Published in final edited form as:

IEEE Trans Biomed Eng. 2013 September ; 60(9): 2401–2410. doi:10.1109/TBME.2013.2257769.

Motion Correction for MR Cystography by an Image Processing Approach

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Abstract

Magnetic resonance (MR) cystography or MR-based virtual cystoscopy is a promising new technology to evaluate the entire bladder in a fully non-invasive manner. It requires the anatomical bladder images be acquired at high spatial resolution and with adequate signal-to-noise ratio (SNR). This often leads to a long-time scan (> 5 minutes) and results in image artifacts due to involuntary bladder motion and deformation. In this paper, we investigated an image-processing approach to mitigate the problem of motion and deformation. Instead of a traditional single long-time scan, six repeated short-time scans (each of approximately 1 minute) were acquired for the

purpose of shifting bladder motion from intra-scan into inter-scans. Then the inter-scan motions were addressed by registering the short-time scans to a selected reference and finally forming a single average motion-corrected image. To evaluate the presented approach, three types of images were generated: (1) the motion-corrected image by registration and average of the short-time scans; (2) the directly-averaged image of the short-time scans (without motion correction); and (3) the single image of the corresponding long-time scan. Six experts were asked to blindly score these images in terms of two important aspects: (i) the definition of the bladder wall and (ii) the overall expression on the image quality. Statistical analysis on the scores suggested that the best result in both the aspects is achieved by the presented motion-corrected average. Furthermore the superiority of the motion-corrected average over the other two is statistically significant by the measure of a linear mixed-effect model with p -values < 0.05 . Our findings may facilitate the detection of bladder abnormality in MR cystography by mitigating the motion challenge. The effectiveness of this approach depends on the noise level of acquired short-time scans and the robustness of image registration and future effort on these two aspects is needed.

Keywords

Bladder imaging; MR cystography; motion correction; repeated short-time scans; image registration

I. INTRODUCTION

Bladder carcinoma is the most common malignancy of the urinary system [1][2]. According to the latest report from the American Cancer Society, bladder cancer has been ranked as the 5th leading cancer incidence (after lung/bronchus, prostate, breast and colon) and the 8th leading cause of cancer-related deaths in the United States. An estimated 73,510 new cases of bladder cancer and 14,880 death cases were expected to occur in 2012 in the United States alone, which increased by 30% and 18% respectively compared with the numbers in 2002 [3][4]. Early detection of bladder abnormalities is crucial for improving patient prognosis and treatment. In addition to the early detection task, management of a detected bladder tumor is another task and can be more challenging because of its high recurrence rate (as high as 80%) after local tumor resection [5]. Because of the high recurrence rate and lack of convenient detection methods, the lifetime treatment costs associated with bladder cancer is probably the highest among all cancers [6]. Therefore, a reliable, non-invasive and easy-performance method for bladder evaluation is clinically desired.

The conventional fiber-optic cystoscopy (OCys) is currently accepted to be the most accurate method for diagnosis and surveillance of bladder cancer, however it is invasive, costly, and uncomfortable with limited field-of-view (FOV) and a risk of 5% to 10% of urinary tract infection [7][8]. In recent years, virtual cystoscopy (VCys) has been developed and suggested to be a promising potential alternative. It mimics the navigation environment of OCys by virtually reconstructing the whole bladder in three-dimensional (3D) space [9]-[13].

Currently computed tomography (CT) and magnetic resonance (MR) imaging are two most important imaging modalities to perform the VCys. The advantages of CT imaging include its high spatial resolution, fast acquisition speed and wide availability. However, its insensitive to soft tissue (including the urine) forbids CT from offering good image contrast in bladder wall [14]. Although the weakness can be partially alleviated by injecting exogenous contrast medium, the CT procedure turns out invasive and uncomfortable. In addition, CT scan delivers a significant amount of X-ray exposure to the patients, which substantially increase the risk on the patients. Compared to CT, MR imaging provides

several advantages for local detecting and staging bladder carcinoma due to its intrinsic superior soft tissue contrast. Especially when the thickness of the bladder wall has been recognized as a biomarker of bladder abnormality, both the inside urine and the outside fat of the bladder can naturally serve as endogenous contrast medium to aid differentiating image intensities of the bladder wall against its surroundings [15][16]. Preliminary studies have demonstrated that there was not statistically significant difference between CT and MR based VCys for bladder cancer detection with the pooled sensitivity of 0.908 (95% CI, 0.827-0.959) and the specificity of 0.948 (95% CI, 0.884-0.983) [17]-[22]. Therefore MR-based VCys or MR cystography is a promising, completely non-invasive (and may be better than CT based VCys) technique for use in the detection and management of bladder lesion.

Tumor in bladder is a malignant overgrowth of cells in the bladder and gradually invades from the mucosa into the muscle layer of the bladder wall. According to the reports [19][20], the thickness of bladder wall, which is measured between the inner and the outer borders, was suggested to be a good indicator of occurrence of bladder abnormalities. Accurately delineating the inner and outer borders is crucial for measuring the thickness [15][23]. Based on the measurements, the normal thickness of bladder wall is around 3 mm when it is moderately distended [19] and the flat and/or small tumors at early stage of penetration of carcinoma are less than 5 mm [22]. Therefore images with high spatial resolution (voxel size is around $1.0 \times 1.0 \times 1.0 \text{ mm}^3$) are required to present the bladder wall. However increasing image resolution is very expensive in signal-to-noise ratio (SNR) in a 3D situation. Anatomical structure details maybe obscured due to insufficient SNR, and then the quality of post-processing work (*e.g.*, delineation of the bladder wall) is considerably influenced by image noise. In an effort to obtain bladder images with high spatial resolution and sufficient SNR, a simple solution in MR scan is to increase the parameter value of signal averaging [24], *i.e.*, the number of acquisitions (NSA) or the number of excitations (NEX), which is a common means to increase SNR by averaging several measurements of the signal in the k -space. In theory, SNR scales approximately with the square root of the NSA or NEX, while scan time scales directly with the NSA. Therefore increasing the NSA value extends the scan time and is prone to image artifacts due to the bladder wall motion, expansion and deformation.

