

## Title

Comparing data smoothing methods for intrinsic actuation Magnetic Resonance Elastography with objective metrics

## Authors

Julian A. Rey<sup>1,2</sup>, Kulam N. Magdoom<sup>1,3</sup>, Peter J. Basser<sup>1</sup>

1. *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, Bethesda, Maryland, USA.

2. National Institute of General Medical Sciences, Bethesda, Maryland, USA.

3. The Henry M. Jackson Foundation for the Advancement of Military Medicine Inc., Bethesda, Maryland, USA.

## Introduction (Min 50 words, Max 250 words)

Magnetic Resonance Elastography (MRE) is a medical imaging technique that maps mechanical properties (e.g., shear modulus) in tissue by analyzing its motion. In the brain, displacement waves induced by external skull vibration or the cardiac cycle (i.e., intrinsic-actuation MRE) are measured and passed through an inversion algorithm that reconstructs property maps. Direct inversion algorithms substitute the measured displacement field into the governing equations of motion and yield the mechanical moduli that produce the best fit to these equations algebraically. Direct inversion is simpler to implement and less computationally demanding than inversion algorithms based on the finite element method, but it involves computing at least 2<sup>nd</sup>-order spatial derivatives of the measured displacement field, which greatly amplifies noise that degrades reconstructed property maps.

Data smoothing is often needed to reduce noise and improve direct inversion. However, various smoothing methods are available, and the optimal amount of smoothing is not known *a priori*. To avoid basing the extent of smoothing on a subjective assessment of inversion quality and to improve consistency across smoothing methods and data sets, we propose objective metrics to evaluate direct inversion performance. These metrics were used to compare the effects of smoothing with splines or Gaussian filters on direct inversion of human brain displacement waves induced by the cardiac cycle.

## Materials and Methods (Min 50 words, Max 250 words)

Physiological brain motion induced by the cardiac cycle was reconstructed by retrospective gating of pulsed gradient spin-echo echo planar imaging (PGSE-EPI) data acquired with a 3T scanner. The complex displacement amplitude at 1 Hz was fit to a 5<sup>th</sup>-order spline to enable analytical computation of 2<sup>nd</sup>-order spatial derivatives. The Navier-Cauchy equation of motion for an isotropic compressible material indicates that the force density field that accelerates material points is a linear combination of the dilatation gradient and the double curl of the displacement, whose coefficients are related to a pair of mechanical moduli. Direct inversion aims to find the mechanical property pair that minimizes the squared error between the predicted force density and the measured force

density field at each voxel. Conceiving of direct inversion as a curve fit to the measured force density field, we propose computing the coefficient of determination,  $R^2$ , over all voxels as a global, objective metric of inversion performance.

Noise amplification by differentiation was mitigated by smoothing the dilatation gradient and double curl of displacement. In this way, the curl-free part and the divergence-free part of the force density can be smoothed independently. Smoothing was achieved by either fitting a “smoothing” spline which may deviate from the data by a prescribed error tolerance or through blurring by a Gaussian filter with a prescribed standard deviation. To compare the extent of smoothing on a standard, objective scale, the  $R^2$  for the fit of the smoothed field to the original field was computed.

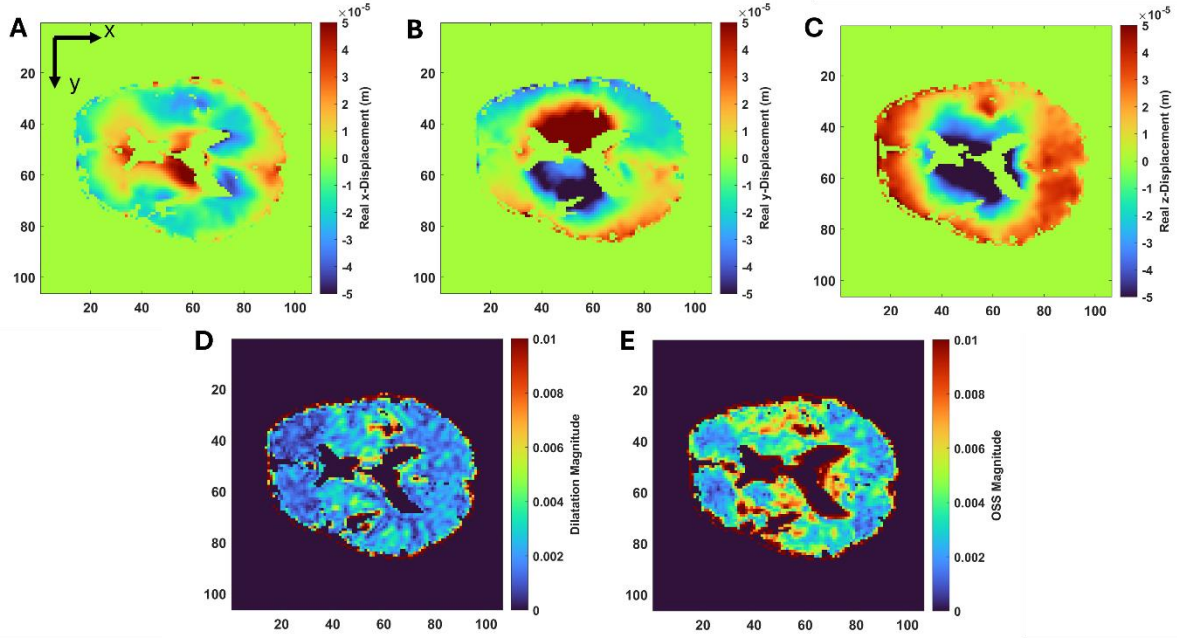
### **Results, Discussion, Conclusions** (Min 50 words, Max 350 words)

