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Abstract. Automatic change detection methods for identifying the changes of serial MR images taken at different times are of great interest to radiologists. The majority of existing change detection methods in medical imaging, and those of brain images in particular, include many preprocessing steps and rely mostly on statistical analysis of magnetic resonance imaging (MRI) scans. Although most methods utilize registration software, tissue classification remains a difficult and overwhelming task. Recently, dictionary learning techniques are being used in many areas of image processing, such as image surveillance, face recognition, remote sensing, and medical imaging. We present an improved version of the EigenBlockCD algorithm, named the EigenBlockCD-2. The EigenBlockCD-2 algorithm performs an initial global registration and identifies the changes between serial MR images of the brain. Blocks of pixels from a baseline scan are used to train local dictionaries to detect changes in the follow-up scan. We use PCA to reduce the dimensionality of the local dictionaries and the redundancy of data. Choosing the appropriate distance measure significantly affects the performance of our algorithm. We examine the differences between L_1 and L_2 norms as two possible similarity measures in the improved EigenBlockCD-2 algorithm. We show the advantages of the L_2 norm over the L_1 norm both theoretically and numerically. We also demonstrate the performance of the new EigenBlockCD-2 algorithm for detecting changes of MR images and compare our results with those provided in the recent literature. Experimental results with both simulated and real MRI scans show that our improved EigenBlockCD-2 algorithm outperforms the previous methods. It detects clinical changes while ignoring the changes due to the patient's position and other acquisition artifacts. © 2014 Society of Photo-Optical Instrumentation Engineers (SPIE) [DOI: 10.1117/1.JMI.1.2.024502]

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1 Introduction

Serial magnetic resonance imaging (MRI) examinations are often performed on patients with chronic diseases, such as cancer and multiple sclerosis. Radiologists routinely look for subtle changes in images of the same anatomical location that may be clinically significant. Trying to find such changes in extent or character by using side-by-side presentation mode of films can be very difficult.^{1,2} Automatic change detection methods for identifying the changes of serial MR images are of great interest to radiologists. Such methods can reduce human error and minimize the enormous amount of data that radiologists have to process to reach a conclusion. There have been many methods proposed to automatically detect changes in MR images. For the purposes of this work, we briefly review a few of these methods and point out the advantages and/or limitations. Bosc et al.³ used an automatic change detection system for serial MRI with applications in multiple sclerosis follow-ups. Their method, based on integrating generalized likelihood ratio test and nonlinear joint histogram normalization, often fails when noise is nonstationary. Patriarche and Erickson^{1,2} implemented an integrated system for detecting changes in serial multispectral MRI examinations. Their algorithm is based on postclassification of image pixels in multispectral MR intensity feature space, with the assumptions that an abnormal tissue may

look like a tissue transitioning from one normal tissue to another in the feature space and that change tends to occur along lines connecting pairs of cluster centroids in the feature space. Preliminary clinical studies show that their system can identify visually subtle changes related to disease. However, the tissue classification task^{1–3} still remains very difficult and the whole process is inherently time consuming. Seo and Milanfar⁴ introduced a general nonparametric statistical framework and a cosine similarity measure to detect changes in two MR images from a single MRI modality. However, their work does not address the effect of misalignment. Also, the existing systems involve a great deal of preprocessing and rely mostly on the statistical analysis of MRI scans.^{1–3}

Dictionary learning is a more recent approach that has been strongly influenced by the latest advances in sparse representation theory and algorithms. The main advantage of trained dictionaries is that they lead to state-of-the-art results in many practical signal processing applications. Sparsity-based methods assume that the foreground image (i.e., changes) is sparse and the background can be learned from a dictionary. The main framework used in such methods is given by Wright et al.^{5,6} and applied by Nguyen and Tran.⁷ These methods cannot be directly adapted to our work because they utilize a database of images to find the perfect match,⁵ or are applied to very sparse images in spatial domain.⁷

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We explored the possibility of utilizing image sparsity and compressive sensing to automatically detect changes between reference and test images by designing the adaptive EigenBlock dictionary learning (AEDL) algorithm.⁸ However, because of the long processing time of l_1 minimization, we adapted the rational behind AEDL and established a simpler but effective new algorithm, namely, EigenBlock change detection (EigenBlockCD).⁹

Both the AEDL and the EigenBlockCD methods extend previous work^{5,7} on dictionary learning techniques in face recognition problems and SAR images. The AEDL and the EigenBlockCD algorithms use local dictionaries learned from one of the images to detect the changes in the consecutive MRI follow-up scans. The key idea for both the AEDL and the EigenBlockCD algorithms is to perform a local image registration for identifying important structural changes, such as appearance, disappearance, growth, or shrinkage of a lesion, while automatically rejecting unimportant changes due to the spatial position of patients and measurement noise. The main difference between these two algorithms is that in the AEDL algorithm, the block of interest is expressed by a sparse linear combination of training blocks from the inquiry block and the best matching block to the block of interest is determined by using l_1 -minimization. The EigenBlockCD aims to find the best matching block from the local dictionary to the inquiry block using l_2 -minimization as the similarity measure. The core of the EigenBlockCD method is minimizing a cost function, which expresses the dissimilarity map between the images. The minimization of the cost function finds the significant changes while ignoring the insignificant ones.

The earlier version of the EigenBlockCD algorithm performs well if the size of the inquiry block is large enough, Ref. 9. As the size of the inquiry block increases, the run-time increases significantly. Also, as the size of the inquiry block decreases, the errors increase leading to the increase of false positives. To overcome these limitations, we added the co-registration step as the key solution to solve this problem and proposed a new and improved version of the EigenBlockCD algorithm for detecting changes between consecutive MR images of the brain, based on dictionary learning techniques, which employ the L_2 norm as the most effective similarity measure and with no-preprocessing steps. By including the co-registration step, the new EigenBlockCD algorithm can automatically correct large shifts and rotations and its performance is significantly improved.

Experiments with synthetic and real MR images show that the improved EigenBlockCD algorithm performs better in cases with large shifts and rotations. The rest of this paper is organized as follows. Section 2 describes the methods used. Section 3 examines the selection of similarity measures and shows that the L_2 norm is more effective than the L_1 norm in our application. Section 4 compares the performance of the new algorithm with the existing methods, Sec. 5 describes simulations and experiments and Sec. 6 discusses the results. The last section provides the conclusions.

2 Methods

In general, a change detection algorithm maps two input images to a third image, namely, the change image, consisting of only the significant changes between the two input images. In this section, we explain the improved version of the initial EigenBlockCD algorithm, named the EigenBlockCD-2. The

EigenBlockCD-2 algorithm is different from the initial version, EigenBlockCD, in the following aspects:

1. We introduce the co-registration step as a very important step for any change detection algorithm.
2. It accounts for large rotations and translations.
3. Reduces the computations significantly.
4. Reduces the error, hence improving the detection accuracy significantly.

First, we describe the EigenBlockCD algorithm for detecting differences between the two consecutive MR images. Then, we describe the EigenBlockCD-2 algorithm and provide a comprehensive comparison of the two algorithms. In both cases, we assume that the differences between the two images may come from disease-related changes that occurred from time t_1 to time t_2 , and/or from misalignment due to subject position shifts and rotations, and other common imaging acquisition artifacts. During this time interval, each block from the reference image has undergone few disease-related changes. Most pixels of the reference image will appear again in the test image either at the same location or nearby. Hence, the insignificant changes in the follow-ups are within a neighborhood.

2.1 EigenBlockCD

In this section, we discuss briefly the initial version EigenBlockCD algorithm used for determining the significant changes between two or more MR images of the same scene taken at different times. The detailed explanation can be found in Nika et al.⁹ The EigenBlockCD extends previous work^{5,7} on dictionary learning techniques in face recognition problems. Although those methods utilize a database of images to find the perfect match, in our method, we use local dictionaries learned from one of the images—the reference image, to detect the changes in the consecutive MRI follow-up scan—the test image. The algorithm divides the test image into many overlapping blocks. We assume that pixels from the reference image will appear again in the test image either at the same location or within a close neighborhood.

This means that for a block $\mathbf{b}$ of size $(2\delta + 1)(2\delta + 1)$ from the test image, centered at (i, j) , its closest block in the reference image will be in some neighborhood of a block centered at the same position (i, j) , referred to here as the inquiry block $\mathbf{B}$ of size $(2\Delta + 1)(2\Delta + 1)$. Therefore, a block $\mathbf{b}$ from the test image can be sparsely represented as a linear combination of a few blocks $\mathbf{a}_k$ from the reference image, over a dictionary Φ of size $n \times p$, which is created by stacking training blocks $\mathbf{a}_k$ into column vectors, where $n = (2\delta + 1)^2$ and $p = (2\Delta + 1)^2$. Also column vectors $\mathbf{y}$ and $\mathbf{x}_k$, $k = 1, \dots, p$ are formed by stacking columns of $\mathbf{b}$ and $\mathbf{a}_k$, respectively. Figure 1 illustrates how a block from the reference image and its inquiry block from the test image are obtained and how the dictionary is learned. Our algorithm seeks to automatically find the best matching block by solving Eq. (1):

$$\mathbf{y} = \Phi\gamma, \quad (1)$$

where γ is a sparse vector with only a few nonzero elements. We find the sparsest vector γ that satisfies Eq. (1), by solving the following minimization problem:

Fig. 1 (a) Dictionary formed by stacking training blocks in column vectors. (b) Inquiry block magnified with many overlapping training blocks $\mathbf{a}_k$. (c) Reference image with “inquiry block” in cyan color. (d) Test image with “block of interest” in cyan color. A magnified version of the block of interest is shown at the bottom right of test image.

