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Effect of off-frequency sampling in magnetic resonance elastography

Curtis L. Johnson[a,*], Danchin D. Chen[a], William C. Olivero[b,c], Bradley P. Sutton[c,d], John G. Georgiadis[a,c]

[a]Department of Mechanical Science and Engineering, University of Illinois at Urbana–Champaign, Urbana, IL 61801, USA
[b]Department of Surgery, University of Illinois at Urbana-Champaign, Urbana, IL 61801, USA
[c]Beckman Institute for Advanced Science and Technology, University of Illinois at Urbana–Champaign, Urbana, IL 61801, USA
[d]Department of Bioengineering, University of Illinois at Urbana–Champaign, Urbana, IL 61801, USA

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Abstract

In magnetic resonance elastography (MRE), shear waves at a certain frequency are encoded through bipolar gradients that switch polarity at a controlled encoding frequency and are offset in time to capture wave propagation using a controlled sampling frequency. In brain MRE, there is a possibility that the mechanical actuation frequency is different from the vibration frequency, leading to a mismatch with encoding and sampling frequencies. This mismatch can occur in brain MRE from causes both extrinsic and intrinsic to the brain, such as scanner bed vibrations or active damping in the head. The purpose of this work was to investigate how frequency mismatch can affect MRE shear stiffness measurements. Experiments were performed on a dual-medium agarose gel phantom, and the results were compared with numerical simulations to quantify these effects. It is known that off-frequency encoding alone results in a scaling of wave amplitude, and it is shown here that off-frequency sampling can result in two main effects: (1) errors in the overall shear stiffness estimate of the material on the global scale and (2) local variations appearing as stiffer and softer structures in the material. For small differences in frequency, it was found that measured global stiffness of the brain could theoretically vary by up to 12.5% relative to actual stiffness with local variations of up to 3.7% of the mean stiffness. It was demonstrated that performing MRE experiments at a frequency other than that of tissue vibration can lead to artifacts in the MRE stiffness images, and this mismatch could explain some of the large-scale scatter of stiffness data or lack of repeatability reported in the brain MRE literature.

Keywords: Magnetic resonance elastography; Tissue vibration; Off-frequency sampling; Dynamic model; Shear waves

1. Introduction

Mechanical properties, such as shear stiffness, have long been utilized as a biomarker for characterizing various pathologies of biological tissue in vivo. Palpation is commonly used to locate stiff lesions in soft tissue by qualitatively assessing the response to generated shear waves. Magnetic resonance elastography (MRE) [1] is an emerging method for quantitatively probing the stiffness of tissues, which is devoid of many of the limitations associated with having to touch the specific organ of interest, and has successfully been used to investigate tissues such as the liver [2–4] and breast [5–7]. The classic dynamic MRE [1,8] experiment involves generating shear waves in the tissue through external harmonic mechanical actuation and capturing the motion of the waves using bipolar gradients that are matched to the period of actuation, thus encoding the motion in the phase of the image. Manipulating the synchronization between the actuation and magnetic resonance imaging sequence allows for time-resolved images of the wave propagation, which are traditionally captured over many periods of motion. By sampling the wave propagation across one period of vibration, a temporal Fourier transform can be used to remove random noise and generate a complex wave image at a frequency of interest. These MRE wave images are the inputs to an inversion algorithm to calculate the mechanical properties of the tissue, such as the shear modulus.

One of the most recent applications of MRE has been the investigation of human brain shear stiffness in vivo.

* Corresponding author.
E-mail address: cjohns73@illinois.edu (C.L. Johnson).

