inputs a close match between the experimental (Fig. 2b) and simulated (Fig. 2c) time-averaged RMS velocity was obtained. The local dynamics as a function of time are available throughout the volume. Four specific points in space were selected to illustrate the local time-dependent wave dynamics in terms of the velocity (Fig. 2d-g), acceleration (Fig. 2h-k), and Lagrangian strain-rate (Fig. 2l-o). At all positions there is a close match between experiments and simulations. For a low velocity, at position 1, the wave propagation is approximately linear and it retains the quasi-monochromatic sinusoidal shape that was originally generated by the shaker. As the particle velocity increases to its maximum, at position 4, the wave undergoes significant distortion that is well described by cubically nonlinear shear-stiffening elastodynamics. This behavior is observable in the waveform since the velocity of the shear wave increases as a function of local amplitude thus generating the characteristic shark fin profile. Propagation movie in velocity for both experiment and simulation is provided in the supplementary material gives a better understanding of the focal effect. The acceleration and strain-rate depend on the computation of a temporal derivative, which can be noise sensitive. These computations have been previously validated experimentally and numerically using simulations that model acoustic wave propagation in a medium undergoing shear wave deformation and they have been shown to be accurate to at least the 11th harmonic of the velocity signal, which coincides roughly to the sensitivity limit of the experimental ultrasound-based displacement estimates. In the linear regime, the acceleration would retain a sinusoidal shape. However, any nonlinear distortion of the wave is magnified by the temporal derivative since it is rapidly amplified at the steep shock-front gradients.
Figure 7. Comparison of linear (top) versus nonlinear (bottom) simulations. Subplot (a,f): Ratio of the maximum acceleration to the initial acceleration for each frequency-amplitude pair. Subplot (b,g): Maximum of the magnitude of acceleration for each frequency-amplitude pair. Subplot (c,h): Maximum of the magnitude strain-rate for each frequency-amplitude pair. Subplot (d,i): Maximum of the magnitude strain for each frequency-amplitude pair. Subplot (e,j): Shortest distance between the point of the maximum acceleration and the surface.

Thus, even the acceleration for the low-amplitude point (Fig. 2h) does not have a purely sinusoidal shape. At large particle velocity amplitudes (Fig. 2k) this effect is explosive and the local acceleration at the shock-front is dramatically amplified. The acceleration at the shaker surface, measured by an accelerometer (PCB Piezotronics, Inc., Depew, NY, USA) was 19g which is 14 times smaller than the 266g acceleration measured at the focal peak. Note that a 19g impact is very rarely injurious and that the lower range of mild traumatic brain injuries occur for impacts above 35g. Estimates of the Lagrangian strain-rate exhibit trends that are similar to the acceleration. At the shock front the strain-rate increases dramatically and at the focus strain-rates up to 551 1/s were observed. Taken together these results thus demonstrate that shear shock waves are focused by the skull geometry and at the focus the nonlinear elastodynamics act to rapidly amplify acceleration and strain-rates albeit in brain-mimicking gelatin.

Simulations of Shock Wave Formation in the Brain

To understand the influence of shear shock formation in the brain, the same head geometry was preserved but simulations were performed with the properties of fresh brain. Compared to gelatin, the measured nonlinear elastic and attenuation parameters are significantly larger in brain ($\beta = 44.24 \pm 14.77$ and $\alpha(\omega) = 0.06\omega^{0.05}$ Np/m, respectively) and the linear elastic properties, by design, remain almost identical ($c_0 = 2.10$ m/s). Nonlinearity acts by transferring energy from low frequencies to higher harmonic frequencies and attenuation opposes this action by preferentially damping higher frequencies. It thus is not immediately obvious how raising the values of both nonlinearity and attenuation impacts the wave propagation dynamics, especially since the nonlinearity is amplitude-dependent whereas the attenuation is not. Simulations were performed for a range of frequencies (12.5 – 200 Hz) and impact velocity amplitudes (0.3 – 1.5 m/s). Additionally, reference linear visco-elastic simulations which were performed by setting the nonlinear parameter to zero ($\beta = 0$). Within this parameter space three regimes emerged driven by this amplitude- and frequency-dependent interplay of nonlinearity and attenuation in the shock formation dynamics.

