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1 Registration of the endoluminal surfaces of the colon derived 2 from prone and supine CT colonography

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Abstract.

Purpose: Computed tomographic (CT) colonography is a relatively new technique for detecting bowel cancer or potentially precancerous polyps. CT scanning is combined with 3-dimensional image reconstruction to produce a virtual endoluminal representation similar to optical colonoscopy. Because retained fluid and stool can mimic pathology, CT data is acquired with the bowel cleansed and insufflated with gas and patient in both prone and supine positions. Radiologists then match visually endoluminal locations between the two acquisitions in order to determine whether apparent pathology is real or not. This process is hindered by the fact that the colon, essentially a long tube, can undergo considerable deformation between acquisitions. We present a novel approach to automatically establish spatial correspondence between prone and supine endoluminal colonic surfaces after surface parameterization, even in the case of local colon collapse.

Methods: The complexity of the registration task was reduced from a 3D to a 2D problem by mapping the surfaces extracted from prone and supine CT colonography onto a cylindrical parameterization. A non-rigid cylindrical registration was then performed to align the full colonic surfaces. The curvature information from the original 3D surfaces was used to determine correspondence. The method can also be applied to cases with regions of local colonic collapse by ignoring the collapsed regions during the registration.

Results: Using a development set, suitable parameters were found to constrain the cylindrical registration method. Then, the same registration parameters were applied to a different set of 13 validation cases, consisting of 8 fully distended cases and 5 cases exhibiting multiple colonic collapses. All polyps present were well aligned, with a mean (\pm std. dev.) registration error of 5.7 (\pm 3.4) mm. An additional set of 1175 reference points on haustral folds spread over the full endoluminal colon surfaces resulted in an error of 7.7 (\pm 7.4) mm. Here, 82% of folds was aligned correctly after registration with a further 15% misregistered by just one fold.

Conclusions: The proposed method reduces the 3D registration task to a cylindrical registration representing the endoluminal surface of the colon. Our algorithm uses surface curvature information as a similarity measure to drive registration to compensate for the large colorectal deformations that occur between prone and supine data acquisitions. The method has the potential to both enhance polyp detection and decrease the radiologist's interpretation time.

1. INTRODUCTION

1.1. Motivation

11 Colorectal cancer is the second-largest cause of cancer mortality in the West, responsible for more than 1 million
12 cases and 639 000 deaths each year¹. Early detection and removal of potentially precancerous polyps (adenomas)
13 arising from the endoluminal colonic surface has been shown to significantly reduce the incidence of subsequent
14 colorectal cancer and thus mortality². Optical colonoscopy (insertion of a video-endoscope into the cleansed colon)
15 is the reference-standard whole-colon diagnostic test and combines diagnosis and treatment (since polyps can be
16 removed). However, the procedure is uncomfortable for the patient, technically difficult to perform, and is occasionally
17 associated with significant adverse events, including colonic perforation³.

18 Computed tomographic (CT) colonography (CTC) is a relatively new alternative technique for imaging the col-
19 orectum which has been shown in large comparative studies to be as sensitive as colonoscopy for larger polyps and
20 cancer^{4,5}. Moreover, studies have shown CT colonography to be more acceptable to patients than colonoscopy⁶, and
21 to be relatively safe⁷. As for colonoscopy, the patient usually undergoes full cathartic bowel preparation prior to imag-
22 ing. Subsequently, multi-detector helical CT is carried out with carbon dioxide colonic insufflation of the bowel (via a
23 small rectal catheter) to maximize the attenuation contrast between the endoluminal surface and the colonic lumen. Im-
24 age rendering software is used to reconstruct a 3-dimensional representation of the endoluminal bowel surface; hence
25 the alternative title, *virtual colonoscopy*⁸. However, residual stool and fluid (or even normal anatomical variants) can
26 sometimes look like polyps, and some regions of bowel may be under-distended, which impairs image interpretation
27 by radiologists. To counteract this, it is standard practice to image the patient in two positions - prone and supine -
28 which redistributes gas and residue within the colon⁹. By comparing corresponding regions from prone and supine
29 datasets, the radiologist can assess whether a potential abnormality perceived on one dataset is a real polyp (i.e. its
30 position remains the same, indicating fixation to the bowel wall) or retained stool (i.e. it moves). However, the colon
31 is a relatively long tubular structure that is loosely attached to the abdominal wall via variable mesenteric attachments.
32 The result is that the colon often undergoes considerable deformation during patient repositioning¹⁰, or even severe
33 local under-distension which can lead to colonic collapse. This complicates the interpretation task; identifying corre-
34 sponding regions of endoluminal surface between prone and supine acquisitions is difficult, prolongs reporting time,
35 and may lead to errors of interpretation. A reliable method for establishing spatial registration between the prone and
36 supine CT colonography datasets has the potential to simultaneously improve diagnostic accuracy and reduce inter-
37 pretation time. Furthermore, its result could be incorporated in computer-aided detection (CAD) algorithms in order

38 to improve their robustness and accuracy.