$$\gamma^* = \arg \min_{\gamma} \|\gamma\|_p \text{ s.t. } \mathbf{y} = \Phi\gamma + \mathbf{e}, \quad (2)$$

where $\mathbf{e}$ are the residual errors in the approximation algorithm. The selection of metric p will be discussed in the next paragraph. The best approximation to the column vector $\mathbf{y}$ is a vector $\mathbf{x}_k$, from dictionary Φ , which is computed by minimizing the residual error $\mathbf{e}$ given as

$$\mathbf{e} = \min_{\gamma} \|\mathbf{y} - \Phi\gamma\|_2. \quad (3)$$

We use principal component analysis (PCA) to reduce the dimensionality of local dictionary Φ and to eliminate the redundancy caused by the highly overlapped blocks. We obtain $\hat{\mathbf{y}}$, $\hat{\mathbf{x}}_k$, and $\hat{\Phi}$ by projecting vector $\mathbf{y}$ and all the corresponding vectors $\mathbf{x}_k$ onto the eigensubspace of the covariance matrix of the dictionary Φ . Equation (3) in the eigensubspace is written as

$$\min_{\hat{\mathbf{x}}_k} \|\hat{\mathbf{y}} - \hat{\mathbf{x}}_k\|_2 \text{ s.t. } \hat{\mathbf{x}}_k \in \hat{\Phi}. \quad (4)$$

The change block $\mathbf{d}$, which has the same size and location (center) as block of interest $\mathbf{b}$, is computed as in Eq. (5):

$$\mathbf{d} = \min_{\mathbf{x}_k} |\mathbf{y} - \mathbf{x}_k|. \quad (5)$$

We obtain all blocks $\mathbf{d}$ and the change image, by repeating the process for all overlapping blocks $\mathbf{b}$. A pixel (i, j) from the test image belongs to n overlapping $\mathbf{b}$ blocks; therefore, pixel (i, j) in the change image belongs to n overlapping $\mathbf{d}$ blocks. To account for overlapping, change image pixels intensities are divided by n .

2.2 EigenBlockCD-2 Algorithm

The improved version of EigenBlockCD algorithm, EigenBlockCD-2, consists of the following main steps:

1. It performs the initial global alignment of images by determining three parameters, two shifts and one rotation, and performing a linear transformation which aligns one of the images with the other one. In this step, the radii of the blocks of interest and the inquiry block are selected to be significantly large to account for large shifts and rotations.

2. It determines significant changes between the two images by running the EigenBlockCD algorithm with fixed small blocks of interest.

2.2.1 Initial global alignment of images

We introduce the co-registration step as a very important step for any change detection algorithm. The co-registration helps in detecting only relevant and significant changes, by decreasing false positives and increasing true positives. The initial global image registration step is a major improvement, which enables the algorithm to identify important structural changes, such as appearance, disappearance, growth, or shrinkage of a lesion, while automatically rejecting unimportant changes due to spatial position of patients and common imaging acquisition artifacts.

In general, the registration problem is to find a transformation that best aligns the two images and it involves the determining and handling of a transformation space and a cost function that quantifies the quality of registration. In our registration problem, the transformation space includes six rigid transformations in three-dimensions with six degrees of freedom; three translations and three rotations, or three transformations with three degrees of freedom in two-dimensions (2D); two for translations and one for rotation. The cost function expresses the dissimilarity map between the images. The minimization of the cost function finds the significant changes while ignoring the insignificant ones.

To align the reference and test images, the EigenBlockCD-2 algorithm automatically selects a few blocks in the test image and their corresponding inquiry blocks from the reference image as shown in Fig. 2.

2.2.2 Blocks of interest selection during the co-registration step

First, we describe how the blocks of interest are selected and then we discuss our co-registration step with more details. The test image is divided into 25 subimages of size 77×77 as shown in Figs. 2(a)–4(a). From nine subimages inside the brain, the EigenBlockCD-2 algorithm selects randomly nine centers, one for each area, for nine blocks of interest. To account for large shifts and rotations, the radii of blocks of interest and corresponding inquiry blocks are chosen to be relatively large. In our experiments, blocks of interest are of size 25×25 and their corresponding inquiry blocks are of size 65×65 . The output

Block of Interest	1	2	3	4	5	6	7	8	9	Median
Vertical shift	-24	-22	-22	-21	-20	-20	-13	-9	22	-20
Horizontal Shift	-1	-3	4	3	-1	0	5	-2	-22	-1
Rotation Angle	1	-3	1	-4	-1	0	4	-4	4	-1

Fig. 2 Top row: three parameters (vertical and horizontal shifts, rotation angle) for nine selected blocks from the test image. bottom row: (a) MR image in 2012 with nine blocks of interest of size 25×25 selected randomly from nine inner areas. (b) An MR image taken in 2010 with corresponding inquiry blocks of sizes 65×65 . (c) Reference image aligned with test image, after two translations and one rotation. In this case, reference image is rotated 1-deg counter-clockwise, shifted 20 pixels down, and one pixel to the left.

of these computations is composed of two translations and one rotation needed to globally co-register images.

More specifically, at the co-registration step, the EigenBlockCD algorithm:

- Determines the shifts and rotations needed to initially align 2-D images with:
 - Input: reference and test images, radius of the block of interest, radius of the inquiry block in the reference image, and a range of rotation angles about x -axis.
 - Output: two translations and one rotation angle needed to globally co-register images, i.e., vertical shift, horizontal shift, and rotation about x -axis.

- Align 2-D images by performing a linear transformation to one MR image to be aligned with its follow-up image. The linear transformation consists of two translations and one rotation.

The EigenBlockCD-2 algorithm identifies the inquiry blocks in the reference image for each given block of interest in the test image. The dictionary learning is created with training blocks from the inquiry block. The dictionary is rotated about the x -axis with an angle selected from a given range of angles, $[-10, 10 \text{ deg}]$ as shown in Figs. 5 and 6. Then, the best matching block for a selected block of interest is computed by minimizing the l_2 differences between the block of interest and all the training blocks projected into the eigensubspace with only 85% of the total variance.

Block of Interest	1	2	3	4	5	6	7	8	9	Median
Vertical shift	-22	-22	-21	-20	-19	-19	-18	-18	-17	-19
Horizontal Shift	-2	-1	0	-3	-1	-2	2	-3	-2	-1
Rotation Angle	-1	-2	-1	2	-2	-3	-3	0	-1	-2

Fig. 3 Top row: three parameters (vertical and horizontal shifts, rotation angle) for nine selected blocks from the test image. Bottom row: (a) MR image in 2012 with nine blocks of interest of size 25×25 selected randomly from nine inner areas. (b) An MR image taken in 2010 with corresponding inquiry blocks of sizes 65×65 . (c) Reference image aligned with test image, after two translations and one rotation. In this case, reference image is rotated 1-deg counter-clockwise, shifted 19 pixels down, two pixels to the left.

Block of Interest	1	2	3	4	5	6	7	8	9	Median
Vertical shift	-32	-22	-22	-21	-20	-19	-18	-9	3	-20
Horizontal Shift	-6	-7	0	2	-1	-2	0	-15	2	-1
Rotation Angle	0	-3	-2	-1	-2	0	-1	4	0	-2

Fig. 4 Top row: three parameters (vertical and horizontal shifts, rotation angle) for nine selected blocks from the test image. bottom row: (a) MR image in 2012 with nine blocks of interest of size 25×25 selected randomly from nine inner areas. (b) An MR image in taken 2010 with corresponding inquiry blocks of sizes 65×65 . (c) Reference image aligned with test image, after two translations and one rotation. In this case, reference image is rotated 2-deg counter-clockwise, shifted 20 pixels down, one pixel to the left.

Parameters	1	2	3	4	5	6	7	8	9	10	11
L_2 min	699	701	712	715	721	722	727	729	729	730	730
sh_v	-22	-24	-22	-22	-22	-24	-24	-22	-24	-24	-22
sh_h	-1	-1	-1	-1	-1	-8	-9	-1	-6	-6	-1
α (degrees)	-3	-2	-1	0	1	2	3	-6	-5	-4	5
β (degrees)	3	2	1	0	-1	-2	-3	6	5	4	-5

Parameters	12	13	14	15	16	17	18	19	20	21
L_2 min-	731	735	736	741	745	750	750	753	757	759
sh_v	-22	-22	-22	-24	-22	-22	-22	-22	-22	-24
sh_h	-1	-1	-1	-11	-1	-1	-1	-1	-1	-13
α (degrees)	6	7	9	-9	-7	10	8	-8	4	-10
β (degrees)	-6	-7	-9	9	7	-10	-8	-8	-4	10

$L_2\text{-min} \Rightarrow \min_{\alpha, \beta, sh_v, sh_h} \|\hat{y} - \hat{x}(\alpha, \beta, sh_v, sh_h)\|_2$
 $sh_v, sh_h \Rightarrow$ Vertical and horizontal shifts with respect to x-y axis
 $\alpha, \beta \Rightarrow$ Rotation angles about x-y axis with which the best matching block is rotated

Fig. 5 Four parameters identified by the algorithm in ascending order of their L_2 minimum.

Parameters	1	2	3	4	5	6	7	8	9	10	11
L_2 min-	414	431	447	458	476	506	514	534	552	587	592
sh_v	-22	-24	-22	-22	-22	-24	-24	-22	-24	-24	-22
sh_h	-1	-1	-1	-1	-1	-8	-9	-1	-6	-6	-1
α (in degrees)	-3	-2	-1	0	1	2	3	-6	-5	-4	5
β (in degrees)	3	2	1	0	-1	-2	-3	6	5	4	-5

Parameters	12	13	14	15	16	17	18	19	20	21
L_2 min-	608	625	643	663	686	729	778	784	793	799
sh_v	-22	-22	-22	-24	-22	-22	-22	-22	-22	-24
sh_h	-1	-1	-1	-11	-1	-1	-1	-1	-1	-13
α (in degrees)	6	7	9	-9	-7	10	8	-8	4	-10
β (in degrees)	-6	-7	-9	9	7	-10	-8	-8	-4	10

$L_2\text{-min} \Rightarrow \min_{\alpha, \beta, sh_v, sh_h} \|\hat{y} - \hat{x}(\alpha, \beta, sh_v, sh_h)\|_2$
 $sh_v, sh_h \Rightarrow$ Vertical and horizontal shifts with respect to x-y axis
 $\alpha, \beta \Rightarrow$ Rotation angles about x-y axis with which the best matching block is rotated

Fig. 6 Four parameters identified by the algorithm in ascending order of their L_2 minimum.