First, for characteristic frequencies below 50 Hz, shear shocks formed deep inside the brain, at the natural geometric foci determined by the overall skull morphology (Fig. 3a,b). In this shock focusing regime the local acceleration values can be enormous. For a 35g, 1.5 m/s, 25 Hz, impact at the surface of the brain, for example, the local acceleration at the focus, deep inside the brain, exceeds 900g (Fig. 7g). This represents surface to focal amplification factor of 41 (Fig. 7f). A linear wave of the same amplitude and frequency will only be amplified by a factor of 2.34 (Fig. 7g), indicating that the majority of the amplification is driven by nonlinearity and not geometrical focusing. The temporal wave form at the surface and at the focus (Fig 4-a) show how the shark-fin shape of the particle velocity produces a very high local acceleration i.e. the time derivative of the velocity at the nearly vertical shock front is large. In the linear regime the quasi-monochromatic wave retains its sinusoidal profile and does not undergo this shark-fin nonlinear distortion which is why its acceleration amplification is modest. In the frequency domain (Fig 4-b) the shape of the shear shock is supported by the odd harmonics, which is a specific feature of the cubic nonlinearity in the governing equations.
Figure 8. Beam plots of the maximum acceleration along x-axis and y-axis in subplots (a) and (b), respectively, for three different frequencies 12.5, 25, 50 Hz of 1.5 m/s. Higher the acceleration peak, smaller the FWHM, for instance, the FWHM for 12.5 Hz is 1.34 mm showing the super-resolved focusing due to the generation of higher harmonics.

Second, between 50 Hz and 75 Hz, shear shocks also appear in a ring that is about a 15.6 mm under the brain surface (Fig. 3c). The focal shock is also present, but its amplitude is reduced. This is due to attenuation which increases as a function of frequency and thus significantly reduces the shear wave amplitude over the long propagation lengths required to reach the focus. The appearance of the shock ring is due to a decrease in the shock formation distance as a function of frequency, i.e. the distance required for the peak of the wave to tip over and reach the trough decreases.52

In fact, as the frequency continues to increase above 75 Hz, the location of the shock ring migrates closer and closer to the brain surface (Fig. 7j). In this third regime, the focal shocks are overwhelmed by attenuation and only the ring shocks occur (Fig. 3d). At 200 Hz, for example, the maximum acceleration occurs in a shock ring at 4.7 mm from the surface where it is 393.2g. This is almost 2 times larger than the 199.5g initial impact acceleration and it is a considerably smaller acceleration amplification factor than at 25 Hz. Propagation movie in acceleration for the 25, 75, 200 Hz provided in the supplementary material clearly differentiate the three different regimes.

A systematic analysis of the amplification factor as a function of frequency and amplitude (Fig. 7f) shows that the acceleration amplification factor peaks at 25 Hz. As the frequency increases the amplification factor decreases due to the effects of attenuation. Note that it also decreases for frequencies below 25 Hz, however this requires a different explanation that will be discussed subsequently in the context of super-resolution. These acceleration amplification factors in the nonlinear regime are consistently larger than the amplification factors in the reference linear visco-elastic regime (Fig. 7a) where there is no shock formation.

The overall maximum acceleration also occurs at 25 Hz (Fig. 7f) and the minimum occurs at 75 Hz. This suggests that the first regime, where the shocks occur only at the focus, is a particularly destructive, unlike the second regime where the shocks are distributed across the focal and ring regions.

The Lagrangian strain-rate distribution (Fig. 5) and maximum Lagrangian strain-rate as a function of frequency and amplitude (Fig. 7f) exhibit trends that closely match the acceleration. The lowest strain rates (175 1/s) occur at 12.5 Hz and the highest strain-rates (928 1/s) occur 25 Hz. At 75 Hz i.e. in the second regime there is a local strain rate minimum (268 1/s). In the third regime, the strain-rates increase with frequency to 525 1/s at 200 Hz. These simulated estimates of the strain-rate are consistent with experimental measurements of the strain-rate at shear shock fronts imaged in fresh porcine brain, where strain-rates as high as 600 1/s were observed at 75 Hz.27

The Lagrangian strain distribution (Fig. 6) and maximum Lagrangian strain as a function of frequency and amplitude (Fig. 7i) behaves in a somewhat counter-intuitive fashion. The strain is often lower in regions of high strain-rate especially in the focal regions (Fig. 6). Furthermore, the maximum strain in the linear regime (Fig. 7d) is about 50% larger than in the nonlinear regime. Nonlinearity generates higher harmonics which are in turn more strongly attenuated thus reducing the overall particle velocity amplitude and strain estimates in comparison to the linear case. Therefore this indicates it is the rate or
time-derivative-dependent behavior that is most strongly affected by the shear shock wave physics rather than strain-dependent estimates directly.

