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Dual registration of abdominal motion for motility assessment in free-breathing data sets acquired using dynamic MRI

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Abstract

At present, registration-based quantification of bowel motility from dynamic MRI is limited to breath-hold studies. Here we validate a dual-registration technique robust to respiratory motion for the assessment of small bowel and colonic motility. Small bowel datasets were acquired in breath-hold and free-breathing in 20 healthy individuals. A pre-processing step using an iterative registration of the low rank component of the data was applied to remove respiratory motion from the free breathing data. Motility was then quantified with an existing optic-flow (OF) based registration technique to form a dual-stage approach, termed Dual Registration of Abdominal Motion (DRAM). The benefit of respiratory motion correction was assessed by (1) assessing the fidelity of automatically propagated segmental regions of interest (ROIs) in the small bowel and colon and (2) comparing parametric motility maps to a breath-hold ground truth. DRAM demonstrated an improved ability to propagate ROIs through free-breathing small bowel and colonic motility data, with median error decreased by 90% and 55%, respectively. Comparison between global parametric maps showed high concordance between breath-hold data and free-breathing DRAM. Quantification of segmental and global motility in dynamic MR data is more accurate and robust to respiration when using the DRAM approach.

[4] These authors contributed equally.

Keywords: small bowel motility, colon motility, dynamic, MRI, motion quantification, registration

(Some figures may appear in colour only in the online journal)

1. Introduction

Artefacts and spatial misalignments caused by respiratory motion represent a major challenge to medical image acquisition and analysis of time series data (Rohlfing *et al* 2004, McClelland *et al* 2013). Many methods have been investigated in order to compensate for the undesirable effects due to motion. Although breath-hold acquisitions remain the most straightforward and common technique for abdominal imaging, they require good patient compliance. Prospective motion correction schemes account for motion directly during acquisition and are predominately used with tracking devices in neuroimaging, or diaphragmatic navigators in cardiac imaging. These techniques require the use of tracking data during acquisition (Maclaren *et al* 2013) and commonly correct only for rigid motion. Respiratory gating using navigators is widely used in cardiovascular imaging (Wang *et al* 1995) at the expense of increased scan time. Retrospective motion correction using image registration is another class of approach commonly used to compensate for the misalignment of features due to respiration (Schmidt *et al* 2011, Buerger *et al* 2011). In particular, several solutions have been introduced in the case of dynamic contrast enhanced (DCE) data with non-rigid deformations and with specific considerations made for the changes in intensity (Melbourne *et al* 2011, Filipovic *et al* 2011, Wollny *et al* 2012). In previous work, we introduced Robust Data Decomposition Registration (RDDR), a novel technique using Robust Principal Component Analysis (RPCA) to separate the (sparse) intensity changes from the (low rank) motion during DCE acquisition (Hamy *et al* 2014). This advance is of particular interest to associated applications where respiratory motion is a limitation. The current study does not involve the use of RDDR in the presence of contrast enhancement. Instead we propose a new application of this technique to free-breathing Magnetic Resonance Enterography (MRE) datasets, prior to small bowel motility quantification. We show that RDDR can be used as a pre-processing step to filter out respiratory motion, with no effect on measurements of peristalsis.

Previous work has demonstrated that it is possible to extract quantitative information related to bowel physiology from dynamic 'cine' MRI images and several methods have been proposed (Ailiani *et al* 2009, Marciani 2011, Odille *et al* 2012, Sprengers *et al* 2012, Farghal *et al* 2012, Bickelhaupt *et al* 2013). An image registration based technique by Odille *et al* used deformation fields to automatically propagate manually placed regions of interest (ROIs) for small bowel segmental analysis and also to provide a global measurement of small bowel motility (Odille *et al* 2012). The technique was developed to be robust to intensity changes caused by intra-luminal flow of intestinal contents and through-plane motion. Further validation of this technique in patients with Crohn's disease (Odille *et al* 2012, Menys *et al* 2012) and in a healthy control cohort suggested this approach is repeatable and sensitive to the effects of motility-altering pharmacological agents (Menys *et al* 2013).

The key motivation driving this study is to introduce and assess a method for quantifying bowel wall motion without the current requirement for a breath-hold protocol. So far, the literature has mainly examined segmental contractile activity taking place over breath-hold time spans, however, a range of peristaltic actions exist in the bowel that take place over longer periods of time or in an episodic fashion difficult to capture with a single breath-hold acquisition. Motility is also of interest in other regions of the gastrointestinal tract including the colon where the contraction rate is far slower than the bowel, again precluding the use of breath-hold protocols. Motility disorders including Crohn's, pseudo-obstruction, various

forms of neuropathy and speculative conditions including Irritable Bowel Syndrome would all benefit from an objective technique capable of evaluating this component of their disease, either to inform basic science, or inform treatment strategies. Finally, and from a practical perspective, breath-hold protocols are difficult for some patients. Collectively, by removing the dependency on breath-hold we can broaden the relevant clinical conditions to which we might investigate and simultaneously increase the technique's practicability.

The principle limitation for many post-processing techniques for small bowel analysis, including Odille's, is the requirement to remove or reduce respiratory motion by using breath-hold acquisition protocols.

This limits the utility for important groups of pathological conditions where aberrant small bowel motility patterns take place over longer time periods or conditions which predominantly affect the colon where the period between peristaltic waves may be greater than a breath hold duration. However, the use of respiratory gating does not seem appropriate in the context of bowel motility analysis because of the loss of temporal resolution leading to an under-sampling of the rapid local contraction of the bowel wall. Also, due to the absence of navigator in the acquisition protocol, retrospective correction using image registration appears as the most suitable choice in our case. We choose to use the iterative registration algorithm described in Hamy *et al* (2013) as it can potentially generate a time series free from breathing-motion without affecting the information on peristalsis, allowing subsequent modelling of small bowel motility with Odille's technique. An ability to accurately quantify bowel motility continuously over several minutes without the interruption caused by repeated breath holds would be a significant advance and open the technique to a broader range of diseases of the small bowel and colon (Fell *et al* 1996, Camilleri *et al* 1998, Pimentel *et al* 2002, Pfeiffer 2010).