39 1.2. Related work

40 The earliest attempt at prone-supine registration involve identifying similar distances along an extracted centerline
41 of the segmented colon in both datasets^{11,12,13,14,15}. This line represents the virtual path through the center of the
42 virtual colonic lumen, from anus to cecum. Methods involve linear stretching and shrinkage of the extracted centerlines
43 based on relative path geometries (for example, local maxima on each centerline's axial coordinate as tie points). Some
44 centerline-based methods can still be effective with colons exhibiting sections of colonic collapse where the segmented
45 colon is disconnected, e. g.^{13,15}.

46 However, these methods provide only one degree of freedom relative to the colonic surface and so can only account
47 for local stretching and shrinking along the length of the colon – they cannot account for torsion or other deformations
48 ‘around’ the colon. Hence, they do not account for all the detailed deformation of the colon surface that we are
49 interested in that commonly occurs between prone and supine positioning such as colonic torsion. Furthermore,
50 aligning the centerline between the prone and supine images is restrained to establish the correspondence between
51 the global shapes of the colon between both views. This shape can vary greatly when the patient changes positions and
52 centerline-based methods might experience difficulties.

53 Alternatively, Näppi¹⁶ defined several anatomical landmarks, using these to align the two datasets. Anatomical
54 locations that are relatively resistant to deformation, such as the anus or colonic flexures, were identified. Other
55 landmarks, including the cecum and recto-sigmoid junction, were inferred relative to the landmarks already defined.
56 However, identification of a limited number of corresponding points is likely to be insufficient to describe the complex
57 colonic deformations that occur when moving between prone and supine positions.

58 Other feature-based methods account for colonic rotation by using the teniae coli (three discrete muscles running
59 longitudinally along the exterior colonic surface) as an additional feature^{17,18}. However, the teniae coli alone are
60 difficult to extract robustly. As with centerline-based methods, they aim to match the global shape of the colon and
61 then have to interpolate to the surface in order to estimate the deformation of the detailed surface structure.

62 A voxel-based approach has been developed by Suh et al.¹⁹. Initially, Suh's method involves rigid dataset alignment,
63 based on the location of the anus and the flexures followed by generation of an initial deformation field using
64 the centerlines. Level-set distance maps from the colonic surface are then used to drive a non-rigid registration.
65 They reported an error of 13.77 (\pm 6.20) mm for aligning polyps in 21 patients. In our experience such voxel-
66 based approaches lack robustness as it is very difficult to adequately constrain the registration to prevent physically
67 implausible deformations while still recovering the large and complex deformations that can occur.

68 They extended their method to handle cases with local colonic collapse where the segmentations are disconnected²⁰.

69 Although they show promise in handling disconnected segmentations, the validation set was limited to 4 CTC cases
70 with only one collapse in one view and fully connected colon segmentation in the other. A reported average registration
71 error of 30.1 mm for 4 polyps suggests limited accuracy. This may be due to their method of handling local collapses
72 which allows the colon to change its topology during the registration. This could cause different structures to appear
73 similar to each other rather than correctly aligning the corresponding anatomical structures, e. g. a fold being flattened
74 rather than shifted.

75 Fukano et al.²¹ aimed to establish correspondence between the detailed colon surface by matching haustral folds
76 extracted from prone and supine data. Although haustral folds can be detected robustly, it is very challenging to
77 establish their correct correspondence between both views as their results indicate. They report 65.1% of corresponding
78 large haustral folds and 13.3% of small haustral folds being matched correctly.

79 Recently, Zeng et al.²² presented a method based on conformal mapping combined with feature matching in order
80 to establish correspondences between the prone and supine surface. They detect four flexures and one teniae coli in
81 order to divide the colon surface into five segments and map each segment to a rectangle. Correspondence between
82 prone and supine surfaces is then established for each rectangular segment individually. Therefore the method relies
83 on being able to accurately determine exactly the same segments on the prone and supine surfaces, which can be very
84 difficult even for fully distended colons, and may not be possible for cases with local colonic collapse. Furthermore,
85 they established correspondence between the mapped segments using only a sparse point set of features extracted from
86 some ‘prominent’ haustral folds, which are unlikely to provide an accurate alignment of the detailed colonic surface.
87 Despite these drawbacks, they report promising results with an average 3D error of 5.65 mm using 20 validated pairs
88 of polyps over 6 patients and a average 3D error of 7.51 mm using feature points.

89 **1.3. Proposed solution**

90 The difficulties described in the previous sections motivated us to develop a method that simplifies the task of
91 establishing full spatial correspondence between prone and supine endoluminal colon surfaces. Since the colon is an
92 extremely flexible structure, the registration task requires a non-rigid transformation but should preserve the topology
93 of the colonic wall. Our method reduces complexity by using cylindrical 2D representations of the endoluminal surface
94 extracted from both prone and supine CTC datasets. This enables us to account for the large deformations and twisting
95 that are inevitable between the two positions in 3D as relatively simple deformations of the cylinder.

