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A combined harmonic phase and strain-encoded pulse sequence for measuring three-dimensional strain

Smita Sampath^{a,*}, Nael F. Osman^b, and Jerry L. Prince^a

^aImage Analysis and Communications Laboratory, Department of Electrical and Computer Engineering, Johns Hopkins University, Baltimore, MD 21218, USA

^bDepartment of Radiology, Johns Hopkins University, Baltimore, MD 21218, USA

Abstract

Measurement of myocardial strain provides direct information about heart function that can be correlated with disease. We present an MRI pulse sequence that acquires in just six heartbeats both harmonic phase (HARP) and strain-encoded (SENC) images and provides dense measurements of radial, circumferential and longitudinal strains within a single short-axis slice. Normal volunteer data confirm the feasibility of this pulse sequence, and acquired data demonstrate the strain measurement reliability.

Keywords

Magnetic resonance tagging; Harmonic phase; Strain encoding; Cardiac strain; FastHARP; SENC; HARP

1. Introduction

Cardiac motion analysis using magnetic resonance imaging is a sensitive diagnostic indicator of regional functional abnormalities in the heart. MR imaging methods based on MR tagging [1,2], phase-contrast velocity imaging [3–5] and stimulated-echo imaging [6,7], combined with post-processing techniques [8,9], have demonstrated the ability to compute 2-D and 3-D displacements, strains, and strain rates in the heart. While advances in imaging strategies [10–15] combined with parallel imaging schemes [16], and faster post-processing techniques [17,18] have improved the clinical applicability of these techniques, the development of a rapid imaging and post-processing system to provide dense 3-D strain visualizations at high spatial and temporal resolutions still remains a challenge.

In this paper, we describe the design and implementation of a fast imaging pulse sequence that integrates two existing MR tag-based methodologies — harmonic phase (HARP) MRI [17, 18] and strain encoded (SENC) MRI [19,20] — to provide dense three-component strain imaging in stacks of short axis slices in the heart with adequate temporal and spatial resolutions in a single, short breath-hold. With this pulse sequence, evolutions of 2-D in-plane normal strains (circumferential and radial) and 1-D out-of-plane normal strains (longitudinal) can be computed from the acquired HARP and SENC images, respectively. Experimental data and results obtained from a normal volunteer study are presented.

* Corresponding author. Department of Diagnostic Radiology, Yale University School of Medicine, PO Box 208043, TACN153, New Haven, CT 06520-8043, USA. Tel.: +1 203 785 6199. E-mail address: smita.sampath@yale.edu (S. Sampath).

2. Methods

2.1. The imaging sequence

The HARP-SENC MRI pulse sequence was designed and implemented on a 1.5-T Signa CV/i whole-body MR system (GE Medical Systems, Waukesha, WI, USA) to provide rapid acquisition of both HARP and SENC images. With this sequence, a typical scan requires just six heartbeats to acquire a single slice. Multiple slices are acquired in a sequential fashion. At the beginning of each heartbeat, 1-1 SPAMM tags are applied at end-diastole triggered by the R wave of the ECG. Let us assume a coordinate system where x is the readout direction, y is the phase-encode direction, and z is the through-plane direction.

Both HARP and SENC use MR tagging, which can be thought of as a modulation of the underlying anatomy into spectral peaks in the Fourier domain [17,18]. By acquiring these spectral peaks during image acquisition, the strain that tissue has undergone since the tag application can be computed [19,20]. Fig. 1 demonstrates how the acquisition of spectral peaks over six heartbeats is accomplished. During the first and second heartbeats, tag planes perpendicular to the slice plane are applied in the y and x directions, respectively, and a sequence of 32×32 square regions in the k_x - k_y plane centered at the k -space origin are acquired (see Fig. 1A and B). These images are referred to as the reference datasets and are used for phase-sensitive reconstruction of the multi-channel receiver coil data [21]. During the third heartbeat, tag planes perpendicular to the slice plane are applied in the y direction and a sequence of 32×32 square regions in the k_x - k_y plane centered at the right harmonic peak (i.e., centered at $k_y=k_z=0$ and $k_x=\text{tag frequency}$) are acquired (see Fig. 1C). During the fourth heartbeat, tag planes perpendicular to the slice plane are applied in the x direction and a sequence of 32×32 square regions in the k_x - k_y plane centered on the top harmonic peak (i.e., centered at $k_x=k_z=0$ and $k_y=\text{tag frequency}$) are acquired (see Fig. 1D). During the fifth and sixth heartbeats, tag planes parallel to the slice plane are applied (z direction) and a sequence of 32×32 square regions in the k_x - k_y plane centered at $k_x=k_y=0$ and with tuning frequencies $k_z=k_{z1}$ and $k_z=k_{z2}$, respectively, are acquired (see Fig. 1E and F).