The purpose of this study is to validate our novel post-processing pathway to correct respiratory motion and then quantify bowel motility in free-breathing cine MRI data sets. We refer to this combined technique as Dual Registration of Abdominal Motion (DRAM).

2. Methods

2.1. Dual registration of abdominal motion

2.1.1. Robust data decomposition registration. Our aim is to use Robust Data Decomposition Registration (RDDR) as a pre-step to register and remove the respiratory component of motion, whilst preserving peristaltic motion in the data. To capture the respiratory motion, we use the RDDR technique. This method uses RPCA to decompose the cine data into low rank (L) and sparse (S) components (Candès *et al* 2011). Contrary to regular principal component analysis which decomposes the data into projections within a multi-dimensional space, RPCA produces only two outputs (L and S). The low-rank component tends to contain the slowly varying respiratory motion and the sparse component the local rapid changes due to peristalsis. However, this decomposition does not perfectly separate the two physiological motions and to remove only the respiratory motion, RDDR applies an iterative registration scheme. Within RDDR, RPCA performs the decomposition in (1):

$$\begin{aligned} &\text{minimize } \|\mathrm{L}\|_* + \lambda\|\mathrm{S}\|_1 \\ &\text{subject to } \mathrm{L}+\mathrm{S}=\mathrm{M} \end{aligned} \tag{1}$$

where $\|.\|_*$ and $\|.\|_1$ respectively represent the nuclear norm (i.e. the sum of the matrix singular values) and the l1-norm (i.e. the sum of the absolute values of the matrix elements). Within the algorithm, the (2D+*t*) input time series is reshaped into a two dimensional matrix M where each column is formed from the pixels of one time frame. Following the RPCA decomposition, this matrix M is expressed as the sum of a low rank matrix L, and sparse matrix S. The

parameter λ appearing in (1) is a trade-off parameter that determines the relative amount of information in L or S: for low values of λ most of the information is in S and as λ is increased, the information is progressively transferred to L. Here we expect that the respiratory component of motion appears in L before the more random or sparse-like peristalsis. Candès *et al* proposed a value for lambda based solely on the data size (Candès *et al* 2011). For the purpose of separating and correcting respiratory motion from peristaltic motion, we vary λ in an iterative scheme that includes successive registrations of the low rank frames as shown in figure 1. For lower values of λ, only elements of respiratory motion appear in L. As λ increases, more respiratory motion is present and peristalsis gradually appears in L as shown in figure 2. At each iteration, the frames contained in the low-rank component are all registered to the frame that minimizes the difference to the pixelwise statistical median (of the low rank frames) over time. The resulting deformation fields are applied to the initial time-series so that a part of the motion can be removed. This process (decomposition + registration) is repeated for increasing values of the trade-off parameter. The deformation fields generated at each registration stage are added to a single global deformation field applied to the initial time series after the last iteration to avoid loss of information caused by multiple resampling.

The registration steps within RDDR use the residual complexity similarity metric (Myronenko and Song 2010) and transformation fields are described using B-spline based free form deformations. The 2D control point grid used here has a relatively large spacing (10 pixels) aimed at capturing the large-scale deformations due to respiratory motion.

2.1.2. RPCA settings. The starting value of λ is chosen such that the rank of L in the first iteration of RDDR is the number of time frames divided by four. This initial value of λ was empirically found to be high enough to include some elements of respiratory motion in L and low enough to keep peristalsis in the sparse component (Hamy *et al* 2014). For lower values of λ, respiratory motion might entirely appear in the sparse component making the first iteration useless. The starting value of λ is logarithmically incremented in subsequent iterations similar to the original version of the algorithm. The same settings were used for all the datasets (both small bowel and colon) analysed in this study.

RDDR was initially developed for DCE-MRI registration, the stopping criterion of the algorithm is modified here to make it suitable for the current application. This criterion is now designed so that no peristalsis would appear in the registered low rank components. We use a threshold on the sparsity of the RPCA sparse component to end the iterations. Given the pseudo-periodical characteristic of respiratory motion and peristalsis, the optimum threshold for λ was chosen using an analysis of test data in the frequency domain, inspired by previous work from Sprengers *et al* (2012). The frequency of peristalsis is expected to be the same in both breath hold and free breathing. Thus the difference between breath hold and free breathing data in the Fourier domain should show only the contribution of respiratory motion. We use such a difference as an indicator of the effect of each iteration in RDDR. Spectral powers were computed by summing the Fourier transform of time-intensity variations for every pixel over the entire field of view. Figure 3 presents the evolution of the spectral power difference with respect to the sparsity of RPCA sparse component. A minimum difference appears clearly when the sparsity is equal to 20%. The spectral difference between the BH and corrected free breathing decreases as respiration is registered out of the free-breathing data and reaches a minimum when all the respiratory motion has been compensated. The difference starts to increase when the sparsity is low because peristalsis is appearing in the low rank component and being registered out of the free breathing data. The threshold is set on the sparsity rather than iteration number. The stopping criterion for RDDR is then chosen to be when the sparsity of S falls below a threshold of 20% (as indicated in figure 1).