The cardiac cycle induces complex 3D displacement waves throughout the brain (Figure 1). Notably the brain undergoes both shear deformation and dilatation of similar magnitude. Although dilatation is smaller than octahedral shear strain, it is not several orders of magnitude smaller as in nearly incompressible materials. For this reason, maps of both shear and bulk moduli were reconstructed, and the curl-free and divergence-free parts of the force density were smoothed independently.

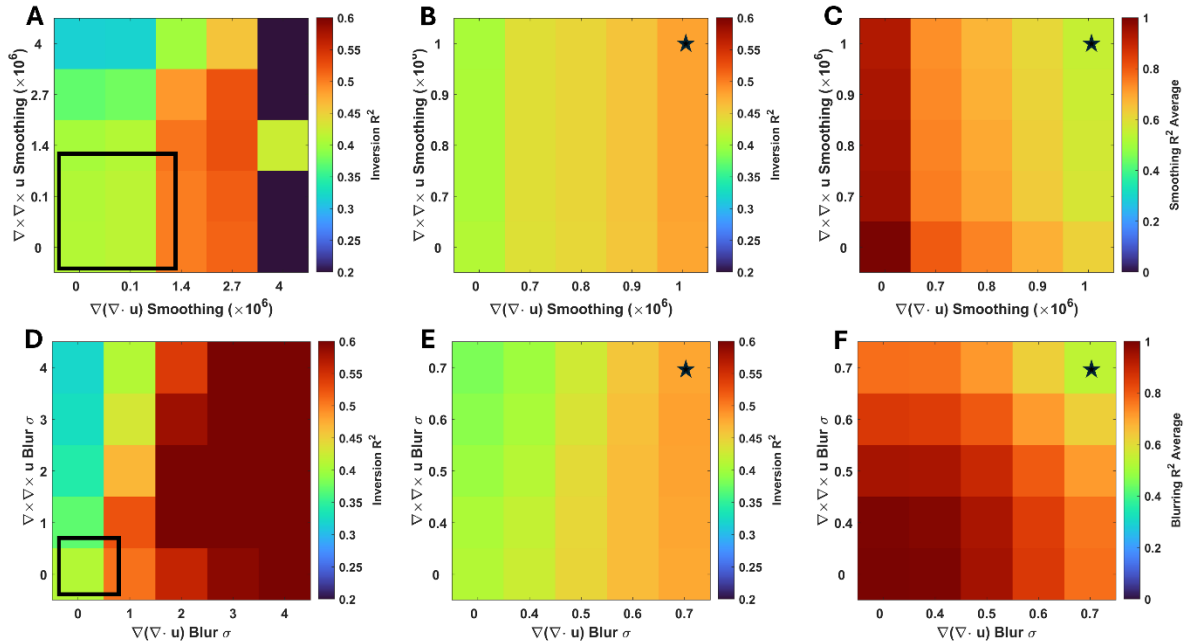
Without any smoothing, brain wide correlation between the measured and predicted force density field had an  $R^2$  of 0.41 (Figure 2). The visual correspondence between the measured y-component of displacement (Figure 1B) and the predicted y-component (Figure 3A) is apparent. In general, smoothing or blurring improved inversion  $R^2$ , although  $R^2$  was not a simple function of smoothing (Figure 2A, 2D). Inversion  $R^2$  was more sensitive to smoothing the gradient of dilatation than the double curl of displacement. When smoothing with splines, there exists a smoothing tolerance beyond which the inversion  $R^2$  begins to decline, whereas inversion  $R^2$  continues to increase with increasing Gaussian blur. However, the smoothed and blurred gradient of dilatation and double curl of displacement in these high inversion  $R^2$  cases were dramatically over-smoothed and were no longer correlated with their unsmoothed forms. The correlation between the original and smoothed fields, the smoothing or blurring  $R^2$ , drops quickly whereas the inversion  $R^2$  continues to rise.

Monitoring smoothing  $R^2$  safeguards against over-smoothing that results from considering inversion  $R^2$  alone. A reasonable average smoothing  $R^2$  of 0.55 increases the inversion  $R^2$  by 17% to 0.48 (Figure 2B, 2C). The modeled displacement and mechanical moduli for this smoothing  $R^2$  and a similar blurring  $R^2$  more closely match the measured displacement (Figure 3B, 3C). The corresponding shear and bulk modulus maps are smoother, but also slightly greater in mean value than the unsmoothed case (Figure 3).