During each heartbeat, a gradient echo-based, Cartesian, echo planar imaging readout scheme is employed to acquire the small k -space regions of interest. Typically, a CINE sequence of around 12–15 images are acquired every heartbeat (depending on the subject's heart rate). For each image, the 32 phase-encode lines are collected in four interleaved groups (shots) of eight lines per group. Each shot is acquired in 9.7 ms using a receiver bandwidth of 62.5 kHz, providing a temporal resolution of 38.8 ms. An optimized incrementing train of imaging flip angles as prescribed in previous literature [22] is used to compensate for the characteristic tag fading caused by longitudinal relaxation and imaging pulses.

2.2. Experiment

The in vivo study was approved by the Institutional Review Board of Johns Hopkins University, and informed consent was obtained. Data presented in this paper are from a normal volunteer of age 29 with no prior history of cardiac disease and a resting heart rate of 60 bpm. A mid-ventricular short-axis (SA) slice was prescribed with a field-of-view of 320 mm. A six-heartbeat-long breath-hold scan was performed during which the reference, HARP (horizontally and vertically tagged) and SENC (with tuning frequencies 0.42 mm^{-1} and 0.48 mm^{-1}) image sequences were acquired. Tag separations (distance between the troughs or peaks of the sinusoidal tag pattern) of 8 and 2.5 mm were used for the HARP and SENC images, respectively. Fig. 2 shows representative reconstructed images at an end-systolic time frame. The images have been interpolated to achieve an in-plane resolution of 1.25 mm. Tags generated by a simple Fourier series expansion of the HARP images (see Ref. [23] for details) are depicted in Fig. 2A and B, while SENC magnitude images are depicted in Fig. 2C and D.

Dense pixel-by-pixel measurement of Eulerian in-plane normal strain (Err or Ecc) is obtained from the HARP images by computing local spatial derivatives of the harmonic phase along the desired orientation (see Refs. [17,18] for details). Pixel-by-pixel measurements of Eulerian out-of-plane strain (Ell) are obtained from the SENC images (see Ref. [19] for details).

2.3. SENC Artifact

In experiments with the pulse sequence, we noticed ghost images of the heart appearing in certain acquired images, as shown in Fig. 3A and B. There were never more than four ghosts and the ghosting pattern was more prominent in images acquired during mid-systole and early diastole, where there are high rates of change in the instantaneous frequencies due to rapid ventricular contraction and rapid ventricular filling. This indicated that the ghosts are caused by an undersampling of the temporal changes occurring during these rapidly changing phases. At these times, shot-to-shot motion variations produced four separate undersampled images of the heart, each aliased by a factor of 4. In standard reconstruction, these four images are grouped together, despite their inconsistencies, causing the wrap around in the phase-encode direction and hence ghosting in the reconstructed composite image. Interestingly, only the heart is ghosted because it is the only object undergoing significant changes in appearance due to its longitudinal strain and SENC encoding.

To further understand the origin and nature of these artifacts, let us consider Fourier planes (say, B and C) acquired during a typical SENC acquisition (see Fig. 4A) at tuning k_z frequencies (say k_{z1} and k_{z2} , respectively) at any given time t . These planes can be mathematically expressed as follows:

$$\begin{aligned} S_B(k_y, t) &= S_S(k, t; k_z = k_{z1}) + S_M(k, t; k_z = k_{z1}) \\ &= W_{S1} S_S(k_y, t) + W_{M1}(t) S_M(k_y, t) \end{aligned} \quad (1)$$

$$\begin{aligned} S_C(k_y, t) &= S_S(k, t; k_z = k_{z2}) + S_M(k, t; k_z = k_{z2}) \\ &= W_{S2} S_S(k_y, t) + W_{M2}(t) S_M(k_y, t), \end{aligned} \quad (2)$$

