Quantification, Validation, and Follow-up of Small Bowel Motility in Crohn’s Disease

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ABSTRACT

The use of magnetic resonance enterography (MRE) has become a mainstay in the evaluation, assessment and follow up of inflammatory bowel diseases, such as Crohn’s disease (CD), thanks to its high image quality and its non-ionizing nature. In particular, the advent of faster MRE sequences less sensitive to image-motion artifacts offers the possibility to obtain visual, structural and functional information of the patient’s small bowel. However, the inherent subjectivity of the mere visual inspection of these images often hinders the accurate identification and monitoring of the pathological areas. In this paper, we present a framework that provides quantitative and objective motility information of the small bowel from free-breathing MRE dynamic sequences. After compensating for the breathing motion of the patient, we create personalized peristaltic activity maps via optical flow analysis. The result is the creation of a new set of images providing objective and precise functional information of the small bowel. The accuracy of the new method was also evaluated from two different perspectives: objective accuracy (1.1 ± 0.6 mm/s of error), i.e., the ability of the system to provide quantitative and accurate information about the motility of moving bowel landmarks, and subjective accuracy (avg. difference of 0.7 ± 0.7 in a range of 1 to 5), i.e., the degree of agreement with the subjective evaluation of an expert. Finally, the practical utility of the new method was successfully evaluated in a preliminary study with 32 studies of healthy and CD cases, showing its potential for the fast and accurate assessment and follow up of CD in the small bowel.

Keywords: Small bowel motility, Crohn’s disease, MR enterography, optical flow, quantification.

INTRODUCTION

According to recent studies, there has been an increase in the incidence of inflammatory bowel diseases at a global level [1]. In particular, Crohn’s disease (CD) affects 14.6 cases per 100,000 person-years in North America. CD typically manifests in the lower part of the small bowel and the colon, with the former involved in 80% of the diagnosed cases. While traditional colonoscopy allows access to the colon, the poor access to the complex anatomy of the small bowel greatly hinders its diagnosis and assessment [2].

Advances in the field of diagnostic imaging have led to the development and clinical implementation of new optimized MR imaging protocols. In particular, magnetic resonance enterography (MRE) has become a mainstay in the evaluation of small bowel disease, thanks to its non-invasive nature, and the absence of ionizing radiation, making it especially useful in the pediatric population and for patients who require serial imaging [3]. Cine sequences, such as Fast Imaging Employing Steady-State Acquisition (FIESTA) sequence, are free-breathing MR sequences in which a single volume of the abdomen is continuously imaged for a few seconds to allow monitoring and quantification the small bowel peristalsis. This cine sequence allows the study and monitoring of the motility patterns of the small bowel to identify potential functional abnormalities related to CD [5][7][11]. Despite the fact that the inclusion of small bowel motility
Optical Haw Avskack ftti evaluation increases the lesion detection rate for CD-related pathological findings [6], the interpretation of MRE remains subjective and variable.

The main goal of this work is to create a new set of images that allows the specialist to objectively analyze the peristaltic activity of the small bowel extracted from free-breathing FIESTA sequences. Since both respiratory and peristaltic motions are present in these images, we first correct the respiratory component via non-rigid image registration. Once the respiratory effects are compensated, we characterize the small bowel peristalsis via optical flow analysis, creating an intestinal activity map of the patient that provides objective quantitative information of the abdominal motility.

To the best of our knowledge, very few studies have addressed the feasibility of automated computerized assessment of small bowel motility via quantitative image analysis [7][8]. However, the validation of these technologies is a question that remains open. Farghal et al.[7] proposed the validation of their framework by means of a score on how well the parametric map they created represented the subjective small bowel activity perceived by an observer. On the other hand, Hamy et al. [8] suggested a more complex but more objective approach, developing a specific phantom able to simulate both respiratory and peristaltic motion.

In this work, we evaluate the new peristaltic activity maps in two different ways. First, we compare the automatically quantified peristalsis with that obtained by manually tracking in-plane motion of selected small bowel segments. We also study the correlation between the automatic peristaltic maps and the qualitative evaluation of clinical experts on the relative motility of the intestine. Finally, the new peristaltic-map images are evaluated by a board certified radiologist to assess the potential for the evaluation and follow up of CD.

Figure 1. Respiratory motion correction for FIESTA data. (a)(b) Pre- and post-registration horizontal intensity projection over time, respectively. (c) Difference between two frames of the original unregistered sequence (gray regions show where the two frames have the same intensities, while colored areas show where the intensities are different). (d) Registration to a frame at the end of the exhalation phase (▼). (e) Registration to a frame in the middle of the respiratory cycle (▼). Note that the correction of respiratory motion should not eliminate peristalsis (the residual motion in (e)).