The process is repeated for all the other angles in that given range, and the block with the minimum L_2 value is selected as the best matching block to the block of interest. The position of this block in the inquiry block, relative to the center of the inquiry block, determines the vertical and horizontal translations, as Figs. 7 and 8 show. The angle for which this minimum is reached determines the rotation angle. The algorithm repeats similar steps for all other selected blocks of interest. The three parameters used to align the images are those that correspond to the median of the parameters determined as described above for all nine blocks of interest as Figs. 2–4 show. Finally, rigid transformations with these three parameters are applied to one of the images to align it with the other image.

The robustness of the registration guarantees our assumption that pixels in the follow-up scan will be either at the same location or nearby. To demonstrate registration accuracy and to show that this assumption holds we run two tests with real MR scans of size 384×384 and with synthetic MR images. More specifically:

a. In the first test, we run the co-registration step experiment 30 times using a pair of real MR images. Three parameters are computed for each experiment, as described above. The mean and standard deviation for each parameter is determined, and the results are displayed in Fig. 9. Vertical and horizontal shifts and their averages from 30 experiments computed from the co-registration step are shown in Figs. 9(a) and 9(b). Rotation angles calculated from the co-registration step of 30 experiments and their averages are shown in Fig. 9(c). The mean of the three parameters and their standard deviation are shown in Fig. 9(d). The error bars in Fig. 9(d) show that all three parameters obtained from 30 trials are closer to their mean, which explains the correctness of the co-registration step.

b. We also tested the co-registration accuracy with synthetic images created from real MR images. To validate the performance of our co-registration step, the test image is created by applying linear transformations on the reference image. The transformation set includes two translations, vertical and horizontal, and a rotation, chosen randomly in a range $[-20, 20]$, $[-16, 16]$, and $[-6, 6]$, respectively. Each triple obtained

Fig. 7 Top row: (a) and (b) Baseline and its follow-up MR images. its inquiry block **B** in cyan. A block of interest of size 25×25 , centered at pixels (198,120) is shown in (i) its corresponding inquiry block of size 65×65 is shown in (b). (c) Enlarged inquiry block with overlapping training blocks to form the learning dictionary. Middle row: four parameters identified by the algorithm in ascending order of their l_2 minimum. Bottom row: (d) block of interest **b**. (e) Inquiry block **B** with the first best eight matching blocks in red from 21 blocks determined by the algorithm for each angle of rotation. (f) the actual best eight blocks closest to the block of interest.

in this way forms the ground truth, meaning the true transformations that need to be applied to reference image to align with the test image. For each pair of synthetic images created in this way, we run the co-registration step which then computes three parameters, vertical and horizontal shifts and a rotation. To compare the computed and the true parameters, the differences between them are calculated; the mean and standard deviation of the differences are also computed, and the results are displayed in Fig. 10. This experiment is run 20 times. The differences of vertical and horizontal shifts and their averages from 20 experiments calculated from the co-registration step are shown in Figs. 10(a) and 10(b). The differences of the rotation angles calculated from the co-registration step of three experiments and their averages are shown in Fig. 10(c). Figure 10(d) shows the mean and standard deviation of the differences. The error bars in Fig. 10(d) show that all three parameters obtained from 20 experiments are closer to their mean. It can be easily seen that the absolute values of the differences for all three parameters ≤ 2 . This guarantees that after the co-registration step, pixels in the follow up will be either at the same location or close enough for any inquiry block of size ≥ 5 to contain the best matching block for a selected block of interest. A visual comparison of images in Fig. 11 clearly shows that the images obtained after the co-registration step, Fig. 11 third column, are aligned with their follow-ups.

2.3 Comparison of EigenBlockCD and Its Improved Version EigenBlockCD-2

In order for the initial EigenBlockCD algorithm to account for large shifts and rotations due to patient position, blocks of interest and their corresponding inquiry blocks need to be large. A small block of interest might not have enough structure that allows the l_2 norm to identify the best matching block from the reference image. Furthermore, if the inquiry block is not large enough, it might not contain the best matching block when the patient's position has significantly changed in the follow-up scan, that is, when shifts and rotations are large. Lesions that initially appear in the follow-up scan might be missed. Similarly, lesions that disappear in the next scan might also be missed. As the size of the inquiry block increases, the run-time of the initial algorithm significantly increases. To make it computationally efficient, the size of the blocks of interest and their corresponding inquiry blocks should be small. The best matching block for a selected block of interest is found by computing the l_2 minimization of the differences between the block of interest and all the training blocks in the projected local dictionary. These differences contain clinical-related changes (true positives), and insignificant changes due to the patient's position in the follow-up scans (false positives). The error of the algorithm consists of these insignificant changes and depends on the size of the inquiry block. As the radius

Fig. 8 Top row: (a) and (b) baseline and its follow-up MR images of sizes 384×384 , its Inquiry block B in cyan. A block of interest of size 25×25 , centered at pixels (198, 120) shown in (a) its corresponding inquiry block of size 65×65 shown in (b). (c) Enlarged inquiry block with overlapping training blocks to form the learning dictionary. Middle row: four parameters identified by the algorithm in ascending order of their l_2 minimum. Bottom row: (d) block of interest b . (e) Inquiry block B with the first best eight matching blocks in red from 21 blocks determined by the algorithm for each angle of rotation. (f) the actual best eight blocks closest to the block of interest.

of the inquiry block decreases, the l_2 norm of the differences between the block of interest and all the training blocks increases; hence, the error increases leading to the increase of false positives.

To overcome these limitations, we added the co-registration step to EigenBlockCD-2 as the key solution to solve this problem. By including the co-registration step, the performance of the algorithm is significantly improved in the following aspects:

- Automatically correcting large rotations and translations.
- Reducing the sizes of blocks of interest and their corresponding inquiry blocks, and hence reducing the computations and significantly improving the detection accuracy.

To compare the two versions of the algorithms, we run three tests with real MR scans of size 384×384 .

- In the first test, we run the experiment 10 times comparing their computational efficiency. Figure 12(a) shows the averages of the 10 run-times versus the radius of the inquiry blocks. As is shown in Fig. 12(a), the EigenBlockCD-2 algorithm detects change images close to the ground truth as confirmed by the radiologist in about 60 s. The two MR images

are of size 384×384 . In such a time, the EigenBlockCD algorithm detects both significant and insignificant changes due to shifts, rotations, and other acquisition-related artifacts, hence it produces more false positives, as shown in Figs. 13–15. It takes 2.49 h to obtain change images with $\delta = 7$ and $\Delta = 17$. And yet the change images have many false positives.

- In the second test, we show how the l_1 norm of the change image identified by both algorithms changes with the size of inquiry blocks as shown in Fig. 12(b), and hence how the error for each algorithm changes. For this pair of MR images used, it is clinically confirmed by the radiologist that the disease-related changes are very small. Therefore, we expect the l_2 norm of the desired change images to be small, hence the l_2 norm of the error to be small.
- This is also consistent with the results in the third test. We run the algorithms for three different pairs of real MR images, baselines and follow ups, with various sizes of inquiry blocks for EigenBlockCD, and with a fixed small size of inquiry blocks for EigenBlockCD-2, in the detection step. The radius of blocks of interest and inquiry blocks for the EigenBlockCD varies as $\delta = 2, 4, 5, 7$, and $\Delta = 5$,

Fig. 9 (a) and (b) Vertical and horizontal shifts from 30 experiments identified from the co-registration step. (c) Rotation angles of 30 experiments identified from the co-registration step. (d) Mean of the three parameters and their standard deviation. Co-registration parameters are along x-axis, vertical shift, horizontal shift, rotation angle. Values of these parameters are along the y-axis.

10, 13, 17. For the EigenBlockCD-2, we use two fixed pairs of δ and Δ . In the co-registration step, δ is 12 and Δ is 20, and then in the detection step both radii are considered small as $\delta = 2$ and $\Delta = 5$. By visually comparing the images given in Figs. 13–15, one can observe that the performance of EigenBlockCD converges to that of EigenBlockCD-2 as the size of the inquiry block increases.

The error between the block of interest from the test image and its best matching block from the reference image depends on the size of the inquiry block. As the radius of the inquiry block decreases, the error increases and vice versa. The co-registration step solves this problem. Figure 12(b) shows that the l_2 minimum value of this error for the EigenBlockCD algorithm is reached when the radius of the inquiry block is greater than the size of the shifts and rotations, $\Delta \geq 30$. The same minimum is reached by the EigenBlockCD-2 for $\Delta \geq 5$.

3 Selecting the Similarity Measure: L_1 Versus L_2

The choice of metric is critical in determining which block from the dictionary Φ is the “closest” to the block of interest **b**. Furthermore, the use of PCA requires that the projection of dictionary atoms onto eigensubspace preserves distances. We exploit the fact that the l_2 norm is invariant under an

orthonormal change of basis in the function space of image functions. This result does not hold for the l_1 norm, that is, the l_1 norm does not preserve the distance and order.

3.1 Similarity Measures- L_1 Norm Versus L_2 Norm

A 2-D MR image can be viewed as a matrix of pixels, where the value of each entry is the grayscale value of the corresponding pixel. An image can be represented as an N -dimensional vector, where N represents the total number of pixels in the image. This representation is the spatial domain and it is one of the infinitely many spaces in which the image can be examined. The eigenspace is one of the most interesting subspaces, which is created by the eigenvectors of the covariance matrix of the training data. Projection of the images into the eigensubspace has been widely used in image recognition or face recognition. First, a subspace is selected to project the images. Then, all the training images and the test images are projected into this subspace. Finally, the projected test image is compared to each projected training image using a distance measure. The training image which is the “closest” to the test image in terms of the selected distance measure is labeled as found. PCA is a linear transformation that can be used for reducing the dimensionality in a dataset. Unlike the other linear transforms, its basis vectors depend on the dataset; therefore, PCA does not have a fixed set of basis vectors. The first principal component is the direction in the feature

Comparison Between Computed and True Co-registration Parameter

Fig. 10 (a) and (b) Differences between true and computed vertical and horizontal shifts from 20 experiments. (c) Differences between true and computed rotation angles of 20 experiments. (d) Mean and standard deviation of the three differences. Co-registration parameters are along x-axis, vertical shift, horizontal shift, rotation angle. Values of the differences of these parameters are along the y-axis.