where $\mathbf{k} \equiv (k_x, k_y, k_z)$ represents the location of each point in 3-D k -space, and $\mathbf{k}_y \equiv (k_x, k_y)$ represents the 2-D projection vector that defines the location of each point in the sampled 2-D k -space plane. The underlying 3-D Fourier spectrum can be expressed as a summation of functions S_S and S_M corresponding to a stationary body (subscript S) and the moving heart (subscript M), respectively. In reality, since the motion of the heart is not uniform, S_M is a summation of several motion spectrums each representing localized regions in the myocardium. For simplicity in discussion, let us, however, assume that the heart moves uniformly. The functions W_{S1} , W_{S2} , $W_{M1}(t)$ and $W_{M2}(t)$ determine the intensity weighting contributions from the underlying stationary or moving spectrum. At any given time in the cardiac cycle, the center of mass of the off-centered 3-D k -space tagging peaks in the moving spectrum S_M shifts from the tagging frequency by an amount that is directly related to the instantaneous frequency of the heart at that time. Thus, for tuning frequencies k_{z1} and k_{z2} , the corresponding image intensity weightings $W_{M1}(t)$ and $W_{M2}(t)$ from the underlying moving spectrum change with the changes in instantaneous frequency of the underlying tissue resulting in a *strain encoded* image [19]. During the course of the heartbeat, if the motion spectrum S_M moves to a point where one of the tuning frequencies does not sample the spectrum, then we cannot obtain an estimate of the center of mass or the strain. But, if this happens, the acquisition can be repeated by choosing a different set of tuning frequencies.

The intensity weighting is primarily dependent on the shape of the spectrum S_M , the distance of the sampling SENC tuning frequency from the peak of the spectrum S_M , and the rate of change in instantaneous frequency. The shape of the desired excitation slice dictates the shape of S_M . We employed sinc-shaped RF pulses with single side lobes to excite a fairly rectangular-shaped slice.

Given this shape, for a constant rate of change in instantaneous frequency, larger variations in intensity weighting in time are observed when the sampling SENC tuning frequency is away from the peak. This is depicted clearly in Fig. 4B. Here, we neglect the side lobes in the sinc curves for simplicity in discussion. The solid curve depicts the motion spectrum $S_M(\mathbf{k}_y, t_1)$ at an early time frame t_1 along k_z for $k_x=k_y=0$. The dotted line depicts the motion spectrum at a later time t_2 . We find that for a SENC tuning frequency of k_{z1} , the changes in intensity weighting ($W_{M1}(t_1) - W_{M1}(t_2)$) are larger as compared to when the sampling tuning frequency is k_{z2} ($W_{M2}(t_1) - W_{M2}(t_2)$). This explains why the artifacts were more prominent for the tuning frequency of 0.48 mm^{-1} .

Next, from Fig. 4C it is clear that for a constant sampling tuning frequency, the larger the changes in instantaneous frequency of the underlying tissue, the larger the variations in intensity weighting during a fixed acquisition interval. In Fig. 4C, the second dotted curve corresponds to a motion spectrum $S'_M(\mathbf{k}_y, t_1)$ of tissue that experiences higher rate of change in frequency during the time interval $t_2 - t_1$. Note how the change in intensity weighting $W'_{M1}(t_1) - W'_{M1}(t_2)$ is much larger than $W_{M1}(t_1) - W_{M1}(t_2)$. This explains why the artifacts occur mainly during mid-systole or early diastole when the rate of change in instantaneous frequency is much larger. A regional heterogeneity in the myocardial longitudinal strain evolutions resulted in a regional differential behavior in the ghosting patterns. For example, the ghosting of just the rapidly moving lateral free wall during early diastole was sometimes observed (see Fig. 3A and B).

2.4. Artifact correction scheme

In this section, we describe the correction scheme that was used to eliminate the ghosting artifacts. Let $I_{z1}(\mathbf{y}, t)$ represent an artifact-free reconstructed image acquired with tuning frequency k_{z1} at time t and image $I'_{z1}(\mathbf{y}, t+40)$ represent an image acquired with the ghosting artifact at a subsequent time frame at $t+40$. The location of each point in the sampled 2-D image plane is represented by $\mathbf{y} \equiv (x, y)$. Note that the second parameter within the braces denotes the time at the end of the image acquisition window expressed in milliseconds. These images can be expressed as a summation of image contributions from the stationary body image (subscript S) and the moving heart (subscript M):

$$I_{z1}(\mathbf{y}, t) = I_S(\mathbf{y}, t) + I_M(\mathbf{y}, t), \text{ and} \quad (3)$$

$$I'_{z1}(\mathbf{y}, t+40) = I_S(\mathbf{y}, t+40) + I'_M(\mathbf{y}, t+40). \quad (4)$$