96 Topologically, the colon is an open-ended cylinder or tube. Hence, any position within the colon can be mapped by
97 two indices: length along the cylinder and angular position. Each 2D point $p(x, y)$ on the cylindrical representation
98 corresponds directly to a 3D point $s(x, y, z)$ in the CTC data. Any measure acquired in 3D and on the surface can be
99 assigned to a corresponding 2D point p which can be used to drive registration. We propose the use of conformal

100 mapping of the endoluminal colonic surfaces from prone and supine CT colonography to obtain a 2D cylindrical
101 representation. A shape measure is assigned to each 2D point p in order to drive a non-rigid cylindrical registration in
102 the parameterized cylindrical space. This simplifies the registration task compared with full 3D volume registration.
103 This registration is represented as a transformation between two cylinders that includes non-linear stretch along
104 the colon, local rotation and local torsion. We propose a cylindrical implementation of the well-known B-spline
105 registration method²³ in order to achieve this for fully connected colon and in the case of local colonic collapse.

106 A similar cylindrical B-spline transformation model was recently proposed by Huysmans et al.²⁴ in order to produce
107 active shape models of tubular structures (e.g. clavicles, tracheae, and thrombi). Although the transformation model is
108 very similar to the one used in this paper, their application is very different (they are trying to determine correspondence
109 for a large population of shapes), and as such their method of assessing correspondence (the minimum description
110 length of the resulting shape model) and their overall framework for performing the registrations cannot be used for
111 registering prone and supine colonic surfaces.

112 We claim novelty for the first use of a cylindrical non-rigid registration method to align image derived representa-
113 tions of the full colon endoluminal surface in order to establish a correspondence between colon surfaces extracted
114 from prone and supine CTC. Our motivation is to simplify the radiologist’s task in interpreting the two datasets, in
115 particular the assessment of possible polyps in the two views, to reduce the incidence of false positives, speed up
116 interpretation and finally to provide correspondence in emerging computer assisted detection (CAD) applications that
117 merge prone and supine datasets in order to reduce false positive detection rates.

2. METHODS

118 Each surface point on the endoluminal colon surface S can be described with two indices x and y using a cylindrical
119 representation. Here, x denotes a position along the length of the colon and y its angular orientation. Several groups
120 have proposed methods to “unwrap” or “virtually dissect” the colon in order to produce flattened 2D images of the
121 endoluminal surface, which were developed to facilitate more rapid interpretation²⁵.

122 Conformal maps are typically applied to surface mesh triangulations in order to find a simpler representation of
123 the three-dimensional object. They provide a one-to-one mapping of a 3D surface to 2D space while preserving local
124 angles²⁶. These methods are based on differential geometry and ensure conformal mapping of the entire surface while
125 preserving appearance of local structures, e.g. polyps and haustral folds.

126 Our registration approach is based on the following principle: a prone endoluminal colon surface S_p in \mathbb{R}^3 can be
127 transformed using the one-to-one mapping f_p to a parameterization P_p in \mathbb{R}^2 . The supine surface S_s is mapped to P_s
128 through f_s , respectively. Here, p and s denotes prone and supine respectively. If the necessary transformation \mathbf{T}_{cyl}
129 between P_p and P_s can be determined, the transformation \mathbf{T}_{ps} between the surfaces S_p and S_s follows as shown in

130 Fig. 1, where the principle is illustrated with the endoluminal colon surfaces extracted from prone and supine CT
 131 colonography.

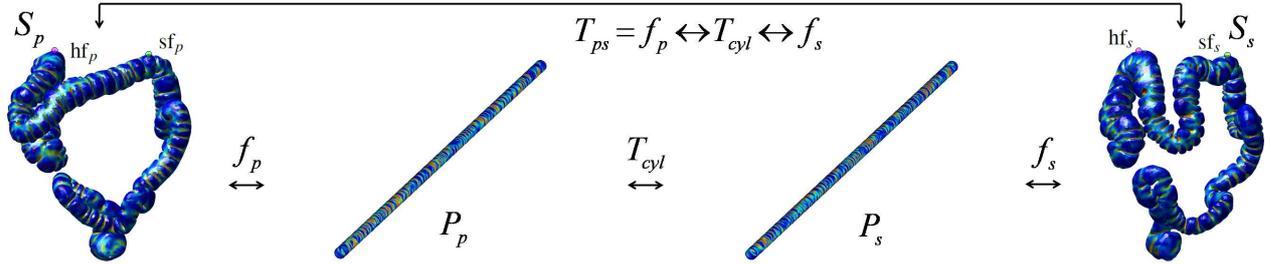


FIGURE 1. The principle of colon surface registration between prone and supine CTC using a cylindrical 2D parameterization (for patient 7), where the color scale indicates the shape index (see equation 2) at each coordinate of the surface computed from the 3D endoluminal colon surfaces. The hepatic and splenic flexures are marked as $hf_{p/s}$ and $sf_{p/s}$ respectively ($_{p/s}$ denotes prone/supine).