Fig. 11 (a) Baseline-reference image. (b) column-follow-up images from the first and fifth experiments with synthetic data. (c) column-corresponding reference aligned with its follow-up image. (d) Values of the ground-truth parameters and their corresponding computed ones by the co-registration step of the EigenBlockCD-2 algorithm.

Fig. 12 (a) Runtime of both algorithms versus the radius of inquiry block. (b) L_2 norm error between each block of interest and its best matching block versus the radius of inquiry block.

Fig. 13 (a) Two real T2 axial MR images of the brain of a patient at the lateral level. Baseline is an MR image taken in 2011, and follow-up scan in 2013. (b) Four change images via the EigenBlockCD. The radii of blocks of interest are $\delta = 2, 4, 5$, and 7 and the corresponding radii of inquiry blocks $\Delta = 5, 10, 13, 17$. (c) Change image obtained by the improved EigenBlockCD-2 with $\delta = 2$, and $\Delta = 5$.

space along which the projections have the largest variance. The second is the direction which maximizes the variance of all directions orthogonal to the first components. Similarly, each k -th principal component is the direction which maximizes the variance among all directions orthogonal to the previous $k - 1$ components. We extend this idea to find the changes between two MR images. Selecting the appropriate distance measure greatly affects the performance of the algorithm. It is useful to examine the performance of two metrics in the algorithms from both theoretical and practical point of views.

In the change detection problem for MR images, we are interested in identifying blocks from the reference image that are similar to the block of interest. In this case, similarity means that they have similar structural features with no or limited distortions in these features. Projecting data into the eigensubspace is similar to rotating the original system around the origin. When selecting the distance measure, or the similarity measure, we

need to keep in mind whether or not that measure preserves distances under an orthonormal change of basis. It can be easily proven that the l_2 norm is invariant under an orthonormal change of basis. The concept of vector space can be generalized to a function space spanned by a set of basis functions. Let us consider the function space of image functions. The inner product in this space is defined as

$$\langle f(x), g(x) \rangle = \int f(x) \overline{g(x)} dx. \quad (6)$$

The following theorem proves the well-known fact that the l_2 norm, as a distance measure, is invariant with respect to orthonormal projections. This means that if a vector is projected into an orthonormal subspace, then its magnitude computed via l_2 would not change. It is also true that the covariance between a set of vectors is invariant with respect to an orthonormal

Fig. 14 (a) Two real T2 axial MR images of the brain of a patient at the lateral level, baseline and follow-up scans. (b) Four change images via the EigenBlockCD. The radii of blocks of interest are $\delta = 2, 4, 5$, and 7 and the corresponding radii of inquiry blocks $\Delta = 5, 10, 13, 17$. Right: change image obtained by the improved EigenBlockCD-2 with $\delta = 2$, and $\Delta = 5$.

Fig. 15 (a) Two real T2 axial MR images of the brain of a patient at the lateral level, baseline and follow-up scans. (b) Four change images via the EigenBlockCD. The radii of blocks of interest are $\delta = 2, 4, 5$, and 7 and the corresponding radii of inquiry blocks $\Delta = 5, 10, 13, 17$. (c) Change image obtained by the improved EigenBlockCD-2 with $\delta = 2$, and $\Delta = 5$.

projection. In other words, the angles between vectors in one domain are equal to angles between their corresponding projections into an orthonormal subspace.

A 2-D image can be viewed as a function: $f: \mathbb{R}^2 \rightarrow \mathbb{C}$ for gray images and $f: \mathbb{R}^2 \rightarrow \mathbb{C}^3$ for color images.

Theorem 1. Let $\mathcal{P} = \{P(x) | x \in \mathbb{R}^2\}$ be an orthonormal basis, i.e., $\overline{P(x)} \times P(y) = 0$, for $x \neq y$ and, $\overline{P(x)} \times P(x) = 1$, for $x = y$. Denote the space spanned by this orthonormal basis as $\text{span}(\mathcal{P})$, $i \in \mathbb{Z}$. If $g(x) = \overline{P(x)} \times f(x)$ is the projected image of $f(x)$ into the orthonormal basis $\mathcal{P}$ then

$$\|g(x)\|_2 = \|f(x)\|_2. \quad (7)$$

Proof. From the definition of the l_2 norm of $f(x)$ and $g(x)$ we have

$$\|f(x)\|_2^2 = \int_{x \in X} |f(x)|^2 dx, \quad \text{and}$$

$$\|g(x)\|_2 = \int_{x \in X} |g(x)|^2 dx,$$

where $X \in \mathbb{R}^2$. Then

$$\begin{aligned}
 \|g(x)\|_2 &= \int_{x \in X} |g(x)|^2 dx \\
 &= \int_{x \in X} \overline{g(x)} g(x) dx \\
 &= \int_{x \in X} \{\overline{P(x)} f(x)\} \overline{P(x)} f(x) dx \\
 &= \int_{x \in X} \overline{f(x)} \{P(x) \overline{P(x)}\} f(x) dx \\
 &= \int_{x \in X} \overline{f(x)} f(x) dx \\
 &= \|f(x)\|_2^2.
 \end{aligned}$$

The result does not hold for the l_1 norm. We will illustrate this with both theoretical and numerical counter-examples in a 2-D space.

3.2 Counter Examples

3.2.1 Counter example 1a: preserving distances in two-dimension

Rotation is an isometric transform, preserving the Euclidean distances between two points or two segments, and it also preserves the angle between two segments. As shown in Fig. 16, when vector $\mathbf{AB}$ is rotated around origin O obtaining vector $\mathbf{A'B'}$, the l_2 norm is the same, but the l_1 norm is different. The only case when the l_1 norm is preserved is when the angle of rotation is a multiple of 90 deg, i.e., $\theta = k \times (\pi/2)$, for $k \in \mathbb{Z}$.

3.2.2 Counter example 1b: preserving distances in two-dimension

Let $\mathbf{x}_1$, $\mathbf{x}_2$, and $\mathbf{y}$ be three vectors in the 2-D space spanned by the traditional orthonormal basis $\mathbf{e}_1$ and $\mathbf{e}_2$.

$$\mathbf{x}_1 = \begin{bmatrix} -2 \\ 0 \end{bmatrix}, \quad \mathbf{x}_2 = \begin{bmatrix} -1 \\ 2 \end{bmatrix}, \quad \mathbf{y} = \begin{bmatrix} -5 \\ 4 \end{bmatrix}, \quad \mathbf{e}_1 = \begin{bmatrix} 1 \\ 0 \end{bmatrix},$$

and $\mathbf{e}_2 = \begin{bmatrix} 0 \\ 1 \end{bmatrix}$.

The distance between pairs $(\mathbf{x}_1, \mathbf{y})$ and $(\mathbf{x}_2, \mathbf{y})$ using l_1 and l_2 norms, respectively, are

Fig. 16 The l_2 norm is preserved when the cartesian system has been rotated around O with angle θ . This demonstrate that l_1 norm is not preserved. Note: θ is chosen such that the transformed vector, $\mathbf{A'B'}$, of $\mathbf{AB}$ under this rotation is vertical vector.

$$\begin{aligned}
 \|\mathbf{y} - \mathbf{x}_1\|_1 &= \sum_{i=1}^2 |y_i - x_{1i}| = |(-5) - (-2)| + |(4) - (0)| \\
 &= |-3| + |4| = 7,
 \end{aligned}$$

$$\begin{aligned}
 \|\mathbf{y} - \mathbf{x}_2\|_1 &= \sum_{i=1}^2 |y_i - x_{2i}| = |(-5) - (-1)| + |(4) - (2)| \\
 &= |-4| + |2| = 6.
 \end{aligned}$$

Similarly, we calculate the l_2 norm of the differences $\mathbf{y} - \mathbf{x}_1$ and $\mathbf{y} - \mathbf{x}_2$.

$$\begin{aligned}
 \|\mathbf{y} - \mathbf{x}_1\|_2 &= \left(\sum_{i=1}^2 |y_i - x_{1i}|^2 \right)^{\frac{1}{2}} \\
 &= \sqrt{[(-5) - (-2)]^2 + [(4) - (0)]^2} \\
 &= \sqrt{(-3)^2 + (4)^2} \\
 &= \sqrt{25} = 5,
 \end{aligned}$$

$$\begin{aligned}
 \|\mathbf{y} - \mathbf{x}_2\|_2 &= \left(\sum_{i=1}^2 |y_i - x_{2i}|^2 \right)^{\frac{1}{2}} \\
 &= \sqrt{[(-5) - (-1)]^2 + [(4) - (2)]^2} \\
 &= \sqrt{(-4)^2 + (2)^2} \\
 &= \sqrt{20} = 2\sqrt{5}.
 \end{aligned}$$

Let $\mathcal{P}$ be a matrix as shown below.

$$\mathcal{P} = \frac{1}{\sqrt{13}} \begin{bmatrix} 2 & 3 \\ -3 & 2 \end{bmatrix}.$$

It is easy to see that the columns, $\mathbf{p}_1$ and $\mathbf{p}_2$, of $\mathcal{P}$ form an orthonormal basis.

$$\langle \mathbf{p}_1, \mathbf{p}_2 \rangle = \begin{bmatrix} 2 & -3 \end{bmatrix} \begin{bmatrix} 3 \\ 2 \end{bmatrix} = 0 \quad \text{and}$$

$$\langle \mathbf{p}_i, \mathbf{p}_i \rangle = \frac{1}{13} [2^2 + (-3)^2] = 1, \quad \text{for } i = 1, 2.$$

