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Viscoelastic properties of the ferret brain measured *in vivo* at multiple frequencies by magnetic resonance elastography

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Abstract

Characterization of the dynamic mechanical behavior of brain tissue is essential for understanding and simulating the mechanisms of traumatic brain injury (TBI). Changes in mechanical properties may also reflect changes in the brain due to aging or disease. In this study, we used magnetic resonance elastography (MRE) to measure the viscoelastic properties of ferret brain tissue *in vivo*. Three-dimensional (3D) displacement fields were acquired during wave propagation in the brain induced by harmonic excitation of the skull at 400 Hz, 600 Hz and 800 Hz. Shear waves with wavelengths on the order of millimeters were clearly visible in the displacement field, in strain fields, and in the curl of displacement field (which contains no contributions from longitudinal waves). Viscoelastic parameters (storage and loss moduli) governing dynamic shear deformation were estimated in gray and white matter for these excitation frequencies. To characterize the reproducibility of measurements, two ferrets were studied on three different dates each. Estimated viscoelastic properties of white matter in the ferret brain were generally similar to those of gray matter and consistent between animals and scan dates. In both tissue types G' increased from approximately 3 kPa at 400 Hz to 7 kPa at 800 Hz and G'' increased from approximately 1 kPa at 400 Hz to 2 kPa at 800 Hz. These measurements of shear wave propagation in the ferret brain can be used to both parameterize and validate finite element models of brain biomechanics.

1 Introduction

Mathematical modeling and computer simulations can illuminate the mechanics of traumatic brain injury (TBI) (Kleiven, 2002; Raul et al., 2008; Zhang et al., 2001), but only if the parameters of the model are accurate. Because of their importance to the understanding of TBI (Risda1 and Menon, 2011), the mechanical properties of brain tissue have been studied for over half a century (Chatelin et al., 2010). Although many *ex vivo* studies of brain tissue have been performed, such as indentation tests (Kaster et al., 2011; van Dommelen et al.,

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Conflict of interest statement

None of the authors has a conflict of interest that could influence the work described in this manuscript.

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2010) or shear testing (Gefen and Margulies, 2004; Hrapko et al., 2008), in vivo data is needed to understand the response of intact, living brain tissue.

Magnetic resonance elastography (MRE) has proven useful for in vivo measurement of biological tissue properties (Muthupillai and Ehman, 1996; Muthupillai et al., 1995). MRE has been applied to study many human organs, including liver (Asbach et al., 2008; Klatt et al., 2007), breast (Sinkus et al., 2005a), and brain (Clayton et al., 2012; Di Ieva et al., 2010; Green et al., 2008; Hamhaber et al., 2010; Klatt et al., 2007; McCracken et al., 2005; Sack et al., 2008; Zhang et al., 2011). The initial inversion methods of MRE were based on the assumption of linear, isotropic, elastic material behavior. Recent studies have extended the application of MRE to more general viscoelastic models (Asbach et al., 2008; Klatt et al., 2007; Sinkus et al., 2005b). Understanding the viscoelastic response of brain tissue is particularly important to the study of TBI, since it is inherently a dynamic phenomenon.

Although studies of the human brain provide essential and directly relevant information for human TBI, animal studies are indispensable. Several groups have used MRE to investigate the mechanical properties of brain tissue in rodents such as mice (Atay et al., 2008; Clayton et al., 2011; Murphy et al., 2012; Schregel et al., 2012) and rats (Boulet et al., 2011) in vivo. However, the rodent brain does not contain large distinct white matter regions. Ex vivo MRE studies have been performed in the brains of large mammals such as the cow (Riek et al., 2011) and pig (Vappou et al., 2007), but tissue parameters may be affected by post-mortem time and tissue handling. Pattison et al. (2010) have used MRE to study the differences between mechanical properties of white and gray matter in a small animal (feline) model in vivo; however they considered only a pure elastic material model.

In the current study we estimate viscoelastic properties of white and gray matter in the ferret brain in vivo at several frequencies. The ferret is the smallest mammal with a folded brain, and its brain has a significant volume of white matter. The ferret is a well-known animal model for the study of brain development processes, such as cortical folding (Barnette et al., 2009; Knutsen et al., 2010; Neal et al., 2007; Xu et al., 2010). In our study, we choose the ferret for its combination of small body size and the features of its brain (folds and white matter tracts) that are shared with larger mammals, including primates. To perform the study, a custom apparatus was designed using an MR-compatible piezoelectric actuator to excite the skull through a vibrating bite bar. Phase contrast MR images proportional to displacement were acquired during the propagation of shear waves in the brain. The 3D displacement fields were then analyzed to estimate viscoelastic properties of white and gray matter.