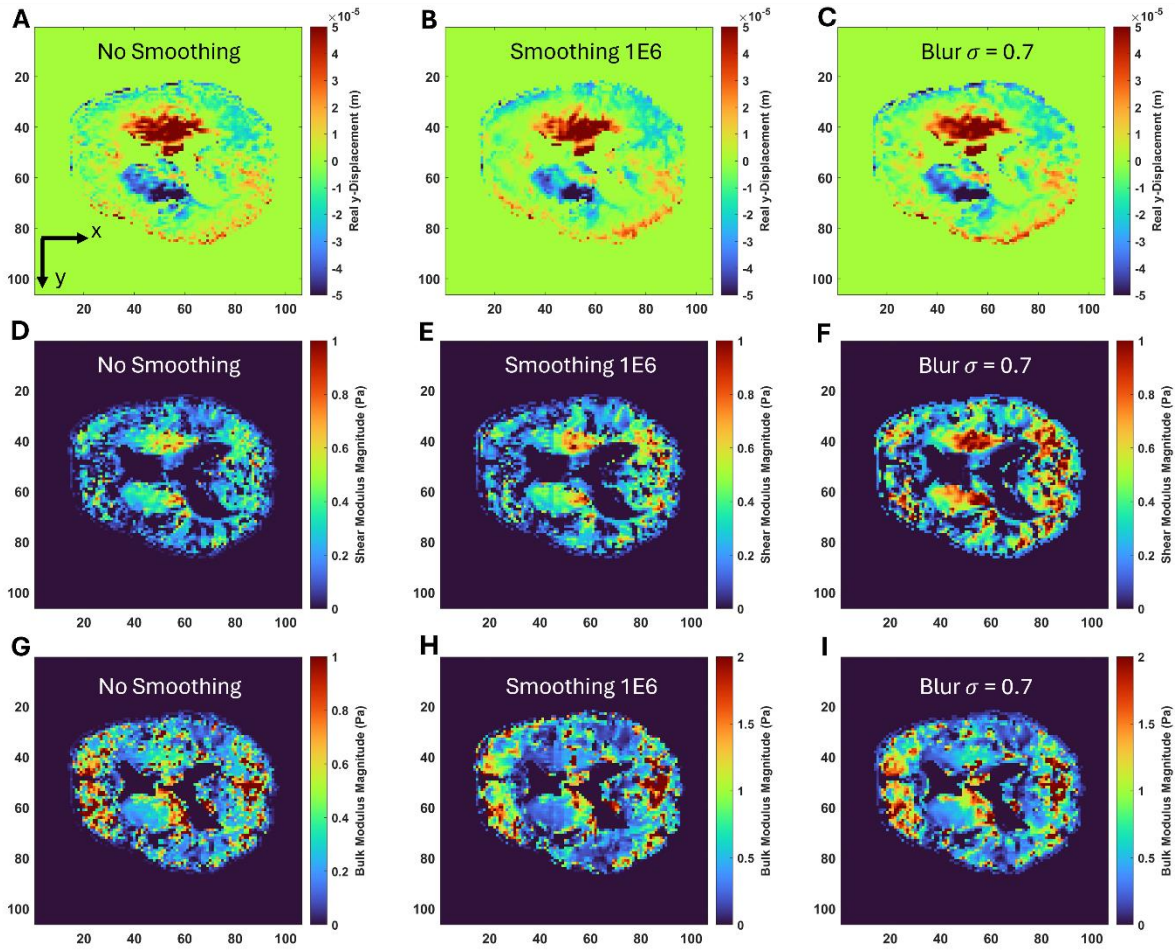
We show that global inversion  $R^2$  and smoothing  $R^2$  are quantitative metrics which can be used to compare smoothing methods and to tether smoothing optimization to the data rather than subjective quality assessments.



**Figure 1.** Measured displacement, dilatation, and octahedral shear strain. A-C) The x, y, and z components of the real part of the displacement amplitude at 1 Hz. D) Dilatation (divergence of displacement) magnitude. E) Octahedral shear strain magnitude.



**Figure 2.** Coefficients of determination. A) Inversion  $R^2$  for a range smoothing spline tolerances. B) Inversion  $R^2$  for the black square in panel A. C) Average of the  $R^2$  for the smoothed dilatation gradient and double curl fields relative to their respective unsmoothed fields. D) Inversion  $R^2$  for a range of Gaussian blur standard deviation  $\sigma$ . E) Inversion  $R^2$  for the black square in panel D. F) Average of the  $R^2$  for the blurred dilatation gradient and double curl fields relative to their respective unblurred fields. Stars indicate  $R^2$  values for smoothed and blurred data shown in Figure 3.



**Figure 3.** Modeled displacement and mechanical moduli. Best fit prediction of the measured y-displacement component assuming compressible isotropic viscoelasticity (A) without any smoothing or blurring, (B) after spline smoothing, and (C) after Gaussian blurring. D-F) Shear modulus magnitude. G-I) Bulk modulus magnitude.