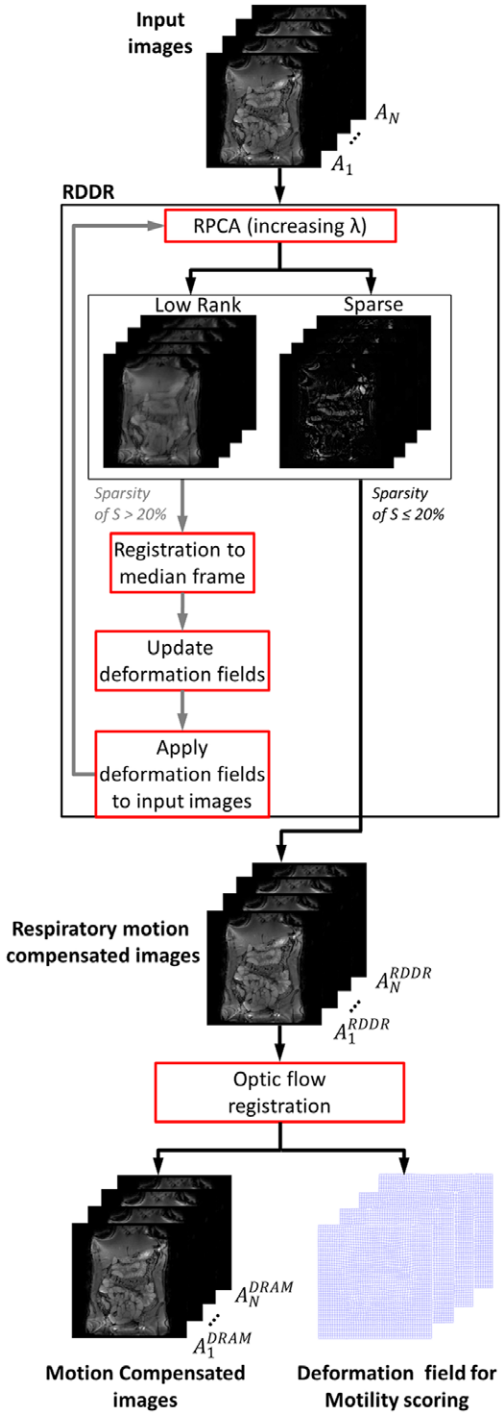

Figure 1. Flow chart illustrating the process of DRAM. The parameter λ is gradually increased in RDDR to let more information appear in the low rank component over iterations.

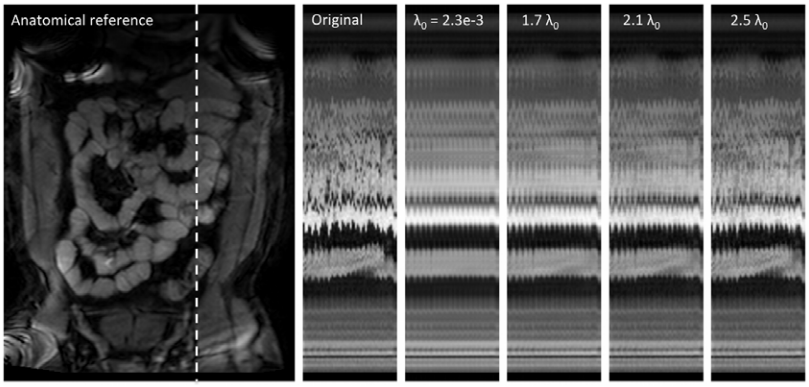

Figure 2. Effect of increasing λ on RPCA low rank component in an example data set: time cuts for the original time series and various low rank components are shown. The location of these time cuts is indicated by a white dashed line in the anatomical reference.

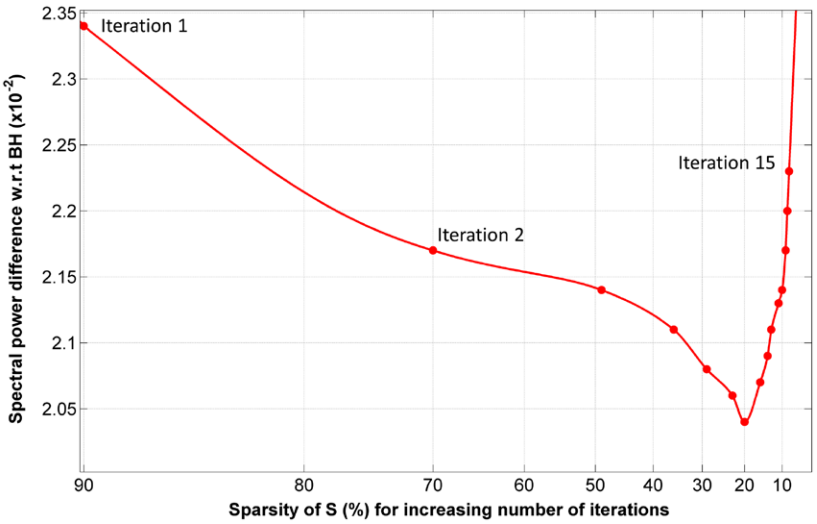

Figure 3. Spectral analysis of a subject for tuning of RDDR stopping criterion. Spectral Differences between gradually corrected data and breath-hold is progressively reduced until a minimum is reached. The sparsity of S at that minimum value (20%) is chosen as lower threshold to stop the iterative registration and avoid deterioration of the information on motility.

2.2. Motility quantification

Following registration using RDDR to reduce respiratory motion, small bowel motility was quantified using the previously reported generalized optic flow registration technique referred to here as Optic Flow (OF) (Odille *et al* 2012). This technique uses a joint non-rigid transformation (multi-resolution) and modelling of intensity changes within a time-series. A dense representation of the 2D deformations (i.e. a displacement field at the pixel resolution) is computed to account for local motion. This model has a higher spatial resolution than the

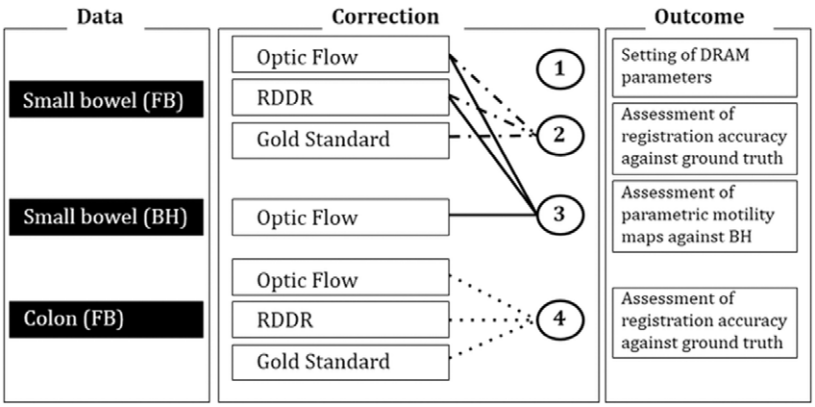

Figure 4. Study overview. (1) Setting of DRAM parameters. (2) Registration accuracy of the two methods was investigated by comparing the ability of the two algorithms to propagate a ROI against a manually adjusted 'gold-standard.' (3) Registration accuracy was assessed as per (2) in the colonic data sets. (4) Parametric motility maps derived from free breathing data sets were compared to a breath-hold pseudo ground-truth.