In order to mitigate the motion artifacts for high spatial resolution on the borders of the bladder wall and adequate SNR on the wall, a retrospective motion correction (RMC) is investigated in this study. The RMC assumes that the intra-scan motions can be shifted into inter-scan motions by dividing a long-time acquisition into several short-time acquisition segments and the inter-scan motions can be corrected retrospectively using image registration techniques. Similar strategies have been successfully applied in functional MRI, digital subtraction angiography and positron emission tomography (PET), etc [25]-[27]. Some recent investigations on RMC strategy were also reported for correction of rigid head motion in MR anatomical imaging. For example, Kochunov, *et. al.*, [28] divided a long-time MR brain acquisition into six segments and employed the FLIRT registration [29] to rigidly align the six segments. The formed average image shows better contrast-to-noise ratio and more boundary details compared to the average image without alignment of segments. Aksoy, *et. al.*, [30] divided the k -space into several segments and considered the motion by individually correcting for the rotation and translation of each segment via minimizing an entropy-based auto-focusing criterion. Sharper edges in the final image were observed after the motion correction. The superiority of the RMC is its simplicity without hardware modification and supplementary equipment, *e.g.*, no specialized coil, is needed during data acquisition.

In this study, we investigated the feasibility of RMC strategy, particularly for the MR imaging of moving, expanding and deforming bladder wall. Considering both the processes

of data acquisition and post image processing, we studied two key points: (1) scan protocols for the short-time acquisition segments; (2) selection of suitable non-rigid registration algorithms. Considering the two main advantages (*i.e.*, shorter scan time and less partial volume (PV) influence on the inner border of the wall) of T_1 -weighted imaging over T_2 -weighted imaging, T_1 -weighted MR scans were used primarily for the purpose of delineating the bladder wall. To generalize the scan settings, no local or surface coil was used during the scanning. To trace the bladder motion among the short-time T_1 -weighted scans, a non-rigid registration algorithm is needed. As is known, the mutual information based registration is commonly used in medical image processing. The registration is automatically achieved based on the maximization of images' mutual information in combination with a parameterized deformation field. Many previous investigations demonstrated that the mutual information based registration to be very powerful and reliable [31][32]. For example: Rueckert *et al.* [33] used normalized mutual information as the voxel-based similarity measure to automatically recover the motion of MR breast scans. Mattes *et al.* [34] registered PET and CT chest images. Balci *et al.* [35] successfully expanded Miller *et al.*'s method [36] to provide a template-free approach of groupwise registration of all images to the common tendency of the population for synthetic proton density data, T_1 , T_2 and fluorescein angiography images respectively. Since a large number of data samples are used to estimate the mutual information, the effects of image noise on the metric are attenuated which is suitable for the MR image registration with lower SNR. On the other hand, many non-rigid registration algorithms are based on physics-based deformation models such as elastic models [37]. However, in our case, the elastic properties of the bladder tissues can differ across patients and with different ages, which makes the application of such models difficult, especially in the presence of tumors. Therefore, in this study, we employed the free-form deformation (FFD) model based on the B-splines. Compared to the physics-based models, B-splines-based FFD model makes no assumption of the elastic properties of the bladder tissues. And it also possess superior "local support" nature, general applicability and computational efficiency [33][38][39].

To evaluate the presented approach on clinical data, two types of images were acquired during a bladder scan: (1) multiple short-time acquisitions with NSA=1; (2) a single long-time acquisition with NSA from 4 to 8. The inter-scan motion of the short-time scans was mitigated by a normalized mutual information non-rigid registration based on the FFD model. The evaluation was implemented among the presented motion-corrected average, the direct average (without motion correction) and the single long-time acquisition. The expectation of this study is that realignment and averaging of multiple short-time acquisitions would mitigate the bladder motion artifacts and provide a better final image when compared to the direct average and the single long-time acquisition of approximately same overall amount of scan time.

II. METHOD

A. Bladder Scan Protocols

In order to obtain an adequate tradeoff between the bladder wall outline and the SNR level in the short-time acquisitions, investigating a suitable MR scanning protocol is an important step. Both T_1 - and T_2 -weighted protocols were investigated. The T_1 -weighted imaging was considered primarily for bladder wall extraction because of the two major reasons mentioned above. In general, T_1 -weighted imaging takes less time and gains contrast by lowering the lumen intensity so the desired signals or bladder wall is enhanced, as shown in Fig. 1(a). In contrast, T_2 -weighted imaging increases the image intensities of the lumen where the enhancement tends to "swallow" small abnormalities on the bladder border due to the PV effect, as shown in Fig. 1(b) [23]. Since T_2 -weighted images provide good pathological information about the tumor invading in the wall, it would be useful for wall

analysis after the bladder extraction [40]. In our experiment, both T_1 and T_2 images were acquired without exogenous contrast medium, *i.e.*, a fully non-invasive procedure.

After investigating several potential data acquisition protocols, we found that the combination of body coil for transmitting and sense-cardiac coil for receiving, and using the 3D THRIVE (T_1 High Resolution Isotropic Volume Examination) pulse sequence with the following scan parameters can achieve an adequate tradeoff between noise and contrast [41]. THRIVE is a Philips MRI pulse sequence using parallel imaging combined with a SPIR (Spectral Saturation with Inversion Recovery) 3D T_1 -weighted turbo spin-echo sequence to obtain images of high resolution and coverage in short breath-hold examinations. SPIR is a method of fat suppression combining both chemical selective and STIR (Short TI Inversion Recovery) methods. A typical high-resolution T_1 -weighted spin-echo image was obtained with 0.9375 mm isotropic, axial orientation, 224×224 matrix, 21 cm FOV, 2 mm section thickness, 1 mm intersection gap, 84 slices, 1 signal acquired, TR[GRH]TE=6.25/3.87 ms, and flip angle=10 degree. An example of the acquired T_1 -weighted images is demonstrated in Fig. 1(a).