Since the composite image in Eq. (3) is not aliased, if each shot in $I_{z1}(\mathbf{y}, t)$ is reconstructed separately, we obtain four undersampled aliased versions of $I_{z1}(\mathbf{y}, t)$. Let these be denoted by $A_1\{I_{z1}(\mathbf{y}, t)\}$, $A_2\{I_{z1}(\mathbf{y}, t)\}$, $A_3\{I_{z1}(\mathbf{y}, t)\}$ and $A_4\{I_{z1}(\mathbf{y}, t)\}$, where $A_1\{\}$, $A_2\{\}$, $A_3\{\}$ and $A_4\{\}$ represent the commutative aliasing functions associated with each shot trajectory. However, if each shot of $I'_{z1}(\mathbf{y}, t+40)$ is reconstructed separately, we obtain four undersampled aliased versions of four separate images $I_{z1}(\mathbf{y}, t+10)$, $I_{z1}(\mathbf{y}, t+20)$, $I_{z1}(\mathbf{y}, t+30)$ and $I_{z1}(\mathbf{y}, t+40)$. Let these

aliased images be denoted by $A_1\{I_{z1}(\mathbf{y}, t+10)\}$, $A_2\{I_{z1}(\mathbf{y}, t+20)\}$, $A_3\{I_{z1}(\mathbf{y}, t+30)\}$ and $A_4\{I_{z1}(\mathbf{y}, t+40)\}$.

Now, let us consider the aliased images $A_1\{I_{z1}(\mathbf{y}, t+10)\}$ and $A_1\{I_{z1}(\mathbf{y}, t)\}$ from the first shot. By subtracting these two aliased images as follows

$$\begin{aligned} & A_1\{I_{z1}(\mathbf{y}, t+10)\} - A_1\{I_{z1}(\mathbf{y}, t)\} \\ &= A_1\{I_{z1}(\mathbf{y}, t+10) - I_{z1}(\mathbf{y}, t)\} \\ &= A_1\{I_M(\mathbf{y}, t+10) - I_M(\mathbf{y}, t)\}, \end{aligned} \quad (5)$$

we see that the stationary body image cancels out and we obtain four aliased ghosts of the image $I_M(\mathbf{y}, t+10) - I_M(\mathbf{y}, t)$, which is the difference of the moving heart image from time t to time $t+10$. Since the ratio of the imaging phase-encode field-of-view to the size of the heart was large enough, the ghosts were found to be nonoverlapping.

Extracting a small region around the heart, we isolate one copy of the above aliased difference image to get the unaliased image $I_M(\mathbf{y}, t+10) - I_M(\mathbf{y}, t)$. This image is now added to $I_{z1}(\mathbf{y}, t)$ to obtain the artifact-free image $I_{z1}(\mathbf{y}, t+10)$. This is repeated for the other three shots to obtain artifact-free images $I_{z1}(\mathbf{y}, t+20)$, $I_{z1}(\mathbf{y}, t+30)$ and $I_{z1}(\mathbf{y}, t+40)$. Fig. 3C and D depicts the artifact-free images at two tuning frequencies (0.42 and 0.48 mm^{-1}), respectively.

3. Results

Fig. 5A–C shows representative end-systolic circumferential, radial and longitudinal strain maps, respectively, with their corresponding color bars. These maps were obtained from one complete HARP-SENC MRI dataset acquired in a mid-ventricular short axis slice in a normal volunteer during a six-heartbeat, breath-hold acquisition. Note the end-systolic circumferential shortening of 25–30%, end-systolic radial thickening of 25–30% and the end-systolic longitudinal compression of around 14–16% in these images. Tag lines generated from the in-plane HARP data are also overlaid on the in-plane circumferential and radial strain maps (see Ref. [23]).

A sequence of twelve images depicting out-of-plane longitudinal strain color maps with in-plane tag overlay for an entire cardiac cycle are shown in Fig. 6. These images provide a qualitative visualization of the evolution of both in-plane motion and out-of-plane strain simultaneously. We note an expected evolution pattern in longitudinal strain as we progress through the heart cycle with higher longitudinal strains at end-systole. We also note that the strains persist longer in the posterio-lateral regions.