2 Materials and Methods

2.1 Experimental methods

Two adult female ferrets (Marshall Bioresources, New York) were used for this study. Each ferret was scanned three times at 1–2 week intervals, each time with 400 Hz, 600 Hz, and 800 Hz vibration frequencies. Anesthesia was induced with 4% isoflurane before the scan, and maintained with 2% isoflurane in 1.0 L/min oxygen during the scan. To keep the ferret physiologically stable, warm water (45°C) was circulated through tubes under its body. The experimental protocol was approved by the institutional Animal Studies Committee and studies were supervised by the Division of Comparative Medicine (DCM) at the Washington University School of Medicine.

The head of the ferret was placed in a custom-built head-holder with ear supports, a nose cone for delivery of isoflurane anesthesia, and a bite bar (Fig. 1). A low-pass, “birdcage” quadrature coil (Chang et al., 2011), which could both transmit and receive radiofrequency

(RF) signals was positioned around the head-holder and the animal. Shear waves in the brain were induced by vibration of skull transmitted via the bite bar. A harmonic signal was generated by a function generator (FG-7002C, EZ Digital Co., Ltd., Korea), amplified by a piezo amplifier (EPA-102, Piezo Systems Inc., Cambridge, Massachusetts) and used to drive a piezo-ceramic actuator (APA150M-NM, Cedrat Technologies, France) connected to the bite bar. The ferret's teeth were hooked over the bite bar; preloading of the teeth against the bite bar was accomplished by sliding the nose cone to provide light pressure against the animal's snout.

A 4.7 T superconducting MRI scanner (Varian, Inc.) was used to acquire MRE images as well as standard anatomical images. For MRE, gradient-echo, multi-slice (GEMS) imaging sequence was modified with motion-sensitizing gradients (Fig. 2) to measure the dynamic displacement of the brain. Motion-encoding gradients were synchronized with mechanical waves at frequencies of 400, 600, and 800 Hz. In each harmonic wave cycle, four or eight temporal points were acquired by varying the phase shift θ between the motion-sensitizing gradient and the mechanical wave. The imaging field of view (FOV) was 48 mm $\times$ 48 mm with an image matrix of 96 $\times$ 96 voxels. A total of 11 slices were acquired, with a slice thickness of 0.5 mm, and no gap between each scanned slices. No cardiac or respiratory gating was used. The scan parameters for each actuation frequency are summarized in Table 1.

2.2 Data processing

The phase ϕ of the MR signal and the displacement $\mathbf{u}$ are related by the magnetic field that the spin packet experiences as it moves. If the displacement and the motion-sensitizing gradient oscillate at the same frequency, a simple relation can be obtained between ϕ and the

projection of displacement onto the direction of the motion-sensitizing gradient: $u_G = \frac{\Omega\phi}{\gamma\pi NG_0}$ (Atay et al., 2008). Here Ω is the vibration frequency, γ is the gyromagnetic ratio for hydrogen, N is the number of motion-sensitizing gradient cycles, and G_0 is the amplitude of the motion sensitizing gradient. By applying the motion-sensitizing gradient in three orthogonal directions, we acquired phase images ϕ_n , $n = 1, 2, 3$ corresponding to the 3D displacement vector field, $\mathbf{u}$ (u_n , $n = 1, 2, 3$).

MR phase images were first unwrapped by a modified 3D quality guided flood-fill phase unwrapping algorithm (Spottiswoode et al., 2007), to eliminate the 2π ambiguity which is inherent in phase measurements. Data were temporally filtered by Fourier transforming in time and keeping only the fundamental frequency (the dominant frequency component). Then the images were spatially filtered with a 3D Gaussian filter (convolution kernel $3 \times 3 \times 3$ pixels, standard deviation 1 pixel).