132

2.1. Colon segmentation

133 In order to extract the endoluminal colonic surface S , the inflated lumen L is segmented using the method described
 134 by Slabaugh et al.²⁷. This method was developed for segmenting intraluminal gas over the entire colonic length. It is
 135 possible that gas-filled regions of small intestine are segmented as either isolated structures or connected to the colonic
 136 segmentation. Because we are only interested in the endoluminal surface of the colon, we reject all other objects by
 137 first eroding the segmentation with a spherical structure element with radius r to remove erroneous connections if
 138 necessary. Then the six-connected object with the largest volume is selected and subsequently dilated with a structure
 139 element of radius r in order to restore its original surface dimensions. Here, six-connected refers to an object in 3D
 140 voxel space which is only connected to direct neighboring voxels on its six sides. For this study, the radius r was
 141 adjusted interactively to produce the best segmentation by visual inspection. The parameter, r , ranged between 1 and
 142 5 voxels for all our cases.

143 The rectal insufflation catheter (used to introduce the colonic gas necessary for luminal distension) is often excluded
 144 from the segmentation and can therefore lead to errors when extracting the endoluminal surface. We use a combination
 145 of morphological operations on a rectal region of interest in order to segment this plastic tube and add it to the colon
 146 segmentation L if necessary.

147

2.2. Topological correction

148 The colonic lumen L is now represented as a single six-connected object, ideally with a surface of genus zero which
 149 is topologically equivalent to a sphere. However, topological errors could be present in the segmentation due to noise

150 or reconstruction artifacts in the CT colonography data. This occurs particularly at adjacent folds or where the colon
151 folds back against itself, resulting in erroneous connections in the surface as shown in Fig. 2 (left).

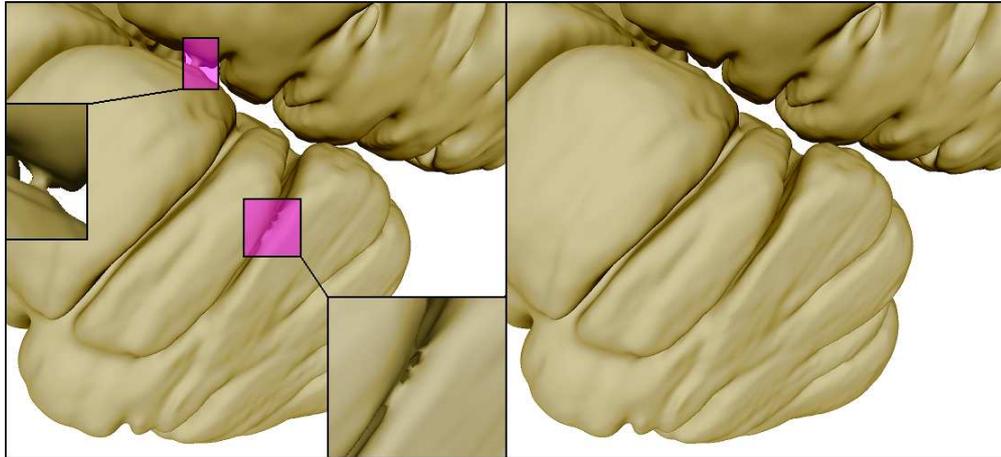


FIGURE 2. Left: handles and an erroneous connection caused by limitation of the segmentation quality, resulting in incorrect topology. Right: the same surface region after topological correction.

152 We use a thinning algorithm^{28,29} starting at the centerline (running at the virtual center of the colonic lumen from
153 cecum to rectum) and guided by a distance based priority map. This centerline can be extracted with the method
154 described by Deschamps et al.³⁰ based on evolving a wave front through the colon using the fast marching method³¹.
155 This method of centerline extraction requires a defined start- and end-point. If the insufflation tube has been detected,
156 we use the most caudal point inside the tube. Otherwise the most caudal point in the colonic lumen L is used. This
157 corresponds to the patient's ano-rectal junction in both projections. A point in the cecum is currently selected manually.
158 Good correspondence for centerline start and end points is not essential for topological correction but improves rectal
159 and cecal mapping to a cylindrical representation as described in section 2.4.

160 The extracted centerline is used to generate an image C with each voxel on the centerline labeled as foreground.
161 A topology preserving region growing algorithm is then applied to the foreground of C maintaining its topological
162 characteristics. In this case, the centerline object is topologically equivalent to a sphere (genus zero). The region
163 growing will thus fill L whilst leaving voxels untouched which would introduce a topological change, e.g. handles.
164 This produces one-voxel-wide cuts through handles at the minimum distance position, resulting in a topologically
165 correct genus-zero segmentation L_{corr} of the endoluminal colon lumen (see Fig. 2).