To obtain a more quantitative correlation of the 3-D strains, we compared the temporal evolutions of average circumferential, radial and longitudinal strains in four regions of interest — anterior (see Fig. 7A), lateral (see Fig. 7B), posterior (see Fig. 7C) and septal (see Fig. 7D). From these curves, we find that peak circumferential strain and radial strain in the lateral region are greater than those in the other three regions. We also note that peak longitudinal strain occurs earlier and persists longer in the lateral and posterior regions than in the anterior and septal regions of the heart.

4. Discussion and conclusion

In this paper, we have demonstrated the ability to measure the dynamic evolution of three normal components of myocardial strain using the HARP-SENC MRI pulse sequence within a six-heartbeat acquisition per imaging slice. The calculation of the true 3-D strain tensor cannot

be obtained using the technique described as longitudinal shear components are not measured. It was shown that post-processing of the datasets acquired from a six-heartbeat breath-hold provides full quantification and visualization of three-component myocardial strains with good temporal resolution in a single SA slice. For a stack of n contiguous SA slices prescribed in the left ventricle, these images are acquired in a single breath-hold lasting $6n$ heartbeats.

The SENC artifact presented in this paper is a very interesting manifestation of the underlying motion characteristics of the tissue for a specific acquisition scheme. The origin and behavior of the artifact point to future investigation of application-specific SENC RF profiles, tuning frequencies and acquisition schemes. For example, in this application, employing a smoother Gaussian SENC RF profile and a multi-scale temporal resolution scheme with higher temporal resolution during the late-systolic and early-diastolic phases could prove to be beneficial. In other work, spiral acquisitions have been used, and these artifacts have not been observed [13]. When the ECG signal is unreliable, for example in patients with arrhythmia, the most common method to address this issue is to either use navigation techniques, or to measure the R-R interval and repeat the acquisition if the measured interval is out of a prespecified range; in this case the number of heartbeats necessary to acquire the data would increase. We also recognize that in patients with higher heart rates, the artifacts may be more prominent and will demand a proportional speed-up in temporal resolutions using parallel imaging techniques along with spiral acquisitions in the future.

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Fig. 1. Image acquisition windows during a typical HARP-SENC MRI scan for a single slice. The first two heartbeats are used to acquire the dc peaks with (A) vertically and (B) horizontally oriented tags. The third and fourth heartbeats are used to acquire the harmonic spectral peaks with (C) vertically and (D) horizontally oriented tags. The fifth and sixth heartbeats are used to acquire the harmonic spectral peaks with out-of-plane tags oriented parallel to the imaging plane at SENC tuning frequencies (E) k_{z1} and (F) k_{z2} respectively.

Fig. 2. Representative images from the HARP-SENC MRI scan for one slice at an end-systolic time frame. Synthetically tagged harmonic images with (A) vertically oriented tags and (B) horizontally oriented tags. SENC magnitude images acquired at tuning frequencies of (C) 0.42 mm^{-1} and (D) 0.48 mm^{-1} .

Fig. 3. Images depicting the SENC ghosting artifact for tuning frequencies of (A) 0.42 mm^{-1} and (B) 0.48 mm^{-1} for an early diastolic representative time frame. The multiple ghosts are indicated by the solid arrows. The dotted arrow points to a feature in the image that is not a ghost and is seen in all time frames. Artifact-free images for tuning frequencies of (C) 0.42 mm^{-1} and (D) 0.48 mm^{-1} .

Fig. 4.

(A) Diagram depicting the SENC planes B and C sampled at tuning frequencies k_{z1} and k_{z2} , respectively. (B) The solid and dotted curves depict the projection of the motion spectrum on the k_z axis at time frames t_1 and t_2 , respectively. The solid vertical lines indicate the positions of the planes B and C. From this diagram, it is clear that the slope of the underlying spectrum at the sampling tuning frequency determines the change in the intensity weighting over a fixed time interval. (C) This figure depicts that for a fixed tuning frequency, the rate of change in instantaneous frequency (or rate of shift in the motion spectrum) determines the change in intensity weighting over a fixed time interval.

Fig. 5. Color-coded Eulerian (A) circumferential, (B) radial and (C) longitudinal strain maps for a SA slice at an end-systolic time frame. There is an overlay of in-plane synthetic tags on the in-plane strain maps.

Fig. 6. Left ventricular color-coded longitudinal strain maps with synthetic tag overlay in 12 selected time frames of a SA slice.

Fig. 7. Evolution of circumferential (solid), radial (dashed) and longitudinal (dotted) strains for (A) anterior, (B) lateral, (C) posterior and (D) septal regions in a SA left ventricular slice over a complete cardiac cycle.