control point grid based deformation in RDDR and can capture local deformations caused by peristalsis. An additional intensity correction map is included in the algorithm's cost function to account for intensity changes related to through-plane motion and flow of intra luminal content (Odille *et al* 2012). The function is formulated as follows:

$$C\left(\mathrm{u_x},\ \mathrm{u_y},\ I_{\mathrm{map}}\right) = \left\| I_{\mathrm{src}}\left(T_{\mathrm{u_x,u_y}}\right) + I_{\mathrm{map}} - I_{\mathrm{trg}}{}^2 \right\| + R\left(\mathrm{u_x},\ \mathrm{u_y},\ I_{\mathrm{map}}\right) \tag{2}$$

I_{src} and I_{trg} respectively denote the source and the target images for registration, I_{map} is the intensity correction field and $T_{\mathrm{u_x,u_y}}$ is the displacement field in the two directions of the 2D image space represented by the vectors $\mathrm{u_x}$and $\mathrm{u_y}$. An additional regularization parameter R is included to enforce spatial smoothness on $\mathrm{u_x}$ and $\mathrm{u_y}$ based on their second order derivatives.

Quantitative assessment of motility can be computed from the Jacobian determinants of the displacement fields obtained after registration with OF. This metric provides information on local expansion or compression of features. For each pixel, the standard deviation of the Jacobian determinant through time provides a surrogate measure of local bowel contraction and expansion. This metric is close to zero where no deformation exists and increases according to standard deviation of fractional change in area over a time series of n images. Such a measure is insensitive to rigid transformations (e.g. translation). However the non-rigid deformations related to respiration, if not corrected for, have an effect on the measurements. It is this effect that DRAM aims to reduce. Note that the OF deformation field can also be used for the automatic propagation of ROIs through the different time frames.

2.3. Study overview

In this study motility is quantified in dynamic small bowel and colonic data with the OF registration algorithm—originally designed to process data in breath-hold alone. We evaluate here the ability of a pre-processing registration step RDDR to correct free breathing motion before OF processing with the combination of the two processes here referred to as DRAM.

We provide two main results that focus on (1) the ability of OF-alone and DRAM to faithfully propagate a line ROI (i.e. a 1D line drawn across the bowel lumen, perpendicular to the central axis of the bowel) through processed small bowel and colonic time series data using the average of two independent manually propagated ROIs as a gold standard. (2) Free breathing parametric motility maps in small bowel data sets registered with OF-alone and DRAM, using breath hold OF data as a gold standard. A summary is provided in figure 4.

2.4. Subject population

Two data sources were used for the validation of this technique. The first was from a prospective study of small bowel motility in 20 volunteers (Menys *et al* 2013), and the second in a study of colonic motility in 6 volunteers. Small bowel and colonic data sets were acquired under ethical approval from the respective institutions' Research Ethics Committees.

2.4.1. Small bowel. Twenty small bowel subjects were scanned (mean age 28, range 22–48, 14 Male). Volunteers were included according to the study inclusion criteria where they were able to give informed consent and were non-smokers and had abstained from caffeinated and alcoholic drinks on the day of the scan. Volunteers were excluded where they had chronic intestinal disease or were on long term medication excluding the oral contraceptive pill. Volunteers were also excluded if they reported abnormal GI (gastrointestinal) symptoms or had a history of GI surgery. Volunteers were recruited prospectively by advertisement and interview.

2.4.2. Colon. Colon data sets for 6 healthy volunteers were used in this study with subject demographics as follows, mean age 27, range 19–43 years, 1 Male. Volunteers were included in the study where they were able to give informed written consent, were non-smokers and had abstained from alcohol for 24 h prior to the study day. Volunteers were excluded if they had any history of serious acute or chronic illness, especially gastro-intestinal, if they regularly used medication which interfered with GI function or had previous GI surgery (excluding appendectomy). Volunteers were recruited prospectively by advertisement.

2.5. MRI protocol

2.5.1. Small bowel. Volunteers fasted for 4 h prior to ingesting 1 L of 2.5% Mannitol solution over the 50 min prior to the MRI scan. Subjects drank at regular intervals such that the last of the Mannitol solution was consumed immediately before entering the scanner. Subjects lay in the prone position and were scanned using a Philips Achieva 3T Multi-transmit MRI scanner (Philips Healthcare, Netherlands) using the manufacturer's torso coil (XL-TORSO). Each subject underwent planning sequences followed by a multi-slice balanced Turbo Field Echo (bTFE) motility sequence (coronal plane, voxel size 2.5 × 2.5 × 5 mm^3, FOV 420 × 420 × 30 mm^3, FA 20°, TE = 1.85 ms, TR = 3.7 ms dual channel RF transmit with adaptive RF shimming), no slice gap with 6 slices in a volume and temporal resolution of 1 volume per second. The study coordinator (AM) positioned the volume that best displayed the small bowel in the coronal plane deep to the abdominal musculature as guided by the planning sequence.

The motility sequence was run first on inspiration breath-hold to collect a total of 20 images of the same anatomical slice. This process was repeated following a 10 s recovery period with the subject this time instructed to 'gently free-breathe' whilst a total of 60 images were acquired in the same anatomical position unchanged from the breath-hold scan.

2.5.2. Colon. The volunteers arrived after an overnight fast. Scans were carried out at baseline and at hourly intervals following consumption of either 1 L or 2 L Polyethlene glycol (PEG) formulation. A total of nine data sets from six subjects are included in this work to highlight differing amounts of colonic motility and breathing effects, selected subjectively by the study scientist (CH). All volunteers underwent a baseline scan and then hourly scans after ingestion of PEG. The data in this study comprises of two baseline scans and seven scans at various time points post ingestion. Subjects lay in the supine position and were scanned using a Philips Achieva 1.5T MRI scanner using the XL-Torso receiver coil.

The colon motility scan consisted of a single slice bTFE sequence positioned in the sagittal plane through the ascending colon (sagittal plane, voxel size $1.5 \times 1.5 \times 15\,mm^3$, FOV $330 \times 228 \times 15\,mm^3$, FA 70°, TE = 1.5 ms, TR = 3.0 ms). Temporal resolution was 1 slice per second and scans were acquired during 2 min of thoracic free breathing.