166 2.3. Colonic surface extraction

167 The endoluminal colonic surfaces S are then modeled as triangulated meshes on the surfaces of L_{corr} , lying on the
168 gas-tissue border in the CTC images. Those surfaces are now guaranteed to be topologically correct (of genus zero).
169 In order to extract S we use the marching cubes algorithm on L_{corr} with a subsequent smoothing using a windowed

170 sinc function interpolation kernel³². This approximates a continuous surface which facilitates the convergence to a
 171 2D parameterization using the Ricci flow method (as described in section 2.4). Furthermore, the mesh is decimated
 172 using a quadric edge collapsing method³³ in order to reduce computation time. Finally, Loop’s subdivision method³⁴
 173 is applied in order to achieve approximately uniformly sized and non-skewed faces over the entire surface S . This
 174 procedure results in a simply connected genus-zero surface S of the colonic lumen L_{corr} . For all cases used in this
 175 study, the surface meshes had typical edge lengths of 3.3 (\pm 1.3) mm and about 60,000 faces.

176 2.4. Cylindrical representation of the endoluminal colonic surface

177 As described above, the endoluminal colon surfaces S can be modeled as piecewise-linear meshes composed
 178 of vertices v_i that are connected using triangular faces. Those surfaces S can be parameterized using a discrete
 179 conformal mapping method. One method to parameterize arbitrary discrete surfaces was introduced by Hamilton³⁵ for
 180 Riemannian geometry based on Ricci flow. It deforms the surface proportionally to its local Gaussian curvature similar
 181 to a heat diffusion process until it converges towards a desired Gaussian curvature³⁶. Rather than mapping the surface
 182 to a rectangle as with other methods²², the Ricci flow does not require a border and therefore reduces distortion. Qiu
 183 et al.³⁷ were the first to apply it to a colonic surface using volume rendering for the purpose of visualization, and
 184 we follow their approach here with a small modification to the planar embedding (see below). We use Ricci flow to
 185 produce a conformal mapping onto a 2D plane. The Ricci flow is defined as

$$\frac{d\mathbf{u}_i(t)}{dt} = \bar{K}_i - K_i, \quad (1)$$

186 where K_i is the Gaussian curvature at vertex v_i , \bar{K}_i the desired Gaussian curvature and \mathbf{u}_i a weighting function,
 187 computed from a circle packing metric³⁶. Ricci flow can be described as the gradient flow of an energy function³⁸
 188 which can be minimized using the steepest gradient descent method. For the purpose of parameterization of the colon
 189 surfaces S in two-dimensional space, the target curvature K_i should be zero at all vertices v_i .

190 The original genus-zero surfaces S have to be converted to a surface SD of genus one³⁶ for this purpose, e.g.
 191 converting a sphere-like surface to a torus-like surface. Therefore, we create holes in the surface mesh by removing
 192 vertices and connected triangular faces closest to the previously selected cecal and rectal points. The remaining surface
 193 is doubled, inverted and glued with the original mesh onto the vertices and edges along the previously produced holes
 194 in a similar manner to³⁹. The resulting surface SD is then parameterized using the Ricci flow while minimizing the
 195 global maximum difference error between all current K_i and \bar{K}_i , E_{max} . This is computed until E_{max} convergence below
 196 a pre-set value, resulting in a mesh P in \mathbb{R}^2 with two-dimensional coordinates of each surface location on S .

197 For all patients used in this study, the Ricci flow was minimized below an error of $E_{\text{max}} = 1e^{-6}$ which results

198 in a surface mesh with its local Gaussian curvatures K_i tending to zero everywhere. This mesh can be embedded
 199 into two-dimensional space \mathbb{R}^2 using the resulting edge lengths of each triangle, starting from a random seed face
 200 and then iteratively adding neighboring faces, in a similar manner to³⁶. This is achieved by computing the position
 201 of each triangle vertex based on the intersection of two circles which have radii equal to the corresponding edge
 202 lengths. However, as K_i is not exactly zero at every vertex v_i , the resulting accumulated 2D mesh can have cracks
 203 and overlapping faces. These errors in computing the planar embedding P can be reduced if the Ricci flow converges
 204 towards smaller values of E_{\max} , but needs to be balanced against the computation time required for the Ricci flow.
 205 Segments of 2D surfaces, generated from the same endoluminal colon surface after convergence to different error
 206 levels E_{\max} , are shown in Fig. 3 (left, middle). However, if the errors in the planar embedding are small enough, the
 207 Ricci flow can be stopped and corresponding vertices of neighboring triangles can be joined together by averaging
 208 their two-dimensional positions. This results in a closed 2D mesh P without discontinuities as in Fig. 3 (right).