According to the Helmholtz theorem (Romano et al., 2005; Sinkus et al., 2005b; Soutas-Little, 1973; Tong et al., 2003), the displacement vector field $\mathbf{u}$ can be decomposed into a curl-free ("longitudinal") component ($\mathbf{u}_L$) and a divergence-free ("transverse") component ($\mathbf{u}_T$). The transverse, or shear, displacement component ($\mathbf{u}_T$) describes volume-conserving deformation ($\nabla \cdot \mathbf{u}_T = 0$). The curl of the displacement field, which contains no contributions from longitudinal waves is obtained using:

$$\omega = \text{curl}(\mathbf{u}) = \nabla \times \mathbf{u} = \varepsilon_{mnk} \frac{\partial u_n}{\partial x_m} \mathbf{e}_k, \quad (1)$$

where ε_{mnk} is the permutation symbol and $\mathbf{e}_k$ is the base vector of the Cartesian coordinate. The components of the local strain tensor may also be estimated by numerical differentiation:

$$\varepsilon_{mn} = \frac{1}{2} \left(\frac{\partial u_m}{\partial x_n} + \frac{\partial u_n}{\partial x_m} \right). \quad (2)$$

2.3 Parameter estimation

In an isotropic, linearly elastic material the governing equations of wave propagation are (Auld, 1990; Kolsky, 1963):

$$\rho \frac{\partial^2 \mathbf{u}}{\partial t^2} = \mu \nabla^2 \mathbf{u} + (\lambda + \mu) \nabla (\nabla \cdot \mathbf{u}), \quad (3)$$

where μ is the shear modulus (the second Lamé parameter), ρ is the material density, and λ is the first Lamé parameter. For nearly incompressible materials, the parameter λ is much larger than μ , and displacement fields would be dominated by the contributions of shear waves. The shear wave component of displacement, $\mathbf{u}_T$, which is divergence free ($\nabla \cdot \mathbf{u}_T = 0$) is governed by a reduced version of Eq. (3):

$$\rho \frac{\partial^2 \mathbf{u}_T}{\partial t^2} = \mu \nabla^2 \mathbf{u}_T. \quad (4)$$

This linear equation can describe behavior at specific excitation frequencies ($\mathbf{u}_T(\mathbf{r}, t) = \mathbf{u}_0(\mathbf{r})e^{i\Omega t}$, where $\mathbf{r} = x_i \mathbf{e}_i$) or individual frequency components of the general periodic response. Each component of every harmonic of the displacement field (the Fourier component at the actuation frequency, Ω , e.g.) obeys an equation of the form:

$$-\rho \Omega^2 \mathbf{u}_{n0} = \mu \nabla^2 \mathbf{u}_{n0}. \quad (5)$$

The viscoelastic properties of the tissue can be calculated by applying the correspondence principle (Flugge, 1975) to Eq. (5), in which the displacement component u_0 and shear modulus μ are replaced with complex analogs: $u_{n0} = u'_{n0} + iu''_{n0}$ and $\mu = G' + iG''$:

$$-\rho \Omega^2 (u'_{n0} + iu''_{n0}) = (G' + iG'') (\nabla^2 u'_{n0} + i\nabla^2 u''_{n0}). \quad (6)$$

The complex modulus at each voxel may be estimated by solving the linear equation (Eq. (6)) for the unknown components of the complex shear modulus (Clayton et al., 2011):

$$-\rho \Omega^2 \begin{bmatrix} u'_{n0} \\ u''_{n0} \end{bmatrix} = \begin{bmatrix} \nabla^2 u'_{n0} & -\nabla^2 u''_{n0} \\ \nabla^2 u'_{n0} & \nabla^2 u''_{n0} \end{bmatrix} \begin{bmatrix} G' \\ G'' \end{bmatrix}. \quad (7)$$

This is a result that can be used, in theory, to estimate the complex shear modulus at every voxel in the image volume, if the contributions of longitudinal waves and rigid-body motion are negligible.

In practice, the displacement field may include the effects of longitudinal waves and rigid-body motion, and Eqs. (5–7) would thus not strictly apply to the components of total displacement. However, by taking the curl of Eq. (4) analogous equations are obtained for the curl, $\boldsymbol{\omega}$, of displacement, culminating in Eq. (8).

$$-\rho\Omega^2 \begin{bmatrix} \omega'_{n0} \\ \omega_{n0} \end{bmatrix} = \begin{bmatrix} \nabla^2 \omega'_{n0} & -\nabla^2 \omega''_{n0} \\ \nabla^2 \omega_{n0} & \nabla^2 \omega'_{n0} \end{bmatrix} \begin{bmatrix} G' \\ G'' \end{bmatrix}. \quad (8)$$