B. Repeated Short-time Scans

Generally speaking, patient motions can be sorted into two kinds: voluntary and involuntary motions [28]. Voluntary motions are related to the unpredictable movements of patients during scan. In our experiments, the patients were given instructions of keeping still with the help of a belt motion suppression system with pads and immobilization straps during data acquisition. It dramatically reduced the voluntary motions. Involuntary motions are related to heart beat, lung breath, *etc.* To mitigate effect from the involuntary motions, patients were instructed to keep breath smoothly and regularly. Prior to the scan, the subject (*i.e.*, patient or volunteer) was asked to empty the bladder and then drink a bottle of water about 12 fl oz. It took about 15 to 20 minutes to allow the urine to fill in the bladder while the scanner and the subject were preparing for scan. When the bladder is stretched by urine, the small structures on the mucosa of the bladder wall would be more visible. In addition, the urine serves as a natural contrast agent for the imaging. During the scanning, the bladder is being slowly stretching by the urine inflow.

For each subject, up to eight short-time scans with NSA=1 were acquired at an image array of 224×224×84 with voxel size of 0.9375×0.9375×1.0 mm³. The acquisition time for a single short-time scan was approximately one minute. A single long-time scan was acquired with NSA=4, 5, 6, 7, and/or 8, depending on the urine filling situation. If the subject could hold for a longer time, more long-time scans or a single long-time scan with larger NSA value were acquired. The acquisition time for a single long-time scan of NSA=6 is slightly less than the total time of six short-time scans, *i.e.*, between 5 and 6 minutes.

C. Motion Correction

Bladder motion correction is the problem of determining transformations that capture the motion of every point on the bladder wall across the short-time acquisitions. To test the feasibility of RMC for bladder MR imaging, we selected components of a registration method based on popular and well-evaluated algorithms. Figure 2 illustrates an example of histograms inside identical regions of interest (ROIs) enclosing the whole bladder wall from six short-time acquisitions. It is noted that the intensity values almost keep consistent among the short-time acquisitions, thus some simple measures may work for this registration task, such as the sum of squared differences (SSD). Considering that short-time acquisitions are with low SNR, the normalized mutual information (NMI) would be preferred and was utilized in this study, because the noise effects on this metric can be attenuated, because the image statistics is estimated using a large quantity of pixel samples.

Taking into account the prior knowledge that the bladder is a hollow muscular and elastic organ, the motion of bladder wall takes a non-rigid fashion, so that the global transformation models, such as rigid or affine transformations, are not sufficient to capture this kind of motion. Therefore following the work [33], we took a combined transformation to describe the non-rigid motion. The combined transformation consists of a global transformation and a local transformation. The global transformation is a twelve parameter affine transform and the local transformation is a FFD model based on the cubic B-splines. The global transformation describes the overall motion of the bladder and the local transformation captures the bladder's local deformation. The basic idea of FFD is to deform an image by manipulating a regular grid of control points which are distributed across the image. The spacing of control point grid determines the resolution of the control point grid and can be arbitrarily set. When a higher resolution of the control point grid is set, a higher local non-rigid deformation will be obtained at the cost of more computing time. The spacing setting would be determined according to the requirement of accuracy and computational efficiency.

The L-BFGS-B (Limited-memory Broyden-Fletcher-Goldfarb-Shannon minimization with simple Bounds) was employed to optimize the registration algorithm. The L-BFGS-B is a limited-memory algorithm for solving large nonlinear optimization problems, which minimizes a nonlinear function f of m variables subject to simple bounds on the variables. Unlike the traditional BFGS method which stores a dense approximation, the L-BFGS-B stores only a few vectors that implicitly describe the approximation. The moderate requirement of memory makes L-BFGS-B well suitable for the optimization problems with a large number of variables [42][43].

To obtain transformation fields which capture the anatomical variations at different scales, a hierarchical scheme was performed by gradually increasing the complexity of the transformation fields during registration [33]. Firstly the global affine registration was performed. The resultant affine transformation was used to initialize a low-resolution deformation field with a coarse grid of FFD control points. Then we increased the resolution of control points to gradually refine the registration. The implementation of the registration algorithm was based on the Insight Toolkit package [44].

The pipeline of the presented motion correction approach is depicted in Fig. 3. Since larger deformation may degrade the performance of registration, the reference image of registration was selected with an effort to minimize the total discrepancy between itself and other images. In other words, the third short-time acquisition out of the six short-time acquisitions was selected as the reference image of registration. All other short-time acquisitions were aligned to the reference image before averaging them.

III. RESULTS

The presented approach was tested on five subjects (two normal volunteers and three patients). The ages of the volunteer group were around 28, and the ages of the patient group were 71.3 ± 8.4 . All subjects were scanned on a clinical 3T whole body MR scanner at the Stony Brook University Medical Center after informed consent. The high-resolution acquisition protocols were described in section II. A typical dataset contains approximately 84 slices. Before registration, we manually defined a cubic ROI enclosing the whole bladder. In all experiments, we started our registration with a coarse control point grid spacing of 20 pixel units and ended it with a fine control point grid spacing of 10 pixel units on an image slice. The NMI was computed using: (1) number of spatial samples = 20% of total pixels, (2) number of histogram bins = 32, (3) termination criterion with respect to the

projected gradient = 10^{-7} [43], and (4) maximization number of iterations per resolution = 2,000. Each pair of registration reached convergence around 400 iterations.

To assess the effectiveness of the presented approach with comparison to currently available methods, two groups of images were acquired. One group is the short-time acquisitions with NSA=1. The other group is the long-time acquisition with signal excitations (NSA $\geq$ 4) in each subject study. The registration algorithm was applied to align the short-time acquisitions to the selected reference. Hence the comparison was performed among three types of final images: (1) the presented motion-corrected average of short-time acquisitions; (2) the direct average of the short-time acquisitions; (3) the single long-time acquisition.