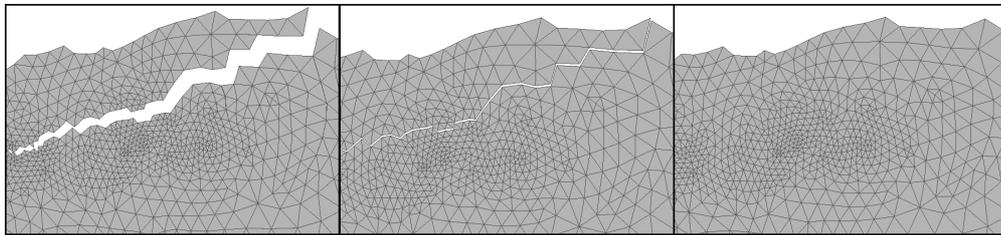


FIGURE 3. Computed planar embeddings P of the endoluminal colonic surface S with convergence errors $E_{\max} = 1e^{-4}$ (left), $E_{\max} = 1e^{-6}$ (middle) and the averaged planar embedding (right) with $E_{\max} = 1e^{-6}$.

209 The 2D mesh P represents a regular cylinder and can be re-sampled between 0 and 360° to generate rectangular
 210 raster images for use in the cylindrical registration as illustrated in Fig 4. Here, the horizontal dimension x corresponds
 211 to a distance along the colon from cecum to rectum and the vertical dimension y to the angular position around the
 212 circumference of the colon.

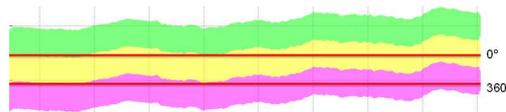


FIGURE 4. Sampling the unfolded mesh to generate rectangular raster-images I suitable for image registration. Each band represents a shifted copy of the planar embedded meshes P which are sampled between the horizontal lines to cover a full 360° of endoluminal colon surfaces S .

213 Sampling curvature information onto the parameterization P results in raster-images I for supine and prone endo-
 214 luminal colon surfaces as shown in Fig. 5 (top, middle). The top and bottom edges of the images I correspond to the
 215 same point on the endoluminal colonic surfaces S , thus representing the endoluminal colonic surface as a cylinder.

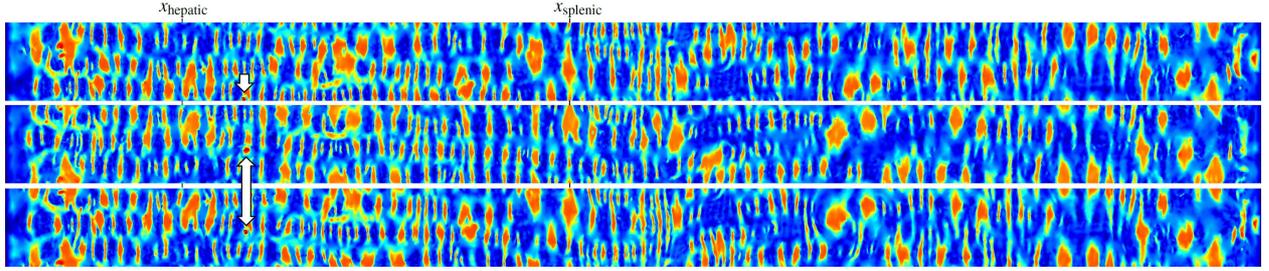


FIGURE 5. Supine (top), prone (middle) and deformed supine deformed to match prone (bottom) raster images of patient 7 where each pixel has the value of the corresponding shape index computed on the endoluminal colonic surface. The x -axis is the position along the colon, while the y -axis is its circumferential location. The x -positions for the detected hepatic and splenic flexures are marked as x_{hepatic} and x_{splenic} . The location of a polyp is marked before (top) and after registration (middle, bottom). Corresponding 3D renderings are illustrated in Fig. 1.

216 The chosen resolution ratio of 16 between $n_x = 4096$ and $n_y = 256$ corresponds approximately to the ratio between
 217 the length of the centerline and the average circumference around the colon. For all un-collapsed cases used in this
 218 study, the average length was 1.7 m and the average circumference was 10.8 cm, giving a ratio of 15.7.

219 For this resolution $n_x \times n_y$, any two neighboring pixels correspond to 3D points which are 0.27 (standard deviation
 220 0.29) mm apart on average, with 99% of neighboring pixels being less than 1.2 mm apart. This suggest that, even
 221 though the circumference of the colon changes along its length, the distortion introduced by mapping S onto a
 222 cylindrical image I with constant width is sufficiently small enough over most of the endoluminal colon surface.
 223 Therefore, any 3D surface location on S can be interpolated with adequate accuracy. Furthermore, our experiments
 224 show that the distortion introduced by this step can be successfully recovered by our cylindrical non-rigid registration
 225 (as described in section 2.5).