At each voxel, we perform a total least squares fit (Okamoto et al., 2011) of the experimental data to the model equation (Eq. 8) using data from that voxel and its neighbors in the surrounding $3 \times 3 \times 3$ kernel. The TLS weighting parameter $\lambda_{TLS} = 10$ (Okamoto et al., 2011). The difference between the model prediction and the measured data at a given voxel is the residual error for that voxel. The squared residual error is averaged over all the voxels in the kernel, and the square root (the root-mean-square residual error) is divided by the root-mean-square value of displacement in the same voxels to give the normalized residual error (NRE) (Clayton et al., 2011). Estimates of parameters at a given voxel were rejected if $NRE > 0.50$. The application of the TLS method to MRE and its validation by comparison to direct mechanical test are described in (Okamoto et al., 2011).

3 Results

All the MRE images were acquired in the coronal plane (Fig. 3). To construct a 3D displacement volume for analysis, 11 slices (Fig. 4) were scanned. The x - y plane of the Cartesian coordinate defines the coronal plane (Fig. 4). By activating the motion-sensitizing gradient along different directions, all three displacement components (u_x, u_y, u_z) in the Cartesian coordinates were acquired during MRE.

Representative 3D displacement fields acquired at actuation frequencies of 400 Hz (Fig. 5a) and 600 Hz (Fig. 5b) show a shear wave propagating in the y -direction (inferior-superior). The dominant displacement component is along the z -direction (anterior-posterior), with a maximum magnitude about $11.2 \mu\text{m}$ for 400 Hz and $7.4 \mu\text{m}$ for 600 Hz. The displacement field at 800 Hz is qualitatively similar, with lower amplitude and shorter wavelength.

Curl fields for 400 Hz (Fig. 6a) and 600 Hz (Fig. 6b) indicate that a volume-conserving transverse wave traveling in the y -direction is the major component of the response to external vibration in the z -direction. At these actuation frequencies the wave field is dominated by the ω_x component of curl. Strain components are of similar magnitude to the curl: approximately 0–0.003 (dimensionless) for 400 and 600 Hz and 0–0.001 for 800 Hz. Since each strain component is approximately sinusoidal, $= \epsilon_0 \exp(i\Omega t)$, its derivative $\dot{\epsilon} = i\Omega \epsilon_0 \exp(i\Omega t)$; from this we estimate typical strain rates of approximately $5\text{--}10 \text{ s}^{-1}$.

Representative elastograms for 400 Hz, 600 Hz, and 800 Hz actuation frequencies are shown in Fig. 7(a–f). Elastogram statistics were obtained for a set of 6 slices spanning consistent anterior and posterior brain regions in each animal on each date (ferret F1 lacked data from the anterior 3-slice set on one date and ferret F2 lacked data from the posterior 3-slice set on one date). White matter and gray matter regions of interest were identified by applying to every such elastogram a selection mask selected manually on the magnitude MRE image of the same slice (Fig. 8i, e.g.). Voxelwise statistics of complex shear modulus estimates for each ferret and scan date are shown in Fig. 8a–f. A summary of shear modulus values for all three frequencies estimated (Fig. 8g–h) shows that the white and gray matter viscoelastic properties are very similar between the two ferrets.

Overall statistics for both animals of the parameters estimated from the curl fields are summarized in Table 2. In general, estimates of both G' and G'' in white matter are similar to the corresponding estimates in gray matter. At 400 Hz estimates of G' in particular are slightly higher in white matter than in gray matter; in contrast, at 800 Hz, estimates of G' are slightly lower in white matter than gray matter. These small differences were statistically

significant only for G' at 800 Hz when data from all six studies were pooled (Students t-test, $p < 0.05$).