A. Bladder Inter-scan Motions

Figure 4 illustrates examples of inter-scan motions of short-time acquisitions in a volunteer scan and a patient study. The corresponding difference images without registration are shown in Figs. 4(c) and 4(g), where the residuals show the underlying noise of the image acquisition and the effect of mis-registration due to bladder motions, which is clearly visible among the short-time acquisitions. Figures 4(d) and 4(h) show the difference images after registration. It is noted that the bladder motions were dramatically mitigated after registration. Since the expectation of this study is that realignment and averaging of multiple short-time acquisitions would provide a better final image when the motion artifact is noticeable, the following sections will compare (i) the average after registration; (ii) the average without registration; and (iii) the corresponding long-time acquisition.

B. Visualization Inspections

The first objective of the test is to determine how many repeated short-time acquisitions are optimal. If the number of repeated scans is more than the need, we may gain nothing, but spending more time for both data acquisition and data processing. To achieve the objective, we acquired up to eight short-time acquisitions in some studies. Correspondingly some long-time scans were acquired with NAS=4, 5, 6, 7, and 8. Based on the studies on these acquisitions, similar to that of Fig. 4 above, we found that the gain after averaging over six repeated short-time scans is not noticeable. In other words, increasing the time to acquire too many short-time scans may not gain much, but would sacrifice the computing efficiency. The same observation concurred in the long-time scans. Then the six short-time scans and the long-time scan with NSA=6 were concluded as an adequate choice.

Given six short-time scans, the next objective of the test is to show the gain by the presented approach in terms of enhancing edge details and preserving SNR (or enhancing SNR and preserving edge details). Figures 5(a)-(f) illustrate an example of normal volunteer studies. Figures 5(g)-(l) show an example of patient studies. By visual judgment, a same conclusion can be drawn from these two figures as follows: Averaging multiple short-time acquisitions enhanced the SNR as compared to the original short-time acquisitions. The averaged image with motion correction preserved better bladder wall definition than the averaged image without motion correction. The bladder walls were blurred without the motion correction.

In addition to the above comparison using the short-time acquisitions, another comparison was made between the average of motion-corrected short-time acquisitions and an equivalent long-time acquisition with signal average by the MR scanner. The signal average by the MR scanner is a *k-space* average which is controlled by the integer value of parameter NSA and is obtained by averaging multiple measurements in the *k-space* before image reconstruction. Figure 6 specially shows the performance of the presented motion-corrected average with comparison to the average by the MR scanner in the three standard image acquisition orientations: transverse, coronal and sagittal. The edge blurring in the

long-time acquisition of Fig. 6(b)-(d) are seen as indicated by the white arrows. By the presented motion correction, as shown in Fig. 6(e)-(g), the bladder wall is more clearly defined in terms of edge details and wall uniformity.

The above visual judgment is based on the commonly accepted assumption that if the bladder wall is more visible by eyes, then it is more recognizable by a computer.

C. SNR and Contrast-to-Noise (CNR) Measures

This experiment is to measure the gain of SNR during the averaging process. Since the bladder lumen is the only uniform region in the bladder, the signal was measured from the bladder lumen. And the noise was measured from a no-signal region outside of the bladder. Based on the method of Henkelman [45] and Kaufman, *et. al.* [46], the SNR value can be calculated as:

$$\text{SNR} = \frac{u_{\text{signal}}}{1.5 \times \sigma_{\text{noise}}} \quad (1)$$

where u_{signal} denotes the mean of signal and σ_{noise} denotes the standard deviation of noise. Since the noise was measured in a no-signal region where the noise follows Rician distribution rather than Gaussian distribution, the factor of 1.5 was included to account for underestimation of σ_{noise} when measured in air in a magnitude MR image [45][46].

The SNR values were measured by mean $\pm$ standard deviations for all five involved subjects (listed in Table 1). It is noted that the measured SNR boosted with the increment of the number of acquisitions in the average as expected, and more importantly, as compared to the long-time acquisitions, the final average of six short-time acquisitions achieved a comparable and possibly a higher SNR values.

The CNR values were measured with respect to the bladder wall and its surroundings. Experts were asked to outline the bladder wall and the bladder lumen. Since the bladder wall has a complicated surrounding outside, then the bladder lumen was used as the background here. The CNR value was calculated by:

$$\text{CNR} = \frac{|u_{\text{wall}} - u_{\text{background}}|}{\sqrt{\sigma_{\text{wall}}^2 - \sigma_{\text{background}}^2}} \quad (2)$$

where u_{wall} and $u_{\text{background}}$ represent the means of the bladder wall and the background, and σ_{wall} and $\sigma_{\text{background}}$ denote the standard deviations of the bladder wall and the background. Figure 7 compares the CNR values between the final average images with and without motion correction of the five subjects. In all subjects, the motion-corrected averages outperformed the averages without motion correction.

In addition to the qualitative visualization inspection and the quantitative SNR and CNR measures above, an evaluation of image quality by radiologist experts was made with statistical analysis in hope to correlate with clinical utility. The experimental study by the experts was conducted in the following section.

D. Evaluation of Image Quality by Observer Study

In an effort to quantitatively compare the image quality acquired from the three different averaging methods: the long-time acquisition (*i.e.*, intrinsic average by the clinical MR scanner), the direct average (without motion correction) and the presented motion-corrected average, six experts were asked to score on the resultant images in terms of two most

important aspects, *i.e.*, (i) definition of the bladder wall, and (ii) the overall impression of images. For each subject, three volume images were obtained by the three different averaging methods, respectively. Three slices were respectively extracted from the same location (the location was randomly chosen) of the three volume images of the same subject, randomized in order and displayed on computer screen. The display did not have any indication on the displayed images of which averaging method was used. Therefore it is a completely blind procedure. Experts scored from 0 (worst) to 10 (best) for the two aspects separately for each displayed image set.