2.6. Assessment of the effect of registration

The effect of respiratory motion correction using RDDR was assessed by investigating the fidelity of the optic flow algorithm to propagate a line ROI through the (1) small bowel and (2) colon free-breathing time series data.

2.6.1. Small bowel. One gastroenterology research fellow and one research scientist (JM—3 years experience MRE, AM—4 years experience small bowel MR) identified, in consensus, a small bowel loop in the upper left quadrant of each subject from one of the six anatomical positions acquired, which remained visible through the time series (i.e. did not move out of plane).

2.6.2. Colon. This process was repeated in the colon data sets, where the same two observers placed in consensus two line ROIs in the ascending portion of the colon.

2.6.3. Assessment of registration accuracy. In both the small bowel and colonic data, the line ROIs were automatically propagated through the time series by both OF alone and the OF component of DRAM based on the registration deformation fields, and the results saved. The ROI was then manually corrected independently by both JM and AM for each time point. Agreement between readers was assessed using Bland-Altman limits of agreement and Intra-class correlation (ICC). An ICC of 0 represents no agreement between observations and 1, perfect agreement. The manually corrected line ROIs for the two observers were averaged for each time point and used to create a ground truth for each data set.

Accuracy of the OF-alone and DRAM algorithms to the ground truth was compared by: (1) assessing change in line length over time in combined 'ground-truth' scores and automatically propagated ROIs using Bland-Altman limits of agreement (LoA) and intra-class correlation (ICC). (2) Assessing the variance of the displacement of ROIs by computing the target registration error (TRE) i.e. the distance between each line end-point of the manually corrected and automatically propagated ROIs. A threshold for TREs was set to 1e–3 mm. Errors below this value were considered as zero.

2.7. Validation of motility scoring

The small bowel was delineated with a polygonal ROI in three data sets for each subject: (1) the breath-hold registered with OF (2) the free breathing registered with DRAM data sets and

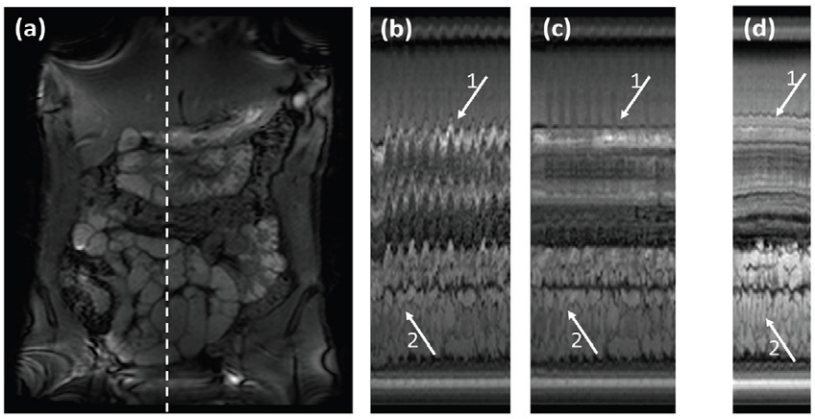

Figure 5. Time cut representation of dynamic time-series of the small bowel in a healthy volunteer: the location of the time cuts is indicated by a white dashed line in (*a*), time cuts before (*b*) and after registration with RDDR (*c*) are presented. Breath-hold data is shown as reference (*d*). Important displacements due to respiratory motion (arrow 1) are accurately corrected by RDDR while preserving bowel motility information (arrow 2).

(3) the free-breathing registered with OF-alone. The 20 s BH data (i.e. without respiratory motion) served as a ground truth.

The ROI for each 2D series was automatically propagated through the time series using deformation fields derived from the OF registration (with and without pre-processing with RDDR). A parametric map was generated by calculating the standard deviation of the Jacobian determinant J of the displacement field, through time, providing a previously validated quantitative surrogate measure of motility expressed in arbitrary units. For each pixel:

$$\sigma_{\mathrm{J}}(x, y) = \sigma\Big(\{\mathrm{J}(x, y, t)\}_{t=[0,N]}\Big) \tag{3}$$

Where x and y are the spatial coordinates,t is time and $\boldsymbol{N}$ is the number of frames. The operator {.} in (3) defines a set of values with respect to a varying parameter, here t.This metric was summarised by taking the mean value of the standard deviation computed for all pixels within a given ROI. The value $\sigma_{\mathrm{J}}(\mathrm{x}, \mathrm{y})$ is expected to be close to zero in regions which do not move (Odille *et al* 2012).

3. Results

3.1. Registration assessment

Example images of time cuts obtained after registration are shown in figure 5. The time cut representation shows correction of breathing motion after RDDR with little apparent effect on peristaltic motion. Global misalignment between figures 5(*c*) and (*d*) are due to the effect of breath holding. In this example the breath hold was carried out at full exhale, thus the liver and the upper bowel are shifted up compared to the average position of the same organs in the registered data. Additional misalignment within figure 5(*d*) corresponds to the fact that breath-holding does not completely freeze motion.

3.1.1. Registration accuracy assessment. In the small bowel, two observers manually propagated a linear region of interest through 60 time points in each of the 20 subjects.

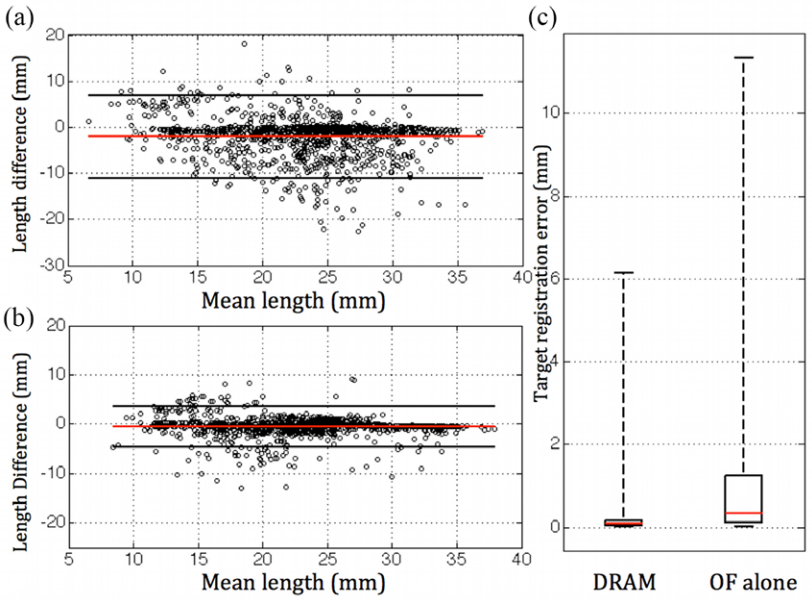

Figure 6. Bland Altman limits of agreement for line ROIs in small bowel data registered with OF against manually corrected ground truth (*a*) and data registered with DRAM against manually corrected ground truth (*b*). Target registration error in DRAM and OF alone (*c*).