Project all three vectors, $\mathbf{x}_1$, $\mathbf{x}_2$, and $\mathbf{y}$ onto this orthonormal basis $\mathcal{P}$ to obtain vectors $\mathbf{x}_1^p$, $\mathbf{x}_2^p$, and $\mathbf{y}^p$

$$\mathbf{x}_1^p = (\mathcal{P}^T)(\mathbf{x}_1) = \frac{1}{\sqrt{13}} \begin{bmatrix} 2 & -3 \\ 3 & 2 \end{bmatrix} \begin{bmatrix} -2 \\ 0 \end{bmatrix} = \frac{1}{\sqrt{13}} \begin{bmatrix} -4 \\ -6 \end{bmatrix},$$

$$\mathbf{x}_2^p = (\mathcal{P}^T)(\mathbf{x}_2) = \frac{1}{\sqrt{13}} \begin{bmatrix} 2 & -3 \\ 3 & 2 \end{bmatrix} \begin{bmatrix} -1 \\ 2 \end{bmatrix} = \frac{1}{\sqrt{13}} \begin{bmatrix} -8 \\ 1 \end{bmatrix},$$

$$\mathbf{y}^p = (\mathcal{P}^T)(\mathbf{y}) = \frac{1}{\sqrt{13}} \begin{bmatrix} 2 & -3 \\ 3 & 2 \end{bmatrix} \begin{bmatrix} -5 \\ 4 \end{bmatrix} = \frac{1}{\sqrt{13}} \begin{bmatrix} -22 \\ -7 \end{bmatrix},$$

then,

$$\mathbf{y}^p - \mathbf{x}_1^p = \frac{1}{\sqrt{13}} \begin{bmatrix} -18 \\ -1 \end{bmatrix}, \quad \text{and} \quad \mathbf{y}^p - \mathbf{x}_2^p = \frac{1}{\sqrt{13}} \begin{bmatrix} -14 \\ -8 \end{bmatrix}.$$

Finally, we calculate the distances between pairs $(\mathbf{x}_1^p, \mathbf{y}^p)$ and $(\mathbf{x}_2^p, \mathbf{y}^p)$ using l_1 and l_2 norms, respectively:

$$\begin{aligned} \|\mathbf{y}^p - \mathbf{x}_1^p\|_1 &= \sum_{i=1}^2 |y_i^p - x_{1i}^p| = \frac{1}{\sqrt{13}} (|-18| + |-1|) \\ &= \frac{19}{\sqrt{13}}, \end{aligned}$$

$$\begin{aligned} \|\mathbf{y}^p - \mathbf{x}_2^p\|_1 &= \sum_{i=1}^2 |y_i^p - x_{2i}^p| = \frac{1}{\sqrt{13}} (|-14| + |-8|) \\ &= \frac{22}{\sqrt{13}}, \end{aligned}$$

$$\begin{aligned} \|\mathbf{y}^p - \mathbf{x}_1^p\|_2 &= \left(\sum_{i=1}^2 |y_i^p - x_{1i}^p|^2 \right)^{\frac{1}{2}} \\ &= \frac{1}{\sqrt{13}} \sqrt{(-18)^2 + (-1)^2} \\ &= \frac{1}{\sqrt{13}} \sqrt{325} \\ &= \sqrt{25} = 5, \end{aligned}$$

$$\begin{aligned} \|\mathbf{y}^p - \mathbf{x}_2^p\|_2 &= \left(\sum_{i=1}^2 |y_i^p - x_{2i}^p|^2 \right)^{\frac{1}{2}} \\ &= \frac{1}{\sqrt{13}} \sqrt{(-14)^2 + (-8)^2} \\ &= \frac{1}{\sqrt{13}} \sqrt{260} \\ &= \sqrt{20} = 2\sqrt{5}. \end{aligned}$$

This example shows that for this specific case, the distance between two vectors, calculated using the l_2 norm, is invariant from the change of basis. In other words, it means that the l_2

norm preserves the distances between two vectors projected into any subspace spanned by an orthonormal basis

$$\|\mathbf{y} - \mathbf{x}_1\|_2 = 5 = \|\mathbf{y}^p - \mathbf{x}_1^p\|_2,$$

$$\|\mathbf{y} - \mathbf{x}_2\|_2 = 2\sqrt{5} = \|\mathbf{y}^p - \mathbf{x}_2^p\|_2.$$

A similar claim for the l_1 norm does not hold.

$$\|\mathbf{y} - \mathbf{x}_1\|_1 = 7 \neq \frac{19}{\sqrt{13}} = \|\mathbf{y}^p - \mathbf{x}_1^p\|_1,$$

similarly,

$$\|\mathbf{y} - \mathbf{x}_2\|_1 = 6 \neq \frac{22}{\sqrt{13}} = \|\mathbf{y}^p - \mathbf{x}_2^p\|_1.$$

Moreover,

$$\|\mathbf{y} - \mathbf{x}_1\|_1 = 7 > 6 = \|\mathbf{y} - \mathbf{x}_2\|_1, \quad \text{but,}$$

$$\|\mathbf{y}^p - \mathbf{x}_1^p\|_1 = \frac{19}{\sqrt{13}} < \frac{22}{\sqrt{13}} = \|\mathbf{y}^p - \mathbf{x}_2^p\|_1.$$

This counter example not only shows that the l_1 norm does not preserve distances, but also shows that the l_1 norm is not order invariant from the change of basis, or in other words, it does not preserve the order. In our algorithm, we seek to find the block which is the “closest” to the block of interest.

3.2.3 Counter example 2: real MR data

In this example, we consider data from real MR images. We select the “block of interest” $\mathbf{b}$ of size 2×2 from the test image:

$$\mathbf{b} = \begin{bmatrix} 116 & 123 \\ 128 & 120 \end{bmatrix}.$$

The inquiry block, $\mathbf{B}$, in the reference image, is a block of pixels containing the block similar to the “block of interest.” For this counter example, we consider the inquiry blocks of size 4×4 . As similarity measures we use both l_1 and l_2 norms. We create a dictionary Φ by extracting $\mathbf{a}_k$ blocks from the inquiry block with the same size as the “block of interest,” $k = 1, 2, \dots, 16$. Block $\mathbf{a}_k$ serve as the training blocks. As

Fig. 17 (a) The reference image, upper left is the magnified “Inquiry Block” $\mathbf{B}$ in cyan, with many overlapping training blocks, $\mathbf{a}_k$, in yellow. (b) Dictionary Φ formed by stacking $\mathbf{a}_k$ training blocks into column vectors. (c) Test image showing the “block of interest $\mathbf{b}$ ” enlarged in cyan color.

shown in Fig. 17, both $\mathbf{b}$ and $\mathbf{a}_k$ blocks are stacked into column vectors, denoted as $\mathbf{x}_k$ and $\mathbf{y}$, respectively, and will be projected into the eigensubspace spanned by the eigenvectors of the dictionary atoms (the training blocks). The inquiry block $\mathbf{B}$ is

$$\mathbf{B} = \begin{bmatrix} 114 & 125 & 130 & 117 \\ 111 & 115 & 136 & 114 \\ 115 & 130 & 148 & 139 \\ 135 & 133 & 151 & 167 \end{bmatrix}.$$

$$\Phi = \begin{bmatrix} 114 & 125 & 130 & 117 & 111 & 115 & 136 & 114 & 115 & 130 & 148 & 139 & 135 & 133 & 151 & 167 \\ 111 & 115 & 136 & 114 & 115 & 130 & 148 & 139 & 135 & 133 & 151 & 167 & 95 & 104 & 113 & 77 \\ 125 & 130 & 117 & 93 & 115 & 136 & 114 & 100 & 130 & 148 & 139 & 133 & 133 & 151 & 167 & 148 \\ 115 & 136 & 114 & 100 & 130 & 148 & 139 & 133 & 133 & 151 & 167 & 148 & 104 & 113 & 77 & 57 \end{bmatrix}.$$

We calculate distances, using the l_1 and l_2 norms, between pairs $\mathbf{y}$ and each column $\mathbf{x}_k$ of the dictionary Φ . Similarly, we calculate distances between the corresponded projected pairs into the eigenspace, $\tilde{\mathbf{y}}$ and each column vector $\tilde{\mathbf{x}}_k$ of the dictionary $\tilde{\Phi}$. We are seeking to find

$$\min_k \|\mathbf{y} - \mathbf{x}_k\|_1, \quad \min_k \|\tilde{\mathbf{y}} - \tilde{\mathbf{x}}_k\|_1, \quad \min_k \|\mathbf{y} - \mathbf{x}_k\|_2, \\ \min_k \|\tilde{\mathbf{y}} - \tilde{\mathbf{x}}_k\|_2,$$

for $k = 1, 2, \dots, 16$.

Figure 18 shows the result of these distances.