Statistical analysis was applied to the scores from the six experts on the five studies (two volunteers and three patients). Figure 8 illustrates the pair-wise scatter plots of the scores for comparison of the proposed motion-corrected average against the non-motion correction average. A Jitter plot technique was utilized in the scatter plots, which allows multiple observations with identical plotted values to be observable on the plot by adding a small amount of random noises to the values [47]. Figure 8(a) shows the scores for the definition of the bladder wall. It is noted that, among 90 pairs of scores, there are 50, 21 and 19 pairs that the motion-corrected average obtained higher, equal, and lower scores than the non-motion corrected average, *i.e.*, 55.56% of data points fall above and 23.33% on the 45 degree concordance line in the scatter plot. Similarly, as shown in figure 8(b), 56.67% of data points fall above and 21.11% on the 45 degree concordance. Similar results were observed when the motion-corrected average was compared with the long-time acquisition. In Figure 9(a), 66.67% of data points fall above and 8.33% on the 45 degree concordance line in the plot. In Figure 9(b), 61.11% of data points fall above and 19.44% on the 45 degree concordance line when the criterion is the overall impression of images. Therefore the scatter plots suggested that the motion-corrected average tend to have the best performance among the three average methods for the two important aspects.

In addition to the scatter plots, statistical testing of the comparisons among the three averaging methods at each of two evaluation criteria was also conducted by a liner mixed-effects model that includes nested random effects [48][49]. The considered random effects here included a random subject effect and a random slice effect which were nested within each subject study. Including these random effects helped account for the correlations between evaluation scores from the same subject and its three slices which were randomly extracted from the volume of the subject. The fixed effects in the study included two main effects of expert and method, and their two-way interaction effect. The multiple comparisons among the three averaging methods were adjusted by the Tukey procedure [50]. The results of the linear mixed-effects model showed that the expert-by-method interaction was not significant at either aspect (both $p\text{-values} > 0.86$), which further suggested that six experts were in agreement in terms of ranking these methods. The resultant $p\text{-values}$ for testing the differences in scores from two different methods are also shown in Figs. 8 and 9. The motion-corrected average approach generated significantly higher scores than the non-motion correction average method for the two aspect criteria (both $p\text{-values} < 0.05$ on Fig. 8). The corresponding 95% confidence intervals of the differences between motion-corrected average and non-motion correction average were (0.03, 1.19) and (0.05, 1.24), respectively, for the definition of the bladder wall and the overall impression criteria. When compared to the long-time scan, the motion-corrected average also generated significantly higher scores (both $p\text{-values} < 0.01$ on Fig. 9), with the corresponding 95% confidence intervals of the differences between motion-corrected average and long-time scan of (0.29, 1.99) and (0.33, 2.05), respectively, for the definition of the bladder wall and the overall impression criteria.

Therefore, the presented motion-corrected average approach outperforms both the non-motion correction average method and the long-time scan at the both important aspects.

IV. CONCLUSION AND DISCUSSION

High quality anatomical bladder images are desired by MR cystography for the clinical tasks of measuring the wall thickness (a sensitive biomarker) and establishing a volume of interest (the entire 3D bladder wall) for functional and pathological assessment of early sign of abnormality and management of recurrence. Because of the bladder deformation during scanning, the low SNR in a short-time acquisition (without signal average) and severe motion artifacts in a long-time acquisition (with signal average) have been remaining a challenging problem. To address this issue with an effective and simple way, we proposed an image-processing approach of acquiring repeated short-time acquisitions without signal average, performing non-rigid alignment of the short-time acquisitions to a selected reference, and finally forming a single motion-corrected average image. The approach was validated by experiments on both volunteer and patient studies. The validation demonstrated the feasibility of the approach in reducing motion artifacts and preserving edge details of the bladder wall while enhancing the SNR and CNR of the wall. The advantages of this approach are that: no hardware modification or extra equipment, such as a specialized coil, is needed; the scanning procedure design is relatively simple (fully invasive); it has the capability of correcting for almost any deformations in image domain because it is not specific to scan protocols.

While most of the previous investigations performed the RMC method for rigid motion correction in k -space and some in spatial domain [29][30][51][52], this work demonstrated that the RMC method can be successfully utilized for non-rigid motion correction of bladder MR imaging in the spatial domain. Since the motion correction in the k -space can only effectively compensate for rigid motions, such as: translation, rotation, expansion, and general affine, it is not desired to use direct correction method for non-rigid motions in the k -space. Therefore to correct for the deformable bladder motion in the spatial domain would be a good choice where the bladder motion follows a non-rigid fashion. The experimental results of this study concurred with the expectation. *i.e.*, the average in the k -space generated less desirable results than the image domain average after registration. Although the non-rigid registration procedure is computationally intensive, real time post-process is not required for MR cystography. In addition, optimized registration algorithm and parallel computing can reduce this limitation.

While the SNR increases as the number of signals increases, see Table 1, the final results after the average of the six signals varied. The difference between the k -space average and the image domain average without registration can be attributed to the methodology difference, *i.e.*, the former averages the k -space complex signals while the latter averages the magnitude. Although the difference from 8.77 ± 0.72 to 9.56 ± 1.32 could not be claim significant, the difference is noticeable. The difference between the two image-domain averages (one with and the other without registration) can be attributed to the performance of the registration. The gain seems more from the average from six scans 1.41 than the average from two scans 0.30. The gain in CNR is more noticeable, see Fig. 7, due to the registration.

As shown in Fig. 6, there are no distinct features inside the bladder. This may limit the ability of the registration to some degrees in addressing the motion problem. Physics-based deformation models may add more distinct features to further improve the capability of this proposed approach.