Figure 2. Peristalsis activity map. Three consecutive registered frames (i.e., after correction of abdominal motion) from the FIESTA sequence showing the peristalsis of a small bowel section are presented from left to the right. The average magnitude of the resulting small bowel motility is shown in the right image.
METHODOLOGY

As the FIESTA sequence acquisition is relatively long (>100 s. per sequence), both respiratory and peristaltic motion are present in the MRE images (Fig. 1). Since for motility evaluation in CD the clinical interest is related only to the peristalsis, the respiratory component must first be eliminated. Let \( \{X_{i,t}\} \) represent the set of frames of the FIESTA sequence acquired at position \( i = 1, \ldots, N \) over time \( t = 1, \ldots, T \) (i.e., \( i \) defines the location in the sagittal axis in which the coronal images are acquired), where the time instants \( t \) were discretized for the simplicity of notation. Due to the complexity of the respiratory cycle, its effects cannot be compensated by means of simple rigid registration. Instead, we performed a two-stage B-Spline non-rigid registration over each \( i \)-th set of frames, using a least-square cost function, and the \( t_{\text{ref}} \)-th frame, \( X_{i,t_{\text{ref}}} \), as reference image. In particular, we used a first-order B-Spline for the first stage of the registration followed by a second-order registration [12]. The use of first-order B-Splines allowed us to compensate for the main respiratory motion that affects the entire abdomen without introducing artificial local deformations that could alter the actual peristalsis. Then, the second-order stage allowed correction for the residual respiratory motions. We selected \( t_{\text{ref}} \)-th as a frame in the middle of the breathing cycle (Fig. 1(a)). In this work, we selected \( X_{i,t_{\text{ref}}} \) manually, though the process can be automatized by analyzing the concatenation of the horizontal intensity projection of each frame, \([x_{i,1}, \ldots, x_{i,T}]\), where \( T \) is the number of frames (Fig. 1(a)(b)).

Suppose now \( \{\bar{X}_{i,t}\} \) represents the set of registered frames using \( X_{i,t_{\text{ref}}} \) as a reference. Once the breathing motion has been compensated, we extracted the remaining pattern of apparent motion (i.e., the peristalsis of the small bowel) from this sequence of ordered images. Optical flow theory allowed us to model these deformations in the small bowel as flow patterns, that is a vector field whose components, \( u \) and \( v \), represent the local image flow (motility) at each pixel. In this work, we used the differential-based optical flow approach originally introduced by Horn and Schunk [4]. This method uses the typical flow constraint equation, imposing an additional global smoothness constraint. The resulting global energy function to minimize is

\[
E = \iint \left( \nabla X_{i,t} \cdot V_{i,t} + \frac{\partial X_{i,t}}{\partial t} \right)^2 + \alpha^2 \left( \|\nabla u_{i,t}\|^2 + \|\nabla v_{i,t}\|^2 \right) \, dx \, dy
\]

(1)

where \( V_{i,t} = [u_{i,t}, v_{i,t}] \) is the optical flow field, and \( \alpha \) is the regularization constant. Equation (1) can be minimized by solving the associated Lagrange equation (see [4] for details). At each position, the motility maps of the intestine were created by averaging the magnitude of the optical flow obtained for each frame: \( M_{i,t} = (1/T) \left( \sum_{t=1}^{T} \|V_{i,t}\| \right) \) (Fig. 2).

To evaluate the obtained motility maps, two different user interfaces for evaluation were developed. The goal of these interfaces was to validate our technology to quantify the small bowel motility from two different points of view. Method 1 allows the user to obtain objective information on the motility of the small bowel by manually defining a set of points to track from one frame of the MRE FIESTA sequence to another. Although \( M_{i,t} \) provides information on the whole image, only those segments that exhibit in-plane displacement are prone to be tracked (Fig. 3 and 4). Method 2 aims to study the correlation between the automatic motility maps and the qualitative evaluation of an expert radiologist. In this case a 10×10 grid is overlaid on the FIESTA sequence \( \{X_{i,t}\} \) asking the observer to score each cell on the grid according to its degree of activity using a 5-point scale, with 1 indicating an almost -static area, and 5 indicating high motility (Fig. 5).