Inter-reader variability was assessed through Bland-Altman LoA and ICC. For the manually corrected OF-alone data, mean difference between readers was 0.4 mm (95% LoA ± 7.3 mm). ICC was 0.85. For the manually corrected DRAM data the mean difference between readers was 0.54 mm, LoA ± 3.4 mm. ICC was 0.96. The Bland-Altman analysis of line length ROIs in OF-alone registered and DRAM registered data with the manual measurements (mean of two observers) is shown in figures 6(*a*) and (*b*). For the OF-alone registered data the mean difference between the manually corrected and automatically propagated ROIs was −2.0 mm (95% LoA ± 9 mm). For the DRAM processed images mean difference was −0.48 mm (95% LoA ± 4.15 mm).

In the colon datasets, the mean difference between readers for the manually corrected OF-alone data was 0.2 mm (95% LoA ± 1.1 mm). ICC was 0.98. For the manually corrected DRAM data the mean difference between readers was 0.28 mm, LoA ± 1.7 mm. ICC was 0.99. The Bland-Altman analysis of line length ROIs in OF-alone registered and DRAM registered data with the manual measurements (mean of two observers) is shown in figures 7(*a*) and (*b*). For the OF-alone registered data the mean difference between the manually corrected and automatically propagated ROIs was −1.25 mm (95% LoA ± 7.57 mm). For the DRAM processed images mean difference was −0.13 mm (95% LoA ± 1.96 mm).

3.1.2. Target registration errors. In the small bowel, TREs were below the threshold in 49% of the cases with OF only and in 70% of the cases after pre-processing with RDDR. For nonzero TREs (figure 6(*c*)), OF-alone yielded a median error of 0.5 mm (IQR 2.27 mm) and DRAM yielded a median error of 0.05 mm (IQR 0.1 mm).

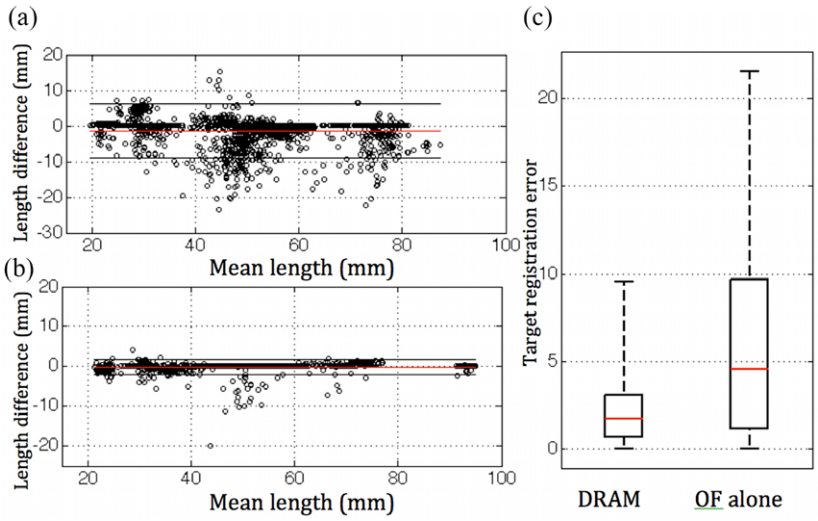

Figure 7. Bland Altman limits of agreement for line ROIs in colon data registered with OF against manually corrected ground truth (*a*) and data registered with DRAM against manually corrected ground truth (*b*). Target registration error in DRAM and OF alone (*c*).

In the colon, TREs were below the threshold in 37% of the cases with OF-alone and in 70% of the cases after pre-processing with RDDR. For nonzero TREs (figure 7(*c*)), OF alone yielded a median error of 4.9 mm (IQR 8 mm) and DRAM yielded a median error of 2.2 mm (IQR 2.1 mm). An example plot of the line lengths through time, propagated by OF and DRAM, is shown in figure 8.

3.2. Motility scoring

The mean global motility score[5] within the manually placed ROIs for the BH data sets across the cohort was 0.340 (range 0.181–0.422). Mean global motility score for DRAM registered data was 0.335 (range 0.189–0.430) and OF alone free-breathing data sets was 0.365 (range 0.268–0.458). Subjective visualisation of motility colormaps is shown in figure 9 with data summarised in figure 10.

4. Discussion

The aim of the work was to validate a two-stage technique that first corrects respiratory motion before applying an existing OF method to register local deformation generated due to peristalsis. Such an approach could allow rapid and robust data analysis from longer datasets acquired in free breathing. The key feature of our technique is the application of RPCA to decompose the dynamic series into low rank and sparse components within an iterative framework, the aim being to register out respiration from the low rank component. The proposed two-stage approach can be considered as a pre-processing followed by a modelling step using different types of registration. It was chosen to use a previously validated metric which required to remove the confounding effects of respiration prior to analysis. This was achieved using RDDR. Such a technique is intended to remove corrupting motion effects (i.e. respiration) and has proved