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Pathologic conditions such as hydrocephalus and Alzheimer's disease have been linked to changes in the mechanical properties of brain tissue, and MRE is a potential method for studying and diagnosing these diseases [9]. There is no other elastographic modality that can penetrate the brain, and vibrating the brain in vivo is challenging owing to the gross anatomy of the human head [10]. However, the brain MRE field is not yet mature, and results have been characterized by inconsistent stiffness values across studies, in addition to large uncertainties within each study [9,11–13]. Kruse et al. [11] found an average white matter stiffness of 13.6 kPa and an average gray matter stiffness of 5.22 kPa in the brains of 25 healthy volunteers, with a standard measurement error of approximately 8.5% between subjects. This is in contrast to the findings of Sack et al. [12], who reported an average stiffness of 1.56 kPa for six subjects from a measurement at 50 Hz, although they did not differentiate between white and gray matter. They also repeated the measurements for each subject at least 20 times and found discrepancies for each individual of up to approximately 8%. Green et al. [13] found the mean stiffness values for white and gray matter across five subjects to be 2.7 and 3.1 kPa, respectively. They also reported standard errors in the estimation across the tissue of up to 30% of the mean stiffness value, which they attributed to heterogeneity in the tissue. Such aggregate results from healthy human brain tissue demonstrate the uncertainty and lack of repeatability in MRE experiments. The discrepancies in published brain MRE results likely arise from different acquisition and analysis methodologies used by different groups, although the variability within each study may either indicate high intersubject variability or point to limitations in brain MRE as a whole.

In general, MRE requires the control of the timing and frequency of both imaging and tissue motion parameters. Tissue is vibrated using an external actuator being driven at a known frequency, now defined as the *actuation frequency*. The resulting motion is encoded using bipolar gradients with a defined duration or frequency, which will be referred to as the *encoding frequency*. In order to temporally sample the wave propagation, the phase offset between actuation and encoding is cycled evenly across a single period, corresponding to what will be referred to as the *sampling frequency*. It is increasingly common for the encoding and sampling frequencies to differ, such as with "fractional encoding" [14], although, in general, both the encoding and sampling frequencies in MRE are matched to the actuation frequency. The reason for matching the imaging frequencies with that of actuation is that it is assumed that tissue motion is at the same frequency as the external driver. However, this study explores the possibility of when that assumption does not hold, and thus, we introduce the term *vibration frequency* to describe the actual tissue motion. It is assumed that encoding and sampling frequencies are the same, and when they differ from the vibration frequency, it is termed *frequency mismatch* or *off-frequency effects*.

There are several potential sources of discrepancy between actuation and vibration frequencies. One possible cause for the frequency mismatch is the coupling between the mechanical actuator and the brain tissue, which is influenced by active components of the dynamic system. These components include the neck muscles and cerebrospinal fluid pulsation, and a simplified model of the dynamic brain system with these components demonstrates how this system can generate vibration frequencies different from the actuation frequency. There may also be vibrations of the tissue at multiple frequencies. One of these frequencies would be the desired actuation frequency, and a second would arise from an extrinsic source, an example of which is the vibration of the scanner bed. Such vibration occurs from the switching of the encoding gradients and is related to the natural frequencies in the scanner [15].

In this work, we investigated the consequences of performing MRE experiments with two simultaneous vibration frequencies, one that matches the actuation frequency and a second that differs, whereas both the encoding and sampling frequencies are matched to the actuation only. Numerical simulations and phantom experiments were performed in order to demonstrate how stiffness estimates could be skewed on both a global and local level by the presence of an extra vibration frequency not accounted for in the MRE protocol. Although in vivo measurements are outside the scope of this study, observations made in brain MRE are the motivation for this work [16].

2. Theory

2.1. Source of vibrations that differ from actuation frequency

In general, it is assumed, during an MRE experiment, that tissue vibrates at a single frequency, and that this vibration frequency matches the actuation frequency controlled by the experimenter. However, there is the potential for the presence of vibrations at frequencies other than the actuation frequency, which can arise from a variety of sources. These sources can be classified as extrinsic or intrinsic, referring to vibrations that result indirectly or directly from the MRE experiment, respectively.

The mechanical vibration of the scanner bed induced by the switching of the gradients is one extrinsic cause. This vibration has been documented as a source of artifacts in diffusion-weighted imaging [15] and, although undesired, has also been used as an actuation method for brain MRE [17]. The characterization of such a vibration has been confined to the case of vibrations stemming from low-frequency switching of gradients, effectively creating a transient vibration related to the natural frequency of the scanner and table structure. In the case of MRE, where gradient lobes are switched with a known encoding frequency, the excited vibration modes of the scanner and