The outcome of the proposed approach is promising for the following tasks: (1) it will facilitate the extraction of bladder wall for detection of bladder abnormality by providing better image quality [23]; (2) it may potentially provide an alternative means to benefit

dynamic MR imaging of other moving organs, such as heart, lungs, *etc.* Given the extracted bladder wall by the use of the anatomic MR imaging technology, other functional imaging modalities, such as diffusion-weighted imaging, contrast-enhanced imaging, *etc.*, can be utilized to provide tissue contrast information inside the wall for functional studies and pathological assessment [40].

Future work needs to assess the impact of the proposed method for detection of bladder abnormality, such as abnormal growth [53], tumor, and cancer. With an effort to improve the performance of the presented bladder motion correction framework, several issues are needed to be investigated in the future work, *e.g.*, refining the short-time scan protocols; incorporating a group-wise registration algorithm in the framework; utilizing more information to guide the motion correction and evaluating the strategies of reference image selection (an unbiased or biased atlas) for the registration algorithms [54].

Acknowledgments

The authors would appreciate the assistance on data acquisition from Drs. Wagshul, PhD, Jambawalikar, PhD, Phillips, MD, Waltzer, MD, Adler, MD, Zawin, MD, and Harrington, MD.

This work was supported in part by the NIH/NCI under Grants #CA082402 and #CA143111. Q. Lin also was supported by the China Scholarship Council under Grant #2009624056. C. Duan, J. Ma, and H. Lu also were supported by the China NSFC under Grant #81230035 & #81271664, and the China Postdoctoral Science Foundation under Grant # 201104115.

REFERENCES

- [1]. Babjuk M, Oosterlinck W, Sylvester R, Kaasinen E, Bohle A, Palou-Redorta J, Roupert M. EAU guidelines on non-muscle-invasive urothelial carcinoma of the bladder. *Eur. Urol.* 2008; 54(2): 303–314. [PubMed: 18468779]
- [2]. Stenzl A, Cowan N, Santis M, Jakse G, Kuczyk M, Merseburger A, Ribal M, Sherif A, Witjes J. The updated EAU guidelines on muscle-invasive and metastatic bladder cancer. *Eur. Urol.* 2009; 55(4):815–25. [PubMed: 19157687]
- [3]. Siegel R, Ward E, Brawley O, Jemal A. Cancer statistics, 2011. *CA Cancer J. Clin.* 2011; 61(4): 212–236. [PubMed: 21685461]
- [4]. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. *CA Cancer J. Clin.* 2012; 62(1):10–29. [PubMed: 22237781]
- [5]. Lamm D, Torti F. Bladder cancer. *CA Cancer J. Clin.* 1996; 46(2):93–112. [PubMed: 8624800]
- [6]. Sievert K, Amend B, Nagele U, Schilling D, Bedke J, Horstmann M, Hennenlotter J, Kruck S, Stenzl A. Economic aspects of bladder cancer: what are the benefits and costs? *World J. Urol.* 2009; 27(3):295–300. [PubMed: 19271220]
- [7]. Mariappan P, Smith G. A surveillance schedule for G1 Ta bladder cancer allowing efficient use of check cystoscopy and safe discharge at 5 years based on a 25-year prospective database. *J. Urol.* 2005; 173(4):1108–11. [PubMed: 15758711]
- [8]. Aa M, Zwarthoff E, Steyerberg E, Boogaard M, Nijssen Y, Keur K, Exsel A, Kirkels W, Bangma C, Kwast T. Microsatellite analysis of voided-urine samples for surveillance of low-grade non-muscle-invasive urothelial carcinoma: feasibility and clinical utility in a prospective multicenter study (cost-effectiveness of follow-up of urinary bladder cancer trial [CEFUB]). *Eur. Urol.* 2009; 55(3):659–67. [PubMed: 18501499]
- [9]. Beer A, Saar B, Zantl N, Link T, Roggel R, Hwang S, Schwaibold H, Rummeny E. MR cystography for bladder tumor detection. *Eur. Radiol.* 2004; 14(9):2311–2339. [PubMed: 15322808]
- [10]. Kim J, Park S, Kim H, Kim S, Cho K. Comparison of virtual cystoscopy, multiplanar reformation, and source CT images with contrast material-filled bladder for detecting lesions. *Am. J. Roentgenol.* 2005; 185(3):689–696.