226 Each pixel of I has a value assigned to it in order to drive a non-rigid registration. These values are estimated (using
 227 barycentric interpolation) from the local surface shape index (SI) computed on each vertex v_i of the three-dimensional
 228 surface S . The shape index SI is a normalized shape descriptor based on local curvature (see Fig. 6) and defined as

$$SI \equiv \frac{1}{2} - \frac{1}{\pi} \arctan \left(\frac{\kappa_1 + \kappa_2}{\kappa_1 - \kappa_2} \right), \quad (2)$$

229 where the principal curvatures κ_1 and κ_2 are the maximum and minimum curvatures computed on the surface S ⁴⁰.

230 The shape index represents the local topological shape of the surface S (as illustrated in Fig. 6). It is a good scalar
 231 measure for describing the local structures on colonic surfaces, such as haustra, folds and polyps. It can be also be
 232 used for polyp detection⁴¹.

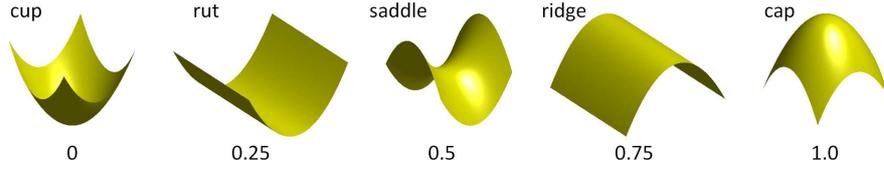


FIGURE 6. The shape index SI is a normalized shape measurement to describe local surface structures⁴¹.

233 Corresponding features, like haustral folds, flexures or the teniae coli are clearly visible in both images of Fig. 5
 234 (top, middle). These images are now aligned using a cylindrical intensity-based non-rigid registration method which
 235 will establish the full spatial correspondence between the endoluminal colon surfaces S_p and S_s .

2.5. Establishing spatial correspondence between prone and supine datasets

237 The two cylindrical representations are now in the same 2D domain but local structures are still misaligned. We will
 238 use a non-rigid registration method to align those local structures accurately. In order to provide good initialization for
 239 the registration algorithms, we use corresponding surface points at the hepatic flexure ($hf_{p/s}$) and splenic flexure ($sf_{p/s}$)
 240 to scale the 2D parameterizations linearly along the x -axis (using $x_{hepatic}$ and $x_{splenic}$). The flexures are detected based
 241 on local maxima of the z -coordinate of the centerline. We detect the hepatic flexure as the first maximum, coming
 242 from the cecum, to be above $t_{hepatic}$ of the maximum centerline z -coordinate. The splenic flexure is detected as the
 243 maximum which is the first to lie above $t_{splenic}$ of the maximum centerline z -coordinate, relative to the rectum. In order
 244 to provide robustness against wrongly detected flexure correspondences, we discard flexures if their centerline distance
 245 vary by greater than t_{var} between prone and supine datasets. Based on our experiments, we found good parameters to
 246 be $t_{hepatic} = 60\%$, $t_{splenic} = 95\%$ and $t_{var} = 5\%$ for all cases used in this study. The corresponding x -positions for the
 247 hepatic and splenic flexures are marked as $x_{hepatic}$ and $x_{splenic}$ in Fig. 5 after linear scaling along the x -direction.

248 The cylindrical representations are used to generate shape index images I_p and I_s , where each pixel corresponds to a
 249 position on the colon surface in 3D. We establish the alignment between I_p and I_s using a cylindrical non-rigid B-spline
 250 registration method. This method is developed from the 3D free form deformation based registration of Rueckert et
 251 al.²³ with the fast implementation provided by Modat et al.⁴².

252 A standard (non-cylindrical) 2D cubic B-Splines deformation model uses a lattice of control points $\{\vec{\phi}\}$. The spacing
 253 between each control point is uniform and noted as δ_x and δ_y along the x - and y -axis respectively. For each pixel \vec{x} in
 254 the domain Ω of the target image. the deformation $\mathbf{T}_{2D}(\vec{x})$ can be computed as:

$$\mathbf{T}_{2D}(\vec{x}) = \sum_{i,j} \beta^3 \left(\frac{x}{\delta_x} - i \right) \times \beta^3 \left(\frac{y}{\delta_y} - j \right) \times \vec{\phi}_{ij}, \quad (3)$$

255 where β^3 represents the cubic B-Spline function.