The minimum for each row is shown in red. In Fig. 18, the last two columns are identical, showing that the l_2 distances between the “block of interest” and each training block from the “inquiry block” in the reference image are equal both in image and in the eigenspace domain. We further observe that in both image domain and the eigenspace, the l_2 minimum is achieved at the ninth original dictionary atom and its projection. That is, the l_2 minimization in either image domain or the eigenspace selects the same training block as the closest to the block of interest. Figure 18 also shows that this does not hold for the l_1 norm. The first two rows of the table show that the l_1 norm does not produce the same values for pairs of vectors in the image domain and pairs of their projections into the eigenspace. Moreover, the l_1 norm does not preserve the order as well. To see this, consider the pairs in blue.

$$45.0 = \|\mathbf{y} - \mathbf{x}_2\|_1 > \|\mathbf{y} - \mathbf{x}_6\|_1 = 44.0,$$

$$41.5 = \|\tilde{\mathbf{y}} - \tilde{\mathbf{x}}_2\|_1 < \|\tilde{\mathbf{y}} - \tilde{\mathbf{x}}_6\|_1 = 57.7.$$

Similarly, consider pairs in green.

$$78.0 = \|\mathbf{y} - \mathbf{x}_{13}\|_1 > \|\mathbf{y} - \mathbf{x}_{14}\|_1 = 76.0,$$

$$\begin{pmatrix} \|\mathbf{y}_{ij} - \mathbf{x}_k\|_1 = 26.0 & 45.0 & 34.0 & 65.0 & 36.0 & 44.0 & 68.0 & 49.0 & 28.0 & 75.0 & 118.0 & 100.0 & 78.0 & 76.0 & 137.0 & 190.0 \\ \|\hat{\mathbf{y}}_{ij} - \hat{\mathbf{x}}_k\|_1 = 32.1 & 41.5 & 27.4 & 70.7 & 35.4 & 57.7 & 68.7 & 53.5 & 27.7 & 75.4 & 110.2 & 95.4 & 69.7 & 75.6 & 115.1 & 145.0 \\ \|\mathbf{y}_{ij} - \mathbf{x}_k\|_2 = 17.9 & 23.6 & 18.2 & 38.7 & 18.9 & 31.0 & 35.2 & 28.7 & 16.4 & 42.5 & 63.4 & 54.2 & 42.5 & 41.2 & 72.4 & 99.0 \\ \|\hat{\mathbf{y}}_{ij} - \hat{\mathbf{x}}_k\|_2 = 17.9 & 23.6 & 18.2 & 38.7 & 18.9 & 31.0 & 35.2 & 28.7 & 16.4 & 42.5 & 63.4 & 54.2 & 42.5 & 41.2 & 72.4 & 99.0 \end{pmatrix}$$

Fig. 18 Rows one and three: results of l_1 and l_2 norm in image domain of the differences between the “block of interest” and training blocks. Rows two and four: results of l_1 and l_2 norm of the differences between the projected “block of interest” and training blocks onto eigenspace domain.

Extract training block $\mathbf{a}_k$ from the “inquiry block” $\mathbf{B}$. Stack $\mathbf{b}$ as a column vector $\mathbf{y}$ and stack $\mathbf{a}_k$ ’s as column vectors to form a dictionary of size 4×6 .

$$\mathbf{y} = \begin{bmatrix} 116 \\ 128 \\ 123 \\ 120 \end{bmatrix}.$$

Dictionary Φ is

$$69.7 = \|\tilde{\mathbf{y}} - \tilde{\mathbf{x}}_{13}\|_1 < \|\tilde{\mathbf{y}} - \tilde{\mathbf{x}}_{14}\|_1 = 75.6.$$

In summary, the choice of metric is vital to reserve consistent solutions from the image space to the eigenspace. The l_1 norm fails to preserve the distance ordering and may produce different solutions in the image space and the eigenspace. Meanwhile, the l_2 norm is certainly invariant from the change of orthogonal basis and preserves the distance ordering. Hence, the solution given by the l_2 minimization is consistent in both the image space and the eigenspace.

3.2.4 Counter example 3: preserving structure real MR data

The next logical question to ask is: does the inconsistency of the l_1 minimization in different spaces matter visually? What is the visual similarity between the solutions given by the l_1 - and l_2 -minimization and the block of interest? To answer these questions, we experimented with blocks of bigger sizes, see Fig. 19, to observe whether the structure, between the “inquiry block” and the block chosen from Φ via l_1 and l_2 norms in both spatial and eigenspace domain, is preserved.

In this example, the size of the “block of interest” and of all the training blocks 19×19 , and the “inquiry block” is of size 37×37 . Figure 19 shows that the block determined via l_2 minimization in spatial and eigenspace domain has a similar structure to the block of interest. We obtain the same block in the image space and in eigensubspace when the l_2 norm is used, but two different blocks if the l_1 norm is used. The block outlined in magenta, as shown in Fig. 19(e), is obtained by l_1 minimization in eigenspace and has significantly different structure from the block of interest [see Fig. 19 (c)] and to the other three solutions given by the l_1 minimization in the image space [see Fig. 19(d)], the l_2 minimization in the image space (see Fig. 19(f)) and in the eigenspace [see Fig. 19(g)].

Fig. 19 (a) and (c) Block of interest **b**. (b) Inquiry block **B**. (d) and (e) Blocks obtained via l_1 norm minimization in spatial and eigenspace domain respectively. (f) and (g) Blocks obtained via l_2 norm minimization in spatial and eigenspace respectively.

4 Performance Analysis

4.1 Performance Analysis Overview

Performance analysis of the change detection methods is essential to the design of automatic change detection systems for MR images. Such an analysis should take all possible nonsignificant changes into account. Here, we provide a complete mathematical characterization of the EigenBlockCD-2 performance in the presence of such changes. We also thoroughly discuss the results of several performance measures as applied to the EigenBlockCD-2 and the AEDL⁸ algorithms. To validate the performance, the obtained performance prediction, or the ground truth, is compared to the results obtained by the algorithms with synthetic MR Images for which the ground truth is known. For the purposes of this study, we have used both quantitative and qualitative performance measures utilized in previous works.^{1,2,10} We calculated the following performance measures: GT/IP (ratio of number of ground truth pixels and the total number of image pixels), percentage correct classification (PCC), Jaccard, Yule, Sensitivity, Specificity, and SSIM (structure similarity). We briefly describe these performance measures in this section and the simulation results are included in Sec. 5.

4.2 Performance Measures

Performance measures tell us how well an algorithm performs when its output is compared with an output from a well-established algorithm, which is called the gold standard or the ground truth, which sometimes is the exact truth. We have designed the ground-truth image for validating the results. These measures are based on the unions, intersections, and complements of the ground-truth images and the computed change images obtained by the algorithms. The first six measures, PCC, Jaccard, Yule, sensitivity, specificity, are, in fact, binary measures with 1 if change or no-change is correctly detected and 0 otherwise. The last measure, SSIM, takes the structure similarity between two images into account. Binary measures which depict change or no change, are computed based on four sets of data.

We denote with IP the total number of image pixels, i.e., $M \times N$ where M and N are the dimensions of an image, e.g., 256×256 . GT stands for the ground-truth image, which contains only significant changes. Ground truth represents the total number of true changed pixels. The computed change (CC) image represents the change image obtained by an

algorithm, or the total number of changed pixels detected by an algorithm.

Let FP be the difference between CC and GT, FN be the difference between GT and CC, TP be the intersection of GT with CC, and TN be the complement of the union of GT with CC.

We describe six quantitative measures and we will apply five of them to validate our algorithms. The PCC measure is the most commonly used performance measure with values in the range $[0,1]$. It represents the ability of the algorithm to correctly detect changes (TP) and nonchanges TN. PCC values close to 1 indicate a higher performance of an algorithm. The PCC ratio approaches 1 if the ground truth change image contains very few changes, or if the ratio $(GT/IP) \leq 0.043$.¹¹ Therefore, it is not a sufficient measure for images that have undergone little change.

$$PCC = \frac{TP + TN}{TP + FP + TN + FN}. \quad (8)$$

Some authors have used only the detection of changed pixels to measure the performance of a change detection algorithm. If TN is excluded from Eq. (8) of the PCC definition, the Jaccard measure is obtained:

$$Jaccard = \frac{TP}{TP + FP + FN}. \quad (9)$$

The Jaccard measure gives values in $[0, 1]$. It is easy to see from Eq. (9) that higher values of this measure indicate a higher performance of an algorithm. Yule is another quantitative performance measure in $[-1,1]$.

$$Yule = \frac{TP}{TP + FP} + \frac{TN}{TN + FP} - 1. \quad (10)$$

Sensitivity measures the probability that an algorithm correctly detects true changes. Equation (11) is used to calculate the sensitivity value:

$$Sensitivity = \frac{GT \cap CC}{GT} = \frac{TP}{TP + FN}. \quad (11)$$

Specificity measures the probability that an algorithm correctly detects nonchanges and it is given by Eq. (12):

$$\text{Specificity} = \frac{\text{TN}}{\text{TN} + \text{FP}} = \frac{(\text{IP} - \text{GT}) \cap (\text{IP} - \text{CC})}{\text{IP} - \text{CC}}. \quad (12)$$

The similarity index (SI) or kappa index with values in [0,1] is defined as the ratio of twice the common area to the sum of individual areas:

$$\text{SI} = 2 \times \frac{\text{GT} \cap \text{CC}}{\text{GT} \cup \text{CC}} = 2 \times \frac{\text{TP}}{\text{TP} + \text{FP} + \text{FN}}. \quad (13)$$

The structural similarity index SSIM¹² measures the similarity between two images by introducing structural information, where one of the images is being compared, provided the other image is regarded as of perfect quality:

$$\text{SSIM}(I_1, I_2) = \frac{(2\mu_1\mu_2 + C_1)(2\sigma_{12} + C_2)}{(\mu_1^2 + \mu_2^2 + C_1)(\sigma_1^2 + \sigma_2^2 + C_2)}, \quad (14)$$

where μ_1, μ_2, σ_1 , and σ_2 , are the mean and the standard deviation of the baseline and its follow-up images, respectively, and σ_{12} is the covariance between them as shown below:

$$\mu_s = \frac{1}{N_1 + N_2} \sum_{i=1}^{N_1} \sum_{j=1}^{N_2} \mathbf{I}_s(i, j), \quad \text{for } s \in \{1, 2\},$$

$$\sigma_s = \left(\frac{1}{N_1 + N_2 - 1} \sum_{i=1}^{N_1} \sum_{j=1}^{N_2} (\mathbf{I}_s(i, j) - \mu_s)^2 \right)^{\frac{1}{2}},$$

for $s \in \{1, 2\}$,

$$\sigma_{12} = \frac{1}{N_1 + N_2 - 1} \sum_{i=1}^{N_1} \sum_{j=1}^{N_2} [\mathbf{I}_1(i, j) - \mu_1][\mathbf{I}_2(i, j) - \mu_2],$$

where $\mathbf{I}_1(i, j)$ and $\mathbf{I}_2(i, j)$ represent the pixel intensity of the baseline image and its follow-up at (i, j) location. $C_1 = (k_1 L)^2$, $C_2 = (k_2 L)^2$, $k_1 = 0.01$, $k_2 = 0.03$, and $L = 2^{(\# \text{of bits per pixel})} - 1$, (i.e., $L = 255$ for gray-scale images).