[5] All motility scores are given in arbitrary units

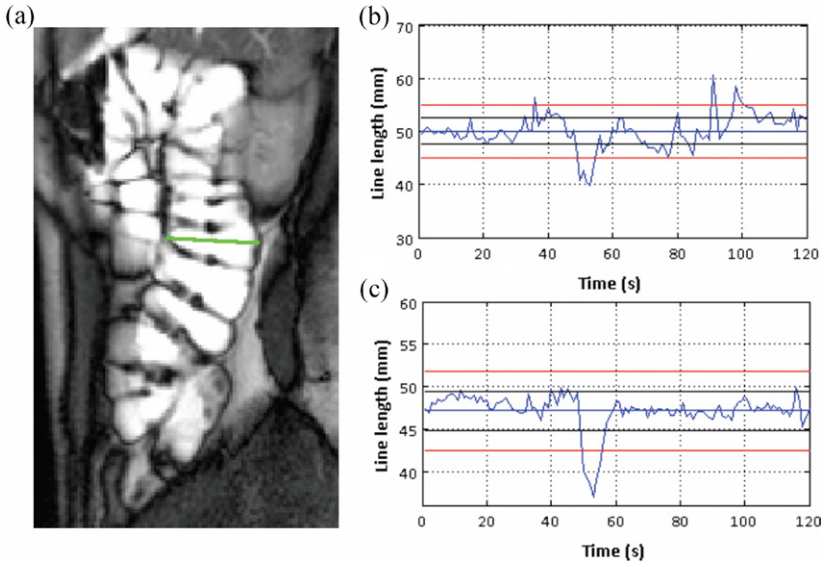

Figure 8. Sagittal view of the ascending colon with line ROI across colon diameter (*a*). Line ROI propagated in data registered with OF (*b*) and DRAM (*c*). Both ROIs remained manually unadjusted. Blue line represents mean line length, black lines represent ±5% and red lines show ±10% of mean diameter. In the absence of respiratory motion correction, plotting a line diameter through the time series shows an ambiguous impression of bowel contractility that becomes resolved using the DRAM revealing a single clear contraction. Importantly, the manual evaluation of this process in large time-series data is time consuming and automated using the DRAM technique.

successful in reducing misalignment in dynamic contrast enhanced MRI (Hamy *et al* 2013). The modelling using OF provides a representation of peristaltic motion as a series of vector fields that can be summarized using the standard deviation of the Jacobian determinant metric. An alternative to the proposed method could include a removal the slow varying component from a single deformation field computed using a single registration step. However, this possibility was not explored in this study.

Within our scheme, parameters were selected empirically once and the same values were used for all datasets providing results that appear generalizable to both the colon and small bowel. Investigating the effect of varying the parameters in RDDR would be of interest in future work.

An iterative scheme was used within RDDR to remove the respiratory component of motion. The risk of losing physiological information related to peristalsis was reduced by modifying the original version of the algorithm to impose a specific stopping criterion. Although the stopping criterion was determined from one example data set, the parameter settings were fixed for all subjects in both the small bowel and colon data sets. The performance of DRAM across these data sets suggests that no further adjustment would be required in another cohort. To quantify the effect of the respiratory motion correction, the motility metric was compared between the pseudo-ground truth breath-hold and the free breathing DRAM data over global small bowel ROIs. We demonstrated comparable results using free breathing DRAM data and the pseudo-ground truth of the BH. Specifically the breath-hold OF registration gave comparable global scores to DRAM and a positive bias in OF-alone registered global motility scores in free breathing datasets was observed. The decrease in registration accuracy was supported by the manual adjustment experiment 3.1.1. This supports our conclusion that DRAM removes respiratory

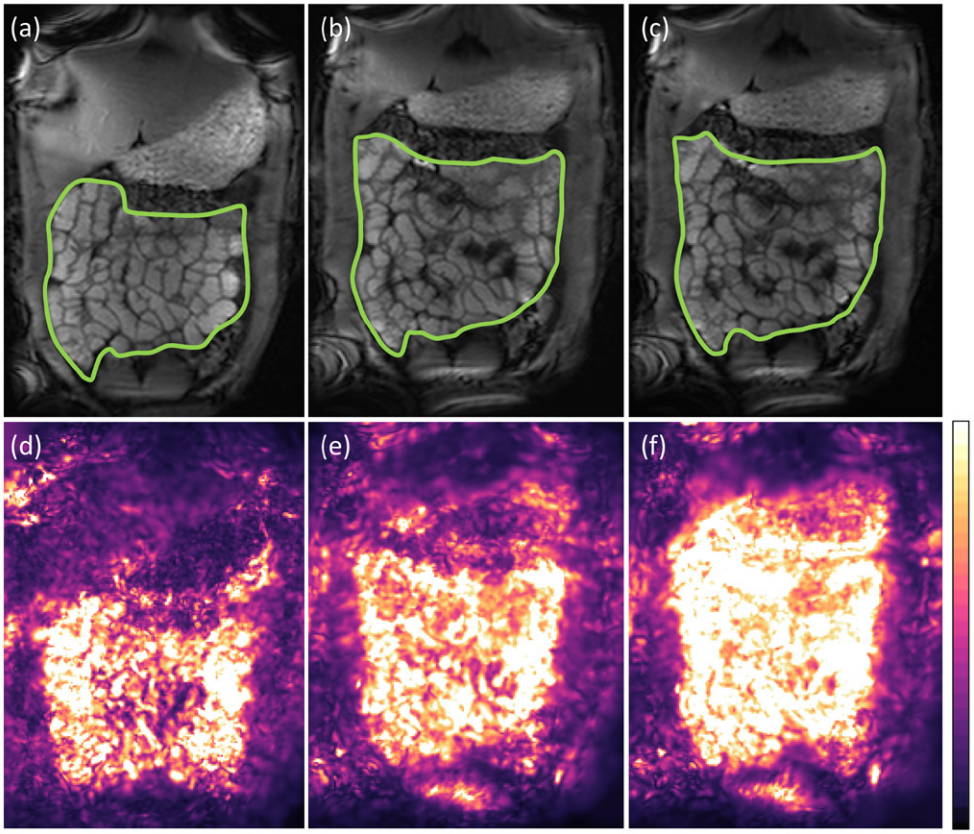

Figure 9. Example data with contoured small bowel region and motility maps for breath-hold ground truth (*a*, *d*), DRAM (FB) (*b*, *e*) and free breathing optical flow registration alone (*c*, *f*), respectively. Respiratory motion compensation is visible as reduced motility in the transverse colon closest to the diaphragm and systemically over the small bowel. The effect of RDDR is less apparent in the lower bowel further from the diaphragm where the effects of free breathing are less pronounced. Motility map shows black as lower motility and white as higher.

motion whilst leaving peristaltic motion largely intact. The breath-hold data was not a perfect ground truth as the data was temporally separated from the subsequent free breathing data collection and we identify this as a study limitation. However the 30 s time difference from the commencement of the breath-hold to the commencement of the free-breathing series is unlikely to impact significantly on a summary measure of bowel motion especially when assessed in a global manner. We do acknowledge that regional differences may be present when visualising the motility maps however this likely corresponds to intrinsic bowel motility variation over time.