To characterize the difference in deformation amplitude at different frequencies, maps of average octahedral shear strain, ϵ_s , were computed using the formula:

$$\epsilon_s = \frac{2}{3} \sqrt{(\epsilon_{xx} - \epsilon_{yy})^2 + (\epsilon_{xx} - \epsilon_{zz})^2 + (\epsilon_{yy} - \epsilon_{zz})^2 + 6(\epsilon_{xy}^2 + \epsilon_{xz}^2 + \epsilon_{yz}^2)} \quad (9)$$

Volumetric strain, ϵ_n , was estimated from:

$$\epsilon_n = \frac{1}{3}(\epsilon_{xx} + \epsilon_{yy} + \epsilon_{zz}) \quad (10)$$

Maps of ϵ_s and ϵ_n are shown in Fig. 9 for 400 Hz, 600 Hz, and 800 Hz actuation frequencies. Octahedral shear strain indicates the magnitude of isochoric deformation, and thus is a good indicator of the contrast-to-noise ratio (CNR) of the measurement (McGarry et al., 2011). Higher octahedral shear strain ϵ_s generally implies higher confidence in local estimates of shear moduli obtained by MRE (McGarry et al., 2011).

4 Discussion

Quantitative measurements of white and gray matter viscoelastic material properties were performed in living ferrets using MRE measurements of harmonic shear wave propagation at 400, 600, and 800 Hz. A clear wave propagation pattern was observed in the ferret brain under external vibration of the skull, which was applied in the anterior-posterior direction via a piezo-electrically-driven bite bar. The complex shear modulus (which comprises both storage and loss moduli) was obtained by fitting the 3D curl fields obtained by MRE to the equations of shear wave propagation in a viscoelastic medium. The curl field was analyzed since it contains no contributions from longitudinal waves.

Our estimates for the viscoelastic parameters of ferret brain (Fig. 8 and Table 2) fall within the range of parameters of elastic and viscoelastic models estimated by MRE in other animal and human studies. Ferret white matter and gray matter appear similar to mouse brain tissue at similar frequencies (Clayton et al., 2011), which exhibited average storage modulus 1.6–8 kPa and loss modulus 1–3 kPa over a frequency range from 600–1800 Hz. MRE estimates of viscoelastic parameters of the human brain, which were obtained at lower frequencies, are also comparable to the current estimates. For example, using MRE at 45–80 Hz, Clayton et al. (Clayton et al., 2012) estimated $G' = 3.3\text{--}4.7$ kPa / $G'' = 1.3\text{--}2.4$ kPa in white matter and $G' = 2.8\text{--}4.4$ kPa / $G'' = 0.8\text{--}2.3$ kPa in gray matter. Using MRE at 90 Hz, Green et al. (Green et al., 2008) estimated $G' = 2.7 \pm 0.1$ kPa / $G'' = 2.5 \pm 0.2$ kPa in white matter and $G' = 3.1 \pm 0.1$ kPa / $G'' = 2.5 \pm 0.2$ kPa in gray matter. Zhang et al. (Zhang et al., 2011) performed MRE at 0 Hz and estimated $G' = 2.41 \pm 0.23$ kPa / $G'' = 1.21 \pm 0.21$ kPa in white matter and $G' = 2.34 \pm 0.22$ kPa / $G'' = 1.11 \pm 0.03$ kPa in gray matter.

The current results extend a recent MRE investigation of the elastic parameters of the feline brain at 85 Hz (Pattison et al., 2010) in which (purely) elastic shear modulus was estimated to be 8.32 ± 3.67 kPa in white matter and 7.09 ± 2.78 kPa in gray matter. Many ex vivo studies of material properties have been performed (Chatelin et al., 2010); our estimates fall within the broad range of observed parameter values from ex vivo studies. Some of the variations in ex vivo parameter estimates are attributable to differences in tissue handling and experimental procedures. Comparison between parameter estimates from different studies

highlights the effect of excitation frequency. In the current study, we observe that the complex shear modulus increases strongly with increasing frequency, which has also been observed in other MRE studies (Asbach et al., 2008; Clayton et al., 2011; Klatt et al., 2010; Klatt et al., 2007; Sinkus et al., 2005b).

We observe that at frequencies from 400 Hz–800 Hz the estimated complex shear modulus (which contains both storage and loss moduli) of white matter is similar to that of gray matter. At 400 Hz the mean loss modulus appears slightly higher in white matter (Table 2), but the difference is not statistically significant (Student's t-test, $p > 0.05$). In contrast, we note that at the highest frequency in the current study (800 Hz), estimated moduli are slightly smaller in white matter than in gray matter. We note that strain amplitudes (and corresponding contrast-to-noise ratios) at 800 Hz were much lower than at 400 Hz.