5 Simulations

Here, we describe the experiments and results. First, we design the reference image. The test image is created by applying two types of changes to the reference image, significant and insignificant. We are able to control both types of changes as shown in Fig. 20. Significant changes regarded as the ground truth include enlargement, shrinkage, disappearance, intensity changes of an existing lesion, and appearance of new shapes or lesions as shown in Fig. 20 Column (c).

5.1 Simulations with Synthetic Images

The reference image as shown in Fig. 20 Column (a) is created by stacking three image strips of size $(L/3) \times L$, where $L = 129$. Therefore, the reference image is of size $L \times L$. For each strip:

- We place three polygons with vertices that are created at random within a given range.

Fig. 20 Column (a): Reference image. Column (b): Test image having the same significant changes and shifts, rotation, noise as insignificant changes. Column (c): Ground truth. Columns (d) and (e) computed change images between reference and test images via EigenBlockCD-2 and Simple Differencing respectively.

- Each polygon is filled with intensities whose distribution is Gaussian, using a maximum intensity chosen at random in $[0.45, 0.55]$, $[0.35, 0.45]$, and $[0.25, 0.35]$, respectively, from left to right.
- Four test images, as shown in Fig. 20 Column (b), are obtained from each reference image by applying two kinds of changes:
 - Insignificant changes: shift, rotation, and noise. These changes will mimic the changes due to patient position, contrast changes, and other acquisition-related artifacts.
 - Horizontal and vertical shift sizes are chosen at random in $[-5, 5]$.
 - Rotation angles are chosen at random in $[-5, 5]$.
 - White Gaussian noise, with signal-to-noise ratio (SNR) chosen at random in $[25, 55]$.
 - Changes in intensity due to changes in field inhomogeneity.
- Significant changes forming the ground truth, as shown in Fig. 20 Column (c), include clinical changes to an existing lesion and the appearance of new lesions.
 - a. We considered the following changes for an existing lesion:
 - Enlargement which mimics whether a lesion has grown between time t_1 and its follow up t_2 .
 - Shrinkage of a lesion showing whether a lesion has shrunk between the two examination times.

Statistical Analysis: Mean of 100 Experiments - Insignificant Changes are due to changes in:								
Measures	Shifts		Rotations		Shifts & Noise		Shifts & Intensity	
	Simple Differencing	EigenBlockCD-2	Simple Differencing	EigenBlockCD-2	Simple Differencing	EigenBlockCD-2	Simple Differencing	EigenBlockCD-2
GT/IP	0.0231	0.0231	0.0295	0.0295	0.0334	0.0334	0.0405	0.0405
PCC	0.9690	0.9934	0.9857	0.9953	0.8246	0.9826	0.9810	0.9903
Jaccard	0.3102	0.5809	0.5427	0.6747	0.3351	0.7377	0.5746	0.6957
Yule	0.3103	0.7383	0.6073	0.8676	0.1522	0.7342	0.6101	0.7713
Sensitivity	0.3381	0.7415	0.6181	0.8693	0.3412	0.7514	0.6260	0.7778
Specificity	0.9961	0.9965	0.9962	0.9969	0.9940	0.9992	0.9962	0.9965
SSIM	0.9998	0.9999	0.9999	1.0000	0.9997	0.9999	0.9998	0.9999

Fig. 21 Mean of the performance measures of the first 100 experiments. The significant changes include enlargement, shrinkage, noise, intensity changes, appearance, and disappearance of shapes. The insignificant changes are due to shifts, rotations, shifts and noise, and shifts and intensity changes.

- Disappearance of a lesion present in the previous scan, but it has disappeared in the follow up.
 - Intensity changes of an existing shape which has clinical significance for a patient.
- b. Appearance of a new shape which mimics the appearance of a new lesion.

The change image, as shown Fig. 20 Columns (d) and (e), is computed via the EigenBlockCD-2 and simple differencing algorithms for each pair of reference and test images. Performance measures are calculated by comparing the ground truth with the change image obtained from each algorithm. We calculate the following performance measures: GT/IP (ratio of number of ground-truth pixels and the total number of image pixels), PCC, Jaccard, Yule, sensitivity, specificity, and SSIM (structure similarity). The experiment runs 100 times and the mean is determined for each measure as shown in Fig. 21. The reference and test image pairs, created as described above, are different for each experiment, because of the randomness of the vertices of the polygons, the randomness of their intensities, noise level, rotation angles, translation sizes, and level of intensity changes.

5.2 Simulations with Serial MR Images

We also created a series of images from real MR images. In order to validate the proposed change detection methods quantitatively and qualitatively, we simulated lesions and applied them to real MR images. Because the exact sizes and locations

of each lesion are known, we regard them as the ground truths. Figure 22 shows an example of a serial MR images created from T2 transversal real MR scan, called the reference image.

Taking into consideration what a radiologist might be looking in a follow-up MR scan, we simulated seven lesions by applying two kinds of changes: insignificant and significant changes. Significant changes, which make up the ground truth, include enlargement, shrinkage, disappearance, intensity changes of an existing lesion, and also the appearance of a new lesion. Four ground-truth images corresponding to pairs (reference, first follow up), (first follow up, second follow up), (second follow up, third follow up), and (third follow up, fourth follow up) are designed as shown in Fig. 22. Insignificant changes include horizontal and vertical shifts, clockwise and counterclockwise rotations, change in contrast, and different noise levels. Horizontal and vertical shift sizes are chosen at random in the range $[-5, 5]$, rotation angles are chosen at random in the range $[-5, 5]$, white Gaussian noise is chosen at random with SNR in range $[25, 55]$. Intensity values are chosen randomly in $[0.2, 0.5]$ and coordinates of the vertices for each polygon are generated randomly.

Six lesions were inserted into the reference image, Fig. 22, labeled with numbers from 1 to 6. Lesion 7 will appear in the first follow up. Some of these shapes act as inactive lesions and the other remaining shapes mimic active lesions. Lesion 1 is inactive in the first follow up, disappears in the second and it remains gone. Lesion 2 stays inactive in the first and second follow ups, then it grows for the next two follow ups. Lesion 3 is inactive and stays inactive during all five scans. Lesion 4 shrinks in the next three scans until it disappears in the last scan. Lesion 5 grows in the first follow up and then it shrinks

Fig. 22 From left to right: reference image, first, second, third and fourth follow-up images, respectively.

Fig. 23 Top row from left to right: reference image, first, second, third, and fourth follow-up images, respectively. Columns (a)–(d) are the changes between two consecutive MR images. Second, third, and fourth rows from left to right: Ground truth containing only significant changes between two consecutive MR images, change images computed via EigenBlockCD-2 algorithm, and change images computed via simple differencing.

until it disappears in the last scan. Lesion 6 is present in the reference image, it disappears in the next follow up and it remains gone in the rest of scans. Lesion 7 appears as a new lesion in the first follow up, it grows in the next two scans, and then it shrinks in the last scan.

The change image, Fig. 23 rows (3) and (4), is computed via simple differencing and EigenBlockCD-2 algorithms. The computed change image is compared to the ground truth based on the performance measures discussed earlier. We performed 48 experiments, with random significant and insignificant changes applied to test images, consisting of horizontal and vertical shifts, rotations, intensity changes of a lesions, enlargements of lesions, shrinkage, appearance, and disappearance of lesions. The mean of the results is shown in Fig. 24. We compared our results with the results of several algorithms as presented by their authors,^{1,2,8,10} which are shown in Table 1.

5.3 Simulations with Real Images

We also ran experiments with real MR data. The initial global co-registration step of two MR images taken in 2010 and 2012, namely the reference and test images both of size 384×384 , are shown in Figs. 2–4. Blocks of interest, selected randomly from nine inner areas from the test image, are of size 25×25 , and their corresponding inquiry blocks in the reference image are of size 65×65 . The maximum values of vertical and horizontal translations are half of the inquiry block **B** linear dimension, i.e., translation parameters of Figs. 2–4 are in the range $[-32, 32]$ pixels and rotation angles $\in [-10, 10]$ deg.

For each selected angle, the block picked is among $65^2 = 4225$ blocks, yielding 21 blocks picked for all angles. In Fig. 2, the l_2 minimum was reached for vertical shift = -20 , horizontal shift 1, and rotation angles about x of -1 .

Statistical Analysis: Mean of 48 Experiments with Serial MR Images							
Measures	GT/IP	PCC	Jaccard	Yule	Sensitivity	Specificity	SSIM
Differencing	0.0082	0.35952	0.0327	-0.6218	0.03267	1.00000	0.99832
EigenBlockCD-2	0.0082	0.99883	0.75584	0.75467	0.75584	1.00000	0.99999

Fig. 24 Mean for the performance measures of 48 experiments. The significant changes include enlargement, shrinkage, noise, intensity changes, appearance, and disappearance of shapes. The insignificant changes are due to shifts, rotations, noise level, and changes in the contrast.

Table 1 Performance measures comparing algorithms presented in Ilsever and Unsalan,¹⁰ Patriarche,^{1,2} AEDL⁸ and EigenBlockCD-2.