- [11]. Panebianco V, Sciarra A, Martino M, Bernardo S, Vergari V, Gentilucci A, Catalano C, Passariello R. Bladder carcinoma: MDCT cystography and virtual cystoscopy. *Abdominal Imaging*. 2009; 35(3):257–264. [PubMed: 19471998]
- [12]. Gohseth A, Lerner P. Application of new technology in bladder cancer diagnosis and treatment. *World J. Urol*. 2009; 27(3):301–307. [PubMed: 19234856]
- [13]. Duan C, Yuan K, Liu F, Xiao P, Lv G, Liang Z. Volume-based features for detection of bladder wall abnormal regions via MR cystography. *IEEE Trans. Biomed. Eng*. 2011; 58(9):2506–2512. [PubMed: 21642039]
- [14]. Rousson M, Khamene A, Diallo M, Celi JC, Sauer F. Constrained surface evolutions for prostate and bladder segmentation in CT images. *Comp. Viso. for Biomed. Imag. App.*, Beijing, China. 2005; 3765:251–260.
- [15]. Liang Z, Chen D, Button T, Li H, Huang W. Feasibility studies on extracting bladder wall from MR images for virtual cystoscopy. *Proc. International Society of Magnetic Resonance in Medicine*. 1999; 3:2204.
- [16]. Totaro A, Pinto F, Brescia A, Racioppi M, Cappa E, D'Agostino D, Volpe A, Sacco E, Palermo G, Valentini A, Bassi P. Imaging in bladder cancer: present role and future perspectives. *Urologia Internationalis*. 2010; 85(4):373–380. [PubMed: 20962513]
- [17]. Song J, Francis I, Platt J, Cohan R, Mohsin J, Kielb S, Korobkin M, Montie J. Bladder tumor detection at virtual cystoscopy. *Radiology*. 2001; 218(1):95–100. [PubMed: 11152786]
- [18]. Bernhardt T, Rapp-Bernhardt U. Virtual cystoscopy of the bladder based on CT and MRI data. *Abdominal Imaging*. 2001; 26(3):325–332. [PubMed: 11429965]
- [19]. Lämmle M, Beer A, Settles M, Hannig C, Schwaibold H, Drews C. Reliability of MR imaging-based virtual cystoscopy in the diagnosis of cancer of the urinary bladder. *Am. J. Roentgenol*. 2002; 178(6):1483–1488. [PubMed: 12034625]
- [20]. Bernhardt T, Schmidl H, Philipp C, Allhoff E, Rapp-Bernhardt U. Diagnostic potential of virtual cystoscopy of the bladder: MRI vs CT. Preliminary report. *Eur. Radiol*. 2003; 13(2):305–312. [PubMed: 12598995]
- [21]. Tekes A, Kamel I, Imam K, Chan T, Schoenberg M, Bluemke D. Dynamic MRI of bladder cancer: evaluation of staging accuracy. *Am. J Roentgenol*. 2005; 184(1):121–127. [PubMed: 15615961]
- [22]. Qu X, Huang X, Wu L, Huang G, Ping X, Yan W. Comparison of virtual cystoscopy and ultrasonography for bladder cancer detection: A meta-analysis. *Euro. J. Radiology*. 2010; 80(2): 188–197. 2.
- [23]. Duan C, Liang Z, Bao S, Zhu H, Wang S, Zhang G, Chen J, Lu H. A coupled level set framework for bladder wall segmentation with application to MR cystography. *IEEE Trans. Med. Imag*. 2010; 29(3):903–915.
- [24]. McRobbie, D.; Moore, E.; Graves, M.; Prince, M. *MRI from Picture to Proton*. 2nd ed.. Cambridge University Press; Cambridge, UK: 2006. p. 79-107.
- [25]. Meijering E, Niessen W, Viergever M. Retrospective motion correction in digital subtraction angiography: a review. *IEEE Trans. Med. Imag*. 1999; 18(1):2–21.
- [26]. Glover G, Li T, Ress D. Image-based method for retrospective correction of physiological motion effects in fMRI: RETROICOR. *Mag. Reson. in Med*. 2000; 44(1):162–167.
- [27]. Wardak M, Wong K, Shao W, Dahlbom M, Kepe V, Satyamurthy N, Small G, Barrio J, Huang S. Movement correction method for human brain PET images: application to quantitative analysis of dynamic ^{18}F -FDDNP scans. *J. Nucl. Med*. 2010; 51(2):210–218. [PubMed: 20080894]
- [28]. Kochunov P, Lancaster J, Glaha D, Purdy D, Laird A, Gao F, Fox P. Retrospective motion correction protocol for high-resolution anatomical MRI. *Human Brain Mapping*. 2006; 27(12): 957–962. [PubMed: 16628607]
- [29]. FLIRT-a very robust and accurate automated linear (affine) registration tool. provided in the FSL package [Online]. Available: <http://www.fmrib.ox.ac.uk/>
- [30]. Aksoy M, Forman C, Straka M, Cukur T, Hornegger J, Bammer R. Hybrid prospective and retrospective head motion correction to mitigate cross-calibration errors. *Magn. Reson. Med*. 2012; 67(5):1237–51. [PubMed: 21826729]

- [31]. Pluim J, Maintz J, Viergever M. Mutual-information-based registration of medical images: a survey. *IEEE Trans. Med. Imag.* 2003; 22(8):986–1003.
- [32]. Klein S, Staring M, Pluim J. Evaluation of optimization methods for nonrigid medical image registration using mutual information and B-Splines. *IEEE Trans. Med. Imag.* 2007; 16(12): 2879–2890.
- [33]. Rueckert D, Sonoda L, Hayes C, Hill D, Leach M, Hawkes D. Non-rigid registration using free-form deformations: application to breast MR images. *IEEE Trans. Med. Imag.* 1999; 18(8):712–721.
- [34]. Mattes D, Haynor D, Vesselle H, Lewellen T, Eubank W. PET-CT image registration in the chest using free-form deformations. *IEEE Trans. Med. Imag.* 2003; 22(1):120–128.
- [35]. Balci, S.; Golland, P.; Wells, W. Non-rigid groupwise registration using B-spline deformation model; MICCAI 2007 Open Science Workshop; Brisbane, Australia. 2007; p. 105-121.
- [36]. Miller, E.; Marius, N.; Viola, P. Learning from one example through shared densities on transforms; *Proc. IEEE Conf. on Comput. Visualization and Pattern Recog.*; Hilton Head, SC. 2000; p. 464-471.
- [37]. Crum W, Hartkens T, Hill D. Non-rigid image registration: theory and practice. *The British J. Radiology.* 2004; 77(2(s)):s140–s153.
- [38]. Lee S, Wolberg G, Shin SY. Scattered data interpolation with multilevel B-splines. *IEEE Trans. Visualization Comput. Graph.* Jul; 1997 3(3):228–244.
- [39]. Schwarz, L. Ph.D. dissertation. Dept. C.S., Technische Univ.; Munchen, German: 2007. Non-rigid registration using free-form deformations.
- [40]. Shi Z, Yang Z, Zhang G, Cui G, Xiong X, Liang Z, Lu H. Characterization of texture features of bladder carcinoma and bladder wall on MRI: initial experience. *Academic Radiology.* 2013 to appear.
- [41]. Liney, G. MRI from A to Z – A definitive guide for medical professionals. Cambridge University Press; Cambridge, UK: 2005. p. 236-238.
- [42]. Byrd R, Lu P, Nocedal J. A Limited Memory Algorithm for Bound Constrained Optimization. *SIAM Journal on Scientific and Statistical Computing.* 1995; 16(5):1190–1208.
- [43]. Zhu C, Byrd R, Nocedal J. L-BFGS-B: Algorithm 778: L-BFGS-B, FORTRAN routines for large scale bound constrained optimization. *ACM Trans. on Mathematical Software.* 1997; 23(4):550–560.
- [44]. Ibáñez, L.; Schroeder, W.; Ng, L.; Cates, J. The ITK software guide (updated for version 2.4). Kitware, Inc.; Clifton Park: 2005. p. 189-195.
- [45]. Henkelman R. Measurement of signal intensities in the presence of noise in MR images. *Med. Phys.* 1985; 12(2):232–233. [PubMed: 4000083]
- [46]. Kaufman L, Kramer D, Crooks L, Ortendahl D. Measuring signal-to-noise ratios in MR imaging. *Radiology.* 1989; 173(1):265–267. [PubMed: 2781018]
- [47]. Chambers, J.; Hastie, T. Statistical Models. S. Wadsworth & Brooks/Cole; 1992.
- [48]. Pinheiro, J.; Bates, D. Mixed-Effects Models in S and S-PLUS. Springer; New York: 2000.
- [49]. Chen J, Zhang G, Chen J, Steinhardt G. Simple moment-based inferences of generalized concordance correlation. *Journal of Applied Statistics.* 2011; 38(9):1867–1882.
- [50]. NIST. SEMATECH. e-Handbook of Statistical Methods. [Online]. Available: <http://itl.nist.gov/div898/handbook/prc/section4/prc471.htm>
- [51]. Kadah, Y. Motion artifact suppression in MRI using k-space overlap processing; 25th National Radio Science Conf.; Tanta, Egypt. 2008; p. 1-9.
- [52]. Maclaren J, Lee K, Luenqviriya C, Speck O, Zaitsev M. Combined prospective and retrospective motion correction to relax navigator requirements. *Magn. Reson. Med.* 2011; 65(6):1724–32. [PubMed: 21590805]
- [53]. Duan C, Yuan K, Liu F, Xiao P, Lv G, Liang Z. An adaptive window scheme for detection of bladder tumor surface via MR cystography. *IEEE Trans. on Inform Tech in BioMed.* 2012; 16(4):720–729.
- [54]. Rohlfing T. Image similarity and tissue overlaps as surrogates for image registration accuracy: widely used but unreliable. *IEEE Trans. on Med. Imag.* 2012; 31(2):153–163.