MRE studies performed in human subjects at lower excitation frequencies, report mixed results on the differences between white matter and gray matter. Early MRE studies based on a purely elastic material model (Kruse et al., 2008; McCracken et al., 2005) found elastic parameters of white matter stiffer than gray matter. In MRE studies of viscoelastic properties of the human brain, some authors (Clayton et al., 2012; Zhang et al., 2011) have found storage and loss moduli slightly higher in white than gray matter while others (Green et al., 2008) found gray matter similar to but slightly stiffer than white matter. Although Pattison et al. (2010) did not consider dissipation in their study of the feline brain, they observed that white matter appeared stiffer than gray matter at 85 Hz. Most small animal MRE studies using mice (Atay et al., 2008; Clayton et al., 2011; Murphy et al., 2012) or rats (Boulet et al., 2011) did not analyze white and gray matter tissue properties separately, because of the small amount of white matter. The study of Schregel et al. (2012) is an exception; these authors were able to estimate the shear modulus magnitude separately in white matter and found it to be approximately 10 kPa at 1000 Hz. The relatively large percentage of white matter tissue in the ferret brain, compared to the rodent brain, provides an opportunity to study the mechanical heterogeneity of white and gray matter over larger regions. Quasi-static, *ex vivo*, mechanical tests of adult ferret brain tissue (Xu et al., 2010) suggested that white matter tissue is stiffer than gray matter at low strain rates. In the study by Xu et al. (2010) the effective moduli were observed to be lower than those estimated by MRE in the current study. In dynamic shear tests of lamb brain *ex vivo* at 20–30 Hz (Feng et al., 2012a, b), higher shear moduli were observed in white matter compared to gray matter but these differences depended greatly on the direction of shear. If shear was in the plane of isotropy, the moduli of gray and white matter were similar.

In this study, 3D image volumes of 3D displacement fields were acquired by MRE. 3D MRE provides more accurate estimates of shear modulus than 2D MRE, because only 3D imaging can accurately characterize wave propagation in directions out of the 2D imaging plane. 2D MRE has been suggested to generate upper bounds on estimates of material parameters (Kruse and Ehman, 2003), because 2D projections of 3D wave fields will appear to have longer wavelengths and thus lead to higher estimated moduli.

We acknowledge several limitations and caveats to this study. The shear modulus inversion method in the current study is based on an isotropic viscoelastic material model. Although this model is likely to be accurate for gray matter, which is structurally isotropic, it neglects the anisotropy of white matter, which is composed of myelinated axonal fibers. White matter may exhibit shear moduli that differ by 30–50% for shear in planes parallel or perpendicular to the local fiber direction (Feng et al., 2012a, b; Hrapko et al., 2008; Margulies et al., 2006; Romano et al., 2012). The study by Romano et al. (Romano et al., 2012), performed in humans at lower frequencies than the present study, is the first MRE study to systematically address the issue of anisotropy in white matter; their approach requires the simultaneous

acquisition of diffusion tensor images (DTI). Qin et al. (Qin et al., 2012) propose a similar approach supported by results from a study of an anisotropic gel phantom.

The linear viscoelastic models used for inversion are strictly applicable only to small deformations. The deformations in this study clearly fall within that category. Complementary studies (likely including ex vivo mechanical tests) will be needed to understand the behavior of brain tissue at large strains. However, the in vivo 3D results of the current study provide an important limiting case, since more general models valid for large strain should be consistent with appropriate linear models in the infinitesimal limit.

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Figure 1.

(a) Setup for inducing and imaging mechanical waves in the ferret brain. The piezoelectric actuator generates mechanical vibration at frequencies of 400, 600, and 800 Hz, which was transmitted through the bite bar to the teeth. The teeth were pre-loaded against the bite bar by adjusting the nose cone position. The RF coil served as both the transmitting and receiving coil for MRI. (b) Schematic view showing the position detail of actuator, bite bar, and nose cone. The direction of actuation is along the long axis of the bite bar, which is anterior-posterior with respect to the skull.

Figure 2.

Gradient-echo multi-slice (GEMS) magnetic resonance elastography (MRE) sequence. The motion encoding gradient can be applied in any or all of the three directions in Cartesian coordinates. The phase shift θ between the mechanical excitation and the motion encoding gradient was chosen to be either $[0, \pi/2, \pi, 3\pi/2]$, or $[0, \pi/4, \pi/2, 3\pi/4, \pi, 5\pi/4, 3\pi/2, 7\pi/4]$ within one sinusoidal excitation cycle.

Figure 3.