The focal region for the acceleration (Fig. 3a,b) and strain-rate (Fig. 5a,b) is much smaller than the wavelength of the initial impact. At 25 Hz, for example, the wavelength is 7.52 cm and the full-width half-max of the acceleration focal zone along the x-axis is 1.34 mm (Fig. 8) i.e. 56 times smaller than the impact wavelength. The strain-rate focal zone is similarly super-resolved by a factor of 43 at 25 Hz. The ability to super-resolve to by over an order of magnitude is due to the broad spectral content of the shock wave and the substantial nonlinear energy transfer to frequencies over ten times higher than the initial impact (Fig. 4). At 12.5 Hz the wave is super-resolved by a factor of 13 but the large 14.08 cm wavelength results in a larger focal zone and thus an overall acceleration or strain-rate amplification is smaller than at 25 Hz.

Discussion and Conclusions

Shear shock wave physics, which has been previously unappreciated, has been shown to play a determining role in estimates of brain motion during injurious impacts. Estimates of the acceleration and strain-rate, critical parameters in brain injury biomechanics, are over an order of magnitude larger when taking into account shear shocks. The use of high frame-rate and high motion sensitivity quantitative ultrasound imaging that can directly observe this behavior is a crucial component that is required to inform the local viscoelastodynamics. Here the focus was placed on the shock wave formation and focusing while ignoring other factors that may be relevant to shear wave propagation, such as the heterogeneous composition of the brain, including ventricles, fluid-solid interfaces, and non-polarized 3D propagation. The ability to model and simulate the propagation of linearly polarized shear shock waves in a homogeneous, isotropic, relaxing soft solid, without constraints on the direction of propagation, was shown here. This simulation tool was validated with direct ultrasound-based quantitative imaging of shear shock wave formation at depth within fresh porcine brain and a human head phantom thus establishing a high level of confidence in its ability to model the relevant nonlinear viscoelastodynamics. The extremely nonlinear shear behavior observed here easily yields Mach numbers that are greater than one deep inside the brain for relatively mild impacts. Strong viscosity contributes significantly to the richness of the observed behavior and its frequency-dependence. Based on an analysis of the local velocity, acceleration, strain, and strain-rate three distinct regimes emerged depending on the frequency and amplitude of the impact.

At lower frequencies and higher amplitudes, the long propagation lengths and high nonlinearity work together to generate extremely nonlinear focal shocks. For example, at 25 Hz for a mild 1.5 m/s impact the local particle velocity at the focus is 2.16 m/s which corresponds to a Mach number of 1.14 (=2.16/1.88). The characteristic attenuation length scale (78 mm) is slightly larger than the wavelength (λ = 75 mm) and the shear wave easily propagate to the middle of the human brain, which has a typical diameter of 12 cm. Consequently there is a significant focal gain. At these Mach numbers shocks form very quickly, and the explosive gradients at the shock send the local acceleration to 979g and the strain rate to 927 1/s. Together, focusing and nonlinearity amplify the local acceleration by 41 times compared to the impact acceleration, with nonlinearity accounting for the majority of that amplification and focusing accounting for a factor of 1.74. In fact, the nonlinearity acts on such short length scales that the focal spot size is super-resolved to a FWHM of 1.34 mm which is over 56 times smaller than the 75 mm impact wavelength. The ability to super-resolve beyond linear diffraction limits theory is due to harmonic generation. As the wave develops into a shock higher frequencies or smaller wavelengths are required to support the sharp features. Thus the local frequency content at the focal shock has a substantial amount of energy at frequencies that are over ten times higher then the fundamental. The impact initial conditions that generate this highly nonlinear behavior correspond to a low scale of what is observed in traumatic brain injuries. In NFL players with head injuries the average head impact velocity is 9.3 m/s acceleration is 98g and the corresponding characteristic average impact frequency is 10.6 Hz.

At high frequencies, the attenuation is strong and shocks appear in a ring close to the skull surface and not at all at the geometric focus. At 200 Hz, for example the characteristic attenuation length 9.0 mm is short compared to the size of the brain. At the location of peak acceleration, which is 4.7 mm from the skull surface, the local velocity is 1.11 which corresponds to a Mach number of 0.84, the peak acceleration is 393.2g and the peak strain-rate is 525.5 1/s. Beyond the this distance the attenuation dominates and is insufficient to overcome the focal gain thus sparing deep parts of the brain. However a shock ring forms just under the surface of the brain potentially causing injury in a wide range of superficial regions.