Fig. 1. Typical examples of MR images of the bladder. (a) T1-weighted image. (b) T2-weighted image.

Fig. 2.

An example of histograms of six short-time acquisitions inside an identical ROI's which encloses the whole bladder wall. The image intensity values are normalized to the range [0, 250] (the x-axis) and frequency of each value interval is shown as the counts (the vertical axis). It is noted that the intensity values keep consistent among the short-time acquisitions.

Fig. 3.
Flowchart of the presented motion correction approach.

Fig. 4.

(a)-(e) is an example of volunteer studies. (a) and (b) show example slices of two short-time acquisitions. (c) is the residual of subtraction of (b) from (a) without registration. (d) is the residual of subtraction of (b) from (a) after registration. (e) is the deformation field from (b) to (a). (f)-(j) is an example of patient studies. (f) and (g) show example slices of two short-time acquisitions. (h) is the residual of subtraction of (g) from (f) without registration. (i) is the residual of subtraction of (g) from (f) after registration. (j) is the deformation field from (g) to (f).

Fig. 5.

(a)-(f) is a typical example of volunteer studies. (a) A short-time acquisition without signal average (segment of a slice). (b) The average of 6 short-time acquisitions without motion correction. (c) The average after motion correction by the presented approach. (d)-(f) show the intensity horizontal profiles through the images whose positions are indicated by the red line segment in (a). The edge blurring of the bladder wall is pointed out by the white arrows. The labels “A” and “B” in (a) and (d) are corresponding to the positions of the bladder wall past by the red line segment. (g)-(l) is a typical example of patient studies. (g) A short-time acquisition without signal average. (h) The average of 6 short-time acquisitions without motion correction. (i) The average with motion correction by the presented approach. (j)-(l) are the intensity horizontal profiles through the images whose positions are indicated by the red line segment in (g). The label “A” indicates the position of the bladder wall past by the red line segment. The label “B” represents the tumor on the bladderwall.

Fig. 6.

Comparison between the long-time acquisition (*i.e.*, the k -space average, shown in (b)-(d), NSA=6) and the presented motion-corrected average of 6 short-time scans (*i.e.*, the spatial average, shown in (e)-(g)) in transverse, coronal and sagittal orientations; where the demonstrated sample slices were obtained by re-slicing the acquired volumes in the three standard image acquisition orientations as shown in (a). The edge blurring of the bladder wall is pointed out by the white arrows.

Fig. 7. Comparison of the CNR values between the motion-corrected averages and the non motion correction averages with respect to the bladder wall.

Fig. 8.

The scatter plot of the scores from the motion-corrected method against the non-motion correction method. (a) Scatter plot of the scores of definition of the bladder wall. (b) Scatter plot of the scores of the overall impression. The P -values were based on testing score differences from two methods using linear mixed models.

Fig. 9.

The scatter plot of the scores from the motion-corrected average against the long-time scan. (a) Scatter plot of the scores for definition of the bladder wall. (b) Scatter plot of the scores of the overall impression. The P -values were based on testing score differences from two methods using linear mixed models.

TABLE I

Signal-to-noise ratio measures

SNR	Non motion correction	Motion-corrected
Single short-time scan	4.42±0.43	
Average of 2 short-time scans	6.21±0.72	6.51±0.97
Average of 3 short-time scans	7.57±0.97	8.43±1.40
Average of 4 short-time scans	8.19±1.09	8.74±1.46
Average of 5 short-time scans	9.28±1.26	10.55±2.33
Average of 6 short-time scans	9.56±1.32	10.97±2.42
Long-time scan(NSA=6)	8.77±0.72	