(a) Transverse view, (b) coronal view, and (c) sagittal view of ferret brain anatomy images (spin echo; T2-weighted; TR=4000 ms; TE=25 ms) showing the field of view (FOV) with a voxel size of $0.25 \text{ mm} \times 0.25 \text{ mm} \times 0.25 \text{ mm}$. The dashed white lines on each view indicate the position of the orthogonal planes.

Figure 4.

Eleven coronal image slices obtained in ferret F2 by a standard gradient echo multi-slice (GEMS) imaging sequence. TR=500 ms; TE=20 ms. The same image slices were used in MRE. The FOV is 36 mm $\times$ 36 mm with a pixel size of 0.5 mm $\times$ 0.5 mm. The slice thickness was 0.5 mm with no gap between each slice.

Figure 5.

Displacement fields at (a) 400 Hz and (b) 600 Hz actuator frequencies. Four phases of the periodic motion ($0, \pi/2, \pi, 3\pi/2$) are shown in sequence from left to right. Three displacement components in x (left-right), y (inferior-superior), and z (anterior-posterior) directions in Cartesian coordinates are shown. Panel (a) above is from ferret F2, at a slice position corresponding to slice 2 in Fig. 4. Panel (b) is from an analogous brain section in ferret F1.

Figure 6.

Curl fields $\omega = \nabla \times \mathbf{u}$. The ω_x , ω_y , and ω_z components are shown at four temporal points in one motion cycle at (a) 400 Hz (ferret F2, slice position corresponding to slice 2, Fig. 4) and (b) 600 Hz (ferret F1).

Figure 7.

Example storage (G') and loss (G'') modulus estimates for (a, d) 400 Hz, (b, e) 600 Hz and (c, f) 800 Hz actuation frequency for posterior sections in two ferrets. (a–c) ferret F2 (slice position corresponding to slice 2 of Fig. 4). (d–f) ferret F1. White outlines indicate the region over which modulus estimates were attempted. Estimates were based on fitting of curl fields to Eq. 8, and were rejected if the normalized residual error (NRE) of fitting exceeded 0.50.

Figure 8.

(a–f) Estimated viscoelastic parameters (mean $\pm$ std. dev. storage modulus, G' , and loss modulus, G'') of white matter (white bars) and gray matter (gray bars) at 400 Hz, 600 Hz, and 800 Hz. Statistics were computed over all voxels in segmented elastograms in consistent anterior and posterior brain regions in ferret F1, and ferret F2 on each of three different scan dates for each ferret. (g, h) Summary of storage and loss moduli (mean and std. dev. of mean values from all dates) for each ferret at each frequency. (i) Example segmentation of white matter (WM, red) and gray matter (GM, green) for one ferret brain section (ferret F2, slice position corresponding to slice 2 of Fig. 4).

Figure 9.

Octahedral shear strain (ϵ_s) and volumetric strain (ϵ_n) for (a, d) 400 Hz, (b, e) 600 Hz and (d, f) 800 Hz in image slices corresponding to elastograms in Fig. 7. (a–c) Ferret F2. (d–f) Ferret F1. The octahedral shear strain reflects the magnitude of shear deformation and thus the effective contrast-to-noise-ratio (CNR) of MRE measurements.

Table 1

MRE scanning parameters

Frequency (Hz)	400	600	800
Repetition time -TR (ms)	200	200	350
Echo time - TE (ms)	13	13	26
Flip Angle (°)	25	25	40
Motion encoding cycles (N)	4	6	16
Measurement time (min)	16	16	27

Table 2

Estimates of shear storage and loss modulus in white and gray matter. Values given are the mean $\pm$ standard deviation of the mean moduli estimated from each of six studies (2 animals, 3 scan dates each).

	White matter		Gray matter	
Frequency (Hz)	G' (kPa)	G'' (kPa)	G' (kPa)	G'' (kPa)
400	3.14 $\pm$ 0.27	1.11 $\pm$ 0.15	3.07 $\pm$ 0.28	0.96 $\pm$ 0.26
600	5.30 $\pm$ 0.36	1.88 $\pm$ 0.23	5.20 $\pm$ 0.26	1.88 $\pm$ 0.22
800	6.88 $\pm$ 0.47	2.26 $\pm$ 0.61	7.31 $\pm$ 0.20 *	2.18 $\pm$ 0.46

* Significantly different from white matter ($p < 0.05$)