We assessed the accuracy of the registration technique by comparing algorithm-propagated ROIs through the time series data and comparing their size and position to a manually adjusted ground truth. Assessment of the DRAM corrected data demonstrated greater registration accuracy with a mean error comparable to previous values in breath-hold data by Odille and Bikelhaupt (Odille *et al* 2012, Bickelhaupt *et al* 2014). The DRAM data did however show a slightly larger variance in the Bland-Altman LoA when compared to the original Odille data using breath-hold data. This is likely due to several factors, principally the choice of ROI position which in the current study was the upper left quadrant (i.e. proximal bowel close to the diaphragm) with the specific

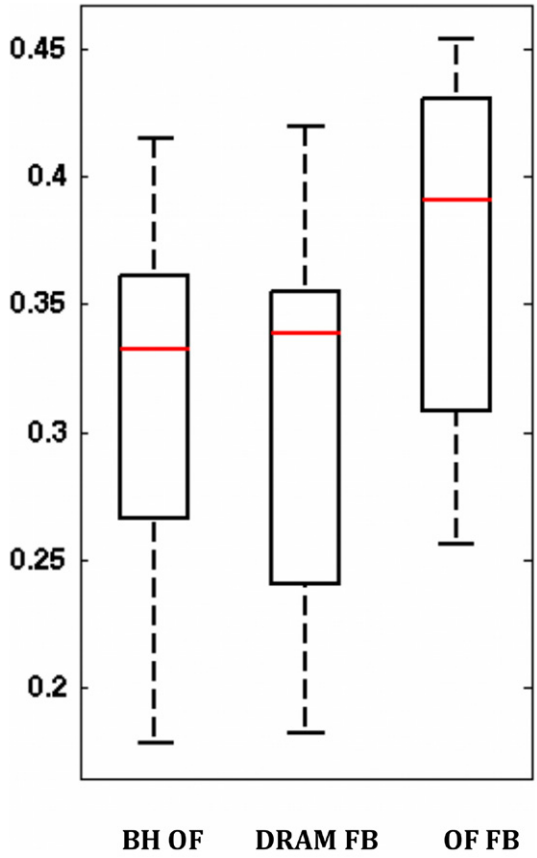

Figure 10. Box plots for OF derived motility scores in the 20 subjects with range (dashed line), interquartile range (box) and median (red horizontal line) for breath hold optic flow registered data (BH OF), free breathing DRAM (DRAM FB) and free breathing optic flow alone (OF FB) registered data.

intention of challenging the capabilities of the respective algorithms with the effects of respiration. We also assessed the displacement distance of the adjusted ROIs to the manual gold standard to identify ROIs that may have been mis-registered to adjacent bowel loops etc. This comparison is a good test for registration as it is based directly on displacements reflecting registration accuracy and has not previously been performed in other small bowel motility validation studies. On average less manual correction was necessary in the DRAM data and when ROIs were adjusted, the median distance and variance was several times lower than that without RDDR pre-processing. By collectively assessing these two components of registration fidelity in a challenging region of bowel, we subjected both DRAM and OF algorithms to a robust test and in both cases we found DRAM performed better in comparison to the ground truth and comparable to existing literature values derived using BH OF. A potential limitation in this study is the absence of simulated small bowel datasets to characterise the decomposition process. However, we chose not to include a simulation experiment for the assessment of the method's performance instead focusing on clinical datasets. The rationale for this choice comes from the extreme difficulty to simulate realistic peristaltic motion (in the small bowel especially). Directly using the deformation field resulting from OF registration is possible. However, this would not include changes absorbed in the algorithm intensity correction field which may lead to a different output in RPCA compared to real clinical data.

An important component of our investigation was the application of our methodology to colonic data sets. Physiologically, the colon is quite different from the small bowel with a less frequent contraction rate (Scott 2003). Using the same parameters employed for the small bowel registration we found again that DRAM performed well, largely correcting the effects of free breathing and permitting the accurate registration of colon wall deformation. Automated propagation of a linear ROI through the time series was possible with seemingly accurate assessment of contraction compared to our ground truth with manual adjustment. Due to the slow contraction rate of the colon, this increase in registration fidelity is important as manual measurements are exceptionally time consuming and not practicable in clinical practice. In this study, we applied the technique to two colonic regions per data set in a total of nine data sets, which is relatively small. Furthermore, with only two contractions expected to occur over the 2 min scan, future work might extend the data acquisition time to around 10 min to more fully explore colonic physiology with MR. However the aim in this preliminary work was to demonstrate the broad applicability of the unaltered DRAM technique to the colon, an organ with different physiological characteristics to the small bowel and using data acquired at a different MRI field strength and over a different number of time frames. Future work will involve the development of improved metrics to summarise colonic motility and assess sensitivity of MR as a modality to investigate this organ.

Finally, from a practical perspective, Magnetic Resonance Enterography is an increasingly popular method for the investigation of disease in the abdomen. MRE does not utilise ionising radiation and is non-invasive with ingestion of Mannitol being largely well-tolerated (Stange *et al* 2006, Horsthuis *et al* 2009). Methods for the analysis of the large quantities of dynamic data are important components of the translation of this non-invasive physiological imaging technique into clinical practice.

5. Conclusions

In this study we validate a new post-processing methodology for extracting quantitative metrics to assess small bowel and colonic motility during free-breathing. Improvement was demonstrated both in segmental and global analyses when using DRAM that will likely be of use in clinical studies investigating the complexity of GI tract motility.

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