RESULTS

Following the procedure described above, the new technology to quantify small bowel motility was evaluated in 32 studies from 17 patients (7 healthy cases with no evidence of inflammatory bowel disease, and 10 cases in which the experts detected intestinal pathology related to CD). This retrospective study was HIPAA compliant and was approved by the IRB Committee at Children’s National Health System, and the requirement for informed consent was waived. The MRE scans were obtained using two different systems: Optima MR450 1.5T and Discovery MR750 3.0T, both from GE Healthcare. Image size was 512 × 512 pixels in the axial plane with resolution from 0.82 to 0.94 mm per pixel. The FIESTA sequences were composed by 18 locations/slices with 15 frames per location and a slice thickness of 8 mm.

Proc. of SPIE Vol. 9414  94141D-3
A total of 25 segments with in-plane motion were identified and manually tracked using Method 1 described above to evaluate the accuracy of the new motility maps (Figs. 3 and 4). The results showed that these automatic maps tend to underestimate the motility of the small bowel in comparison with the data obtained manually with an average difference of $1.1 \pm 0.6$ mm/s. To evaluate the correlation of the motility maps with the subjective evaluation of an expert radiologist using Method 2, the motility values were normalized and quantized to the same discrete range used by the software (from 1 to 5; 1: static - very low motility; 5: high motility), obtaining an average difference of $0.7 \pm 0.7$. The accuracy of our method was higher than values reported in the state of the art literature [10]. As some investigators point out [9], the optical flow estimation is marked by the requirement of the dense sampling in time, and also by the scale of the structures whose motility is being estimated. Thus, the limited temporal resolution of FIESTA (~0.37 seconds per frame) and the reduced size of some segments of the small bowel in these images could be at the origin of these discrepancies between manual and automatic assessments of motility.

Finally, the utility of the motility maps was evaluated by a board certified radiologist to assess the potential for the evaluation and follow up of CD. In particular, the expert was presented with the new maps of the bowel motility that identified and highlighted the regions with reduced motility that may require additional attention. Small bowel areas presenting wall thickening or luminal narrowing were successfully matched with regions with reduced motility in all pathological cases. Areas of reduced motility (<0.6 mm/s) were also identified among the healthy cases, though no evidence of small bowel abnormality was revealed after further structural analysis. Regarding patients’ follow up, the framework allowed successfully the identification of a relative improvement in the motility of the affected areas (from <1mm/s to 1.5 mm/s) for two patients who exhibited a positive clinical response to CD treatment over time. A decrease in the overall motility (from >2.7mm/s to <1.6 mm/s) was observed for other two patients with an interval progression of CD, while no difference in the motility was observed for the rest of our cases. In general, our method allowed to quantify that the healthy small bowel motility can go up to 3 mm/s, while in the areas of reduced motility the motion of

Figure 3. Set of four points manually drawn in two series of FIESTA images of the small bowel describing the in-plane motion of a small bowel segment.

Figure 4. Markers describing the contraction-distension of a longitudinal section of the small bowel.
In the bowel was less than 0.6 mm/s. A shortcoming of our analysis is that it did not account for the inter- and intra-individual variability of small bowel motility.

CONCLUSIONS

Despite the increasing incidence of CD at a global level, tools that characterize MRE images of the abdomen in an objective, quantitative and reproducible manner are lacking. The aim of this study is to establish a proof of concept of the potential of a new quantitative imaging biomarker of small bowel motility to facilitate the objective longitudinal follow up of patients affected by CD, and to provide functional information about small bowel diseases. Firstly, we isolated the peristaltic activity from the breathing motion using non rigid B-spline based registration. This motion correction allowed the application of our method to pediatric population, where the free-breathing FIESTA sequence is the mainstay in the evaluation of the small bowel motility. Next, the new peristaltic activity maps were generated via optical flow analysis.

In this paper, we also introduce two approaches to manually rate the motility of the small bowel. The information provided by these tools allowed us to study the accuracy of the automatic motility maps and the correlation with the subjective perception of an expert observer. The motility maps showed an error of $1.1 \pm 0.6$ mm/s, and a discrepancy with the subjective perception of an expert of $0.7 \pm 0.7$ (in a range of 1 to 5).

Finally, a preliminary study with 32 studies revealed the practical utility of these new data in in-vivo clinical studies, and their potential contribution to CD patient diagnosis and follow up. Further validation is needed to determine if these new imaging biomarkers correlate with patient symptoms and clinical observations.

In the near future, we plan to use the new evaluation tools to further analyze the inter-observer variability in the interpretation of the small bowel motility.

ACKNOWLEDGMENT

This project was supported by a philanthropic gift from the Government of Abu Dhabi to Children’s National Health System. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the donor.
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