At intermediate frequencies, shocks appear at both the focus deep inside the brain and in the ring just under the brain surface. This regime corresponds to a local minimum in acceleration and strain-rates because the energy is distributed between the two regions. For 75 Hz case, for example, the peak acceleration is 167.7g and the peak strain-rate is 268.6 1/s. The location of peak acceleration in the band region, where propagation is still quasi-planar, is 15.65 mm from the skull surface, the local velocity is 1.19 m/s which corresponds to a Mach number of 0.91.

Thus even a small change in the characteristic frequency of the impact can have a large effect on the local acceleration, strain-rate and their distribution within the brain. This also suggests that there is an optimum impact frequency, around 75 Hz, that can minimize local biomechanical injury metrics. Counter-intuitively this also indicates that damping out high frequencies
while preserving low frequencies may be entirely counterproductive. Wearing protective equipment, for example, encourages highly competitive athletes to take more risks and absorb larger impacts\textsuperscript{34}. This is due to the fact that protective equipment will dampen the high frequencies that trigger superficial pain receptors. A boxing glove, for example, will damp out the high frequencies that would otherwise be present in a hard and painful fist-to-face contact. However, the low frequency component of the impact, which is less painful to superficial receptors, is readily transmitted to the brain, where there are no pain receptors. At these low frequencies, even for mild impacts, the local acceleration can be focused into highly destructive and highly localized super-resolved shear shocks that tear and damage tissue. Above local acceleration measurements of 266g in our head phantom, for example, the tissue-mimicking gelatin completely fractured at the focus. However the acceleration at the brain phantom surface was measured to be only 19g i.e. 5 times lower than the average injurious acceleration in the NFL\textsuperscript{35}. The size of this high acceleration region in the focal regime is small. The FWHM extends over an area of just 14.66 mm\textsuperscript{2}, which is about the size of a grain of rice. Thus a single mild impact may incur devastating damage but only to a small region. However, over the course of an athletic career the accumulation of many tiny mm-scale injuries could explain why repeated exposure to mild events can lead to staggering rates of CTE, such as 99% observed in the NFL\textsuperscript{35}. The focal location, which depends on an specific impact, may also explain the wide variety of neurological symptoms that follow a TBI.

In conclusion there is an overwhelming amount of evidence that shear shock wave physics is a necessary and primary component of brain biomechanics and, we hypothesize, brain injury. Local measurements and simulations of this shock wave behavior, which are absent from current biomechanical models of the brain, may fundamentally change the way we approach the design of protective equipment in transportation, sports, playground safety, falls and our understanding of the extreme biomechanical environment to which our brains can be subjected.

Methods

Theoretical and Numerical Model

The system of equations describing the nonlinear propagation of linearly-polarized shear wave, particle displacement is confined to the axis orthogonal to the plane of propagation, in a homogeneous, isotropic, relaxing media is given by:\textsuperscript{33}

$$\begin{bmatrix}
  v \\
  r \\
  s \\
  \xi_{1x} \\
  \xi_{2x} \\
  \xi_{3x} \\
  \xi_{1y} \\
  \xi_{2y} \\
  \xi_{3y}
\end{bmatrix} = \begin{bmatrix}
  -\sigma_{sx}/\rho_0 \\
  -\sigma_{ry}/\rho_0 \\
  -\sigma_{sz}/\rho_0 \\
  0 \\
  -v \\
  0 \\
  -\omega_1 v \\
  -\omega_2 v \\
  -\omega_3 v
\end{bmatrix} + \begin{bmatrix}
  0 \\
  0 \\
  0 \\
  -\sum_{i=1}^{3} \tilde{\tau}_{ix} \xi_{1x} \\
  -\sum_{i=1}^{3} \tilde{\tau}_{iy} \xi_{1y} \\
  -\omega_1 \xi_{1x} \\
  -\omega_2 \xi_{2x} \\
  -\omega_3 \xi_{3x} \\
  -\omega_1 \xi_{1y} \\
  -\omega_2 \xi_{2y} \\
  -\omega_3 \xi_{3y}
\end{bmatrix}, \quad (1)
$$

where \( v \) is the particle velocity, \( r, s \) are strain-like auxiliary variables. Here the first three equations model the lossless propagation with the cubic nonlinear stress terms:

$$\sigma_{sx} = \mu r + \frac{2\mu \beta}{3} r (r^2 + s^2) \quad (2)$$

and

$$\sigma_{sy} = \mu s + \frac{2\mu \beta}{3} (r^2 + s^2) \quad (3)$$

where \( \rho_0 \) is the material density, \( \mu \) is the shear modulus, and \( \beta \) is the coefficient of nonlinearity. On the other hand, the last 6 equations are resulting from a generalized Maxwell body (GMB) consisting of three Maxwell bodies and an elastic element, all connected in parallel. Each relaxation mechanism (Maxwell body) has a variable associated along each direction, which are: \( \tilde{\xi}_{ix}, \tilde{\xi}_{iy}, i = 1, 2, 3 \) corresponding to the three relaxation frequencies \( \omega_i, i = 1, 2, 3 \). The relaxation constants \( \tilde{\tau}_{ix}, \tilde{\tau}_{iy}, i = 1, 2, 3 \) are determined after fitting a GMB with attenuation law: \( \alpha(\omega) = a\omega^b \) along with its dispersion law given by the Kramers-Kronig causality conditions.\textsuperscript{36}

The resulting system of equation was solved using a custom piecewise parabolic method, a high-order finite volume method.\textsuperscript{37} Finite volume methods are the first choice for simulating shock waves. It discretizes the domain into volumes/cells and is designed to conserve the net-flux of the material in and out of the volume. This characteristic is important for shock wave propagation as it ensures that the entropy is conserved which is governed by the Rankine-Hugoniot jump conditions.\textsuperscript{38} A detailed illustration of the theoretical and the numerical model can be found in the references.\textsuperscript{32,33}
The domain was discretized with $\Delta x = 0.19$ mm, it ensured that the highest fundamental-frequency \textit{i.e.} 200 Hz had at least 50 points per wavelength. The time $t \in [0, 0.12]$ s was discretized using $\Delta t = \frac{CA_t}{c_0}$ = 15.8 $\mu$s with CFL number $C = 0.3$, amplitude $A = 1.5$ m/s, and linear shear speed $c_0 = 2.1$ m/s. A monochromatic sine-pulse of its respective frequency and amplitude was taken with a 3-period Chebyshev window (−80 dB cut-off). Nonlinear simulations were performed using $\beta = 44.24 \pm 14.77$ and $\alpha(\omega) = 0.06\omega^{1.05}$ Np/m. Equivalent linear simulations were also performed by forcing $\beta = 0$.

**Experimental Method**

The experimental design used to measure shear wave propagation within the 2D human skull geometry is shown in Fig:2 (Top-left). The inner boundary of a horizontal section of the human skull was detected from CT scans shown in Fig:1. The skull section boundary was extruded and 3D printed into a mold for fabricating a fiberglass skull cylinder (Fig:2(a)). Over the mold surface, two plies of a fiberglass fabric were laid up using an epoxy resin and allowed to cure for 24 h. The resulting skull-cylinder was subsequently filled with a brain mimicking gelatin mixture (5% by volume), that was tuned to have the same acoustical and linear elastic properties as brain\textsuperscript{27}. The shear wave speed, nonlinear parameter, and attenuation of gelatin were measured to be 1.90 m/s, $\beta = 3.5 \pm 0.4$, and $\alpha(\omega) = 0.012\omega^{1.12}$ respectively, at an excitation of 75 Hz. The skull phantom was vibrated with a VTS-100 electromechanical shaker (Vibration Test Systems, Aurora, Ohio) to generate controlled shear impacts at an excitation frequency of 75 Hz. The resulting 2D shear wave propagation was observed by imaging throughout the gelatin surface using a Verasonics Vantage ultrasound scanner (Verasonics, Kirkland, WA, USA). The scanning of the gelatin surface was done by attaching a 5.2 MHz ultrasound probe (ATL Philips L7-4) to a programmable ABB robot arm. High frame rate images ($\approx 6200$ frames per second) were acquired using a custom ultrasound imaging sequence developed by our group, for tracking shear shocks.\textsuperscript{27,59,60}

**Brain and Gelatin Parameters**

The physical parameters of brain used for simulations were inferred using the plane wave experiments published in reference.\textsuperscript{27} The inverse uncertainty quantification, using metropolis Markov chain Monte Carlo analysis along with the deterministic 1D piecewise parabolic method, was performed to estimate the nonlinear parameter $\beta$. Datasets from 3 different brains for 5 different amplitudes each was used in this estimation, a detailed paper is in preparation. Physical parameters of the gelatin were obtained using $L_2$-norm minimization as discussed in previous papers.\textsuperscript{32,33}

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