256 In order to account for the cylindrical nature of the registration we modified the transformation model in a similar

257 fashion to Huysmans et al.²⁴. For standard B-spline registrations the control point grid must extend outside the image
 258 by at least one control point spacing in each direction so that the deformation is defined over the whole image. For
 259 the cylindrical registrations, the control point grid does not extend outside the images in the y -direction (around the
 260 cylinder). Instead, when an extended control point is required, the corresponding value is taken from the opposite side
 261 of the grid. Therefore the equation for the cylindrical deformation is:

$$\mathbf{T}_{\text{cyl}}(\vec{x}) = \sum_{i,j} \beta^3 \left(\frac{x}{\delta_x} - i \right) \times \beta^3 \left(\frac{y}{\delta_y} - j \right) \times \vec{\phi}_{ik}, \quad (4)$$

262 where the control point is indexed by k instead of j , and k is defined as:

$$k = \begin{cases} j + N_{\delta_y} & \text{if } j < 0 \\ j & \text{if } 0 \leq j < N_{\delta_y} \\ j - N_{\delta_y} & \text{if } j \geq N_{\delta_y} \end{cases} \quad (5)$$

263 Here, N_{δ_y} is the number of control points in the y -direction.

264 In addition we prevent any displacement in the x -direction (along the colon) at each end of the image by fixing the
 265 x -displacement of the first and last three control points to be zero. This ensures that the ends of the images are aligned
 266 with each other, while still allowing for twists around the colon.

267 The two cylindrical shape index images I_p and I_s are aligned by finding the transformation which maximizes the
 268 objective function:

$$\mathcal{O} \left(I_p, I_s (\mathbf{T}_{\text{cyl}}); \{\vec{\phi}\} \right) = (1 - \lambda - \mu) C_{\text{similarity}} - \lambda C_{\text{smooth}}(\mathbf{T}_{\text{cyl}}) - \mu C_{\text{volpres}}(\mathbf{T}_{\text{cyl}}) \quad (6)$$

269 which combines a similarity measure, $C_{\text{similarity}}$, and two penalty terms, C_{smooth} and C_{volpres} , weighted against each
 270 other by the user-specified weights λ and μ . The similarity measure used was the mean sum of squared differences
 271 (mean *SSD*):

$$C_{\text{similarity}} = -\frac{1}{N} SSD = -\frac{1}{N} \sum_{\vec{x} \in \Omega} [I_p(\vec{x}) - I_s(\mathbf{T}_{\text{cyl}}(\vec{x}))]^2. \quad (7)$$

272 where $N = n_x \times n_y$ is the number of pixels.

273 Two constraint terms were used to try and prevent unrealistic deformations. The bending energy describes the
 274 smoothness of the deformation and is defined as:

$$C_{\text{smooth}} = \frac{1}{N} \sum_{\vec{x} \in \Omega} \left(\left| \frac{\partial^2 \mathbf{T}_{\text{cyl}}(\vec{x})}{\partial x^2} \right|^2 + \left| \frac{\partial^2 \mathbf{T}_{\text{cyl}}(\vec{x})}{\partial y^2} \right|^2 + 2 \left| \frac{\partial^2 \mathbf{T}_{\text{cyl}}(\vec{x})}{\partial xy} \right|^2 \right), \quad (8)$$

275 The volume-preserving penalty term discourages large expansions/contractions, and is defined as:

$$C_{\text{volpres}} = \frac{1}{N} \sum_{\vec{x} \in \Omega} [\log(\det(\text{Jac}(\mathbf{T}_{\text{cyl}}(\vec{x})))])^2 \quad (9)$$

276 In addition we prevent folding occurring by introducing a folding correction scheme performed concurrently with
277 the registration process⁴³. For each voxel that corresponds to a negative Jacobian determinant we compute its influence
278 on its neighborhood control points and change the control point positions until the determinant value is positive.

279 In order to find optimal parameters for the B-spline registration, we used a sub-set of the available cases for tuning
280 the registration algorithm parameters. The following reported optimal parameters were found empirically by visual
281 examination of the registration results and by assessing the alignment of polyps after registration.

282 We used a coarse-to-fine approach in order to capture first the largest deformations and then the smaller differences
283 between both input images. This is achieved with a seven-level multi-resolution approach using I_p as target and I_s as
284 source. Both the image and B-spline control point grid resolutions are doubled with increasing resolution levels. The
285 final resolution level uses images with 4096×256 ($n_x \times n_y$) pixels. The control point spacing δ is 16 pixels in both
286 directions at each resolution level. The gradient of the cost function is smoothed after each iteration, using a Gaussian
287 kernel with a standard deviation of 3δ . Gaussian smoothing of the 2D images is applied at each resolution level with a
288 standard deviation of two pixels. The objective function weights are set to $\lambda = 1e^{-4}$ and $\mu = 1e^{-4}$. These parameters
289 were found to recover the majority of the deformation between the two images for the data used for tuning, while
290 preventing unrealistic deformations from occurring.

291 The cylindrical B-spline registration results in a continuous transformation around the entire endoluminal colon
292 surface and allows the mapping between S_p and S_s . From this mapping it is straightforward to determine the full 3D
293 mapping \mathbf{T}_{ps} (as shown in Fig. 1).

294 **2.6. Dealing with collapsed