Algorithms	PCC	Jaccard	Yule	Sensitivity	Specificity	SSIM
Image differencing	0.8082	0.1888	0.4451			
Image rationing	0.8054	0.2202	0.4072			
Image regression	0.8024	0.1861	0.3971			
CVA	0.8081	0.1809	0.4512			
Fuzzy XOR	0.8023	0.1044	0.4783			
Background Sub	0.7945	0.2125	0.4285			
CD-change detector				[0.68, 94]	[0.91, 1.0]	
CS-classify subtract				[0.55, 65]	[0.80, 98]	
AEDL	0.9989	0.7653	0.7653	0.755	1.0	1.0
EigenBlockCD-2	0.9988	0.7558	0.7547	0.7735	0.999	0.9999

Hence, the reference image is rotated 1 deg clock-wise, shifted 20 pixels down and one to the left to be aligned with test image as shown in Fig. 2 column (c). Figures 7 and 8 show that the l_2 minimum for one block of interest is reached for a rotation angle with x -axis of -3 deg. A block of interest of size 25×25 and centered at pixels (198, 120) and at (198, 250) and their corresponding inquiry blocks **B** in cyan color of sizes 65×65 from the reference image are selected. Column (e) in the second rows of Figs. 7 and 8 show that the best eight matching blocks from the inquiry block (in red) are positioned at the top middle location of the inquiry block, that is 22 pixels above the center of the inquiry block and one pixel to the right from it. In other words,

this means that the reference image needs to be shifted 22 pixels down, and one pixel to the left to be aligned with the test image.

Change image via EigenBlockCD-2 results with real MR data is shown in Fig. 25. Columns (a)–(c), and the first and second rows show selected axial T2 images of the brain of a patient at the level of the lateral ventricles who had undergone serial MRIs in 2011 and 2013. The third row shows changes obtained by EigenBlockCD-2 algorithm, overlaid onto the MR 2013 image. Column d shows the selected axial T2 image of the brain of another patient who had undergone serial MRIs in 2010 and 2012.

Fig. 25 First row: Axial T2 images of the brain of two patients at the level of the lateral ventricles. Second row: Corresponding follow-up images of the same patients. Third row: Overlay change images computed via EigenBlockCD-2 algorithm onto the follow-up images.

6 Discussions

In this section, we discuss the results of performance analysis for our algorithms and compare the results with several published works. We validate our algorithms based on the performance measures discussed in Sec. 4.

6.1 Performance Analysis for Synthetic Images

It is difficult to provide a fair comparison among automatic change detection algorithms because there is no gold standard and codes of state-of-the-art methods are not publicly available.⁴ Rousseau et al.¹³ evaluated the performance of their methods on simulated lesion images and reported their SI (kapa index) value of around 0.75. Shen et al.¹⁴ tested their lesion detection method based on segmentation to lesions generated from simulated brain database and reported their SI values on the simulated target slices with 20%, 40%, and 60% intensity reduction as 0.867, 0.879, and 0.724, respectively. The Seo and Milanfar method⁴ obtained an average value of 0.879 for SI. As an overall measure of performance, they were able to achieve sensitivity = 0.877, specificity = 0.998, and similarity index (SI) = 0.879. They claim that it performs comparably with the method used by Shen et al. and outperforms the method used by Rousseau.¹³ Ilsever and Unsalan¹⁰ used three measures: PCC, Jaccard, and Yule coefficient.

Patriarche and Erickson^{1,2} also used sensitivity and specificity measures to validate their algorithm. Patriarche and Erickson obtained values of SI in the range [0.54–0.94] with P -value = 0.004 and SI values in the range [0.71–0.96] for P -value = 0.008. The specificity values they obtained are in the range [0.87–1] with P -value = 0.035.

We show the mean of 100 experiments in Fig. 21. The low ratios of the GT/IP yield very high mean values for PCC measure. Mean values of the Jaccard measure for EigenBlockCD-2 are 0.5809, 0.6747, 0.7377, and 0.6957 which are higher than the mean value for Jaccard measure obtained by simple differencing, 0.3102, 0.5427, 0.3351, 0.5746, respectively, and are also much higher than the 0.2202 value reported from Ilsever and Unsalan¹⁰ for the image rationing.

Mean values of Yule measure for EigenBlockCD-2 are 0.7383, 0.8676, 0.7342, and 0.7713, respectively, higher than 0.3103, 0.6073, 0.1522, and 0.6101 which are the mean values for the Yule measure obtained by simple differencing, and much higher than the 0.4783 value reported from Ilsever and Unsalan¹⁰ for a fuzzy XOR algorithm. Mean values of sensitivity measure for EigenBlockCD-2 are 0.7415, 0.8693, 0.7514, and 0.7778, respectively, higher than 0.3381, 0.6181, 0.3412, and 0.6260 which are the mean values for the sensitivity measure obtained by simple differencing, and they are comparable with the 0.877 value reported from Seo and Milanfar⁴ for their own algorithm. Finally, the mean values of SSIM and specificity measure for EigenBlockCD-2 are close to one, showing that the computed change images have similar structures to the ground truth as Fig. 20 shows. In other words, this means that both algorithms detect significant clinical changes from one scan to another while ignoring the insignificant changes due to patient position and other acquisition-related artifacts.

6.2 Performance Analysis for Simulated Serial MR Images

We performed 48 experiments, with random significant and insignificant changes applied to test images, consisting of

horizontal and vertical shifts, rotations, intensity changes of a lesions, enlargements of lesions, shrinkage, appearance, and disappearance of lesions. The reference image and its four follow ups of one of the experiments are shown in Fig. 23. Lesion 1 is inactive at first and then disappears, lesion 2 has grown on the third and fourth follow ups, lesion 3 is always inactive, lesion 4 shrinks until it disappears, lesion 5 grows at first then shrinks until it disappears, lesion 6 disappears, and lesion 7 appears at the second follow up then grows. Our improved algorithm computes change images very close, in terms of their structure, to the ground truth image as confirmed by the radiologist and are shown in Fig. 23. The mean of the results, as shown in Table 1, are compared with the results of several algorithms as presented by their authors.^{1,2,8,10}

6.3 Performance of EigenBlockCD-2 for Real MR Images

The initial global co-registration step of two MR images taken in 2010 and 2012 of sizes 384×384 are shown in Figs. 2–4, 7, and 8. The best matching block is selected by minimizing the l_2 norm of the difference between the block of interest and the columns of the learning dictionary projected into the eigensubspace.

Figures 7(e) and 8(e) show that the best eight matching blocks from the inquiry block (in red) are positioned at the top middle location of the inquiry block, that is 22 pixels above the center of the inquiry block and one pixel to the right. The reference image needs to be rotated 3 deg counter-clock wise, shifted 22 pixels down, and one pixel to the left to be aligned with test image.

In Fig. 25, columns (a) to (c) of the second row, follow-up images demonstrate multiple periventricular foci of the increased signal. A few of these foci show interval enlargement with the largest on the follow-up images, which are shown on the corresponding overlay image highlighting these regions in the third row as significant changes between the two scans as is confirmed by the radiologist. Images shown in column (c) are at the level of the lateral ventricles and demonstrate a large and several smaller hyperintense foci in the periventricular region on both the initial (first row) and follow-up (second row) images without an interval change in size or intensity evident. The corresponding overlay image, third row, shows no interval change.

7 Conclusions

In this paper, we proposed an improved version of change detection algorithm, the EigenBlockCD-2, for MR images. It is based on the l_2 minimization and dictionary learning techniques. We tested the performance of our algorithm by using both quantitative and qualitative performance measures. To the best of our knowledge, our algorithm is one of the few that detects the changes of MR images without preprocessing steps. The improved EigenBlockCD-2 algorithm accounts for large translations and rotations by updating its parameters from the data at the local block level. We provide a complete performance analysis and discuss the benefits of using the l_2 norm over l_1 norm. The results show that our method performs better than existing change detection methods.

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References

1. J. Patriarche and B. Erickson, "Part 1. Automated change detection and characterization in serial MR studies of brain-tumor patients," *J. Digital Imaging* **20**(3), 203–222 (2007).
2. J. Patriarche and B. Erickson, "Part 2. Automated change detection and characterization applied to serial MR of brain tumors may detect progression earlier than human experts," *J. Digital Imaging* **20**(4), 321–328 (2007).
3. M. Bosc et al., "Automatic change detection in multi-modal serial MRI: application to multiple sclerosis lesion evolution," *NeuroImage* **20**(2), 643–656 (2003).
4. H. Seo and P. Milanfar, "A non-parametric approach to automatic change detection in MRI images of the brain," in *Proc. IEEE International Symposium On Biomedical Imaging: From Nano to Macro*, pp. 245–248, IEEE, Boston, MA, (2009).
5. J. Wright et al., "Robust face recognition via sparse representation," *IEEE* **31**(2), 210–227 (2009).
6. J. Wright et al., "Sparse representation for computer vision and pattern recognition," *Proc. IEEE* **98**(6), 1031–1044 (2010).
7. L. Nguyen and T. Tran, "A sparsity driven joint image registration and change detection technique for SAR imagery," in *Proc. Int. Conf. on Acoustic Speech and Signal Processing*, pp. 2798–2801 (2010).
8. V. Nika, P. Babyn, and H. Zhu, "AEDL algorithm for change detection in medical images an application of adaptive dictionary learning techniques," in *Proc. 15th Int. Conf. on Medical Imaging Computing and Computer Assisted Intervention*, pp. 14–21, MICCAI: STMI, (2012).
9. V. Nika, P. Babyn, and H. Zhu, "EigenBlock algorithm for change detection an application of adaptive dictionary learning techniques," *J. Comput. Sci.* **5**(3), 527–535 (2013).
10. M. Ilsever and C. Unsalan, *Two-Dimensional Change Detection Methods: Remote Sensing Applications*, Springer, New York (2012).
11. T. Aach, A. Kaup, and R. Mester, "Statistical model-based change detection in moving video," *Signal Process.* **31**(2), 165–180 (1993).
12. Z. Wang et al., "Image quality assessment: from error visibility to structural similarity," *IEEE. Trans. Image Process.* **13**(4), 600–612 (2004).
13. F. Rousseau et al., "A contrario approach for change detection in 3D multimodal images: application to multiple sclerosis in MRI," in *Conf. Proceedings IEEE Engineering in Medicine and Biology Society (EMBS)*, pp. 2069–2072 (2007).
14. S. Shen, A. Szameitat, and A. Sterr, "Detection of infarct lesions from single MRI modality using inconsistency between voxel intensity and spatial location-a 3D automatic approach," *IEEE Trans. Inf. Technol. Biomed.* **12**(4), 532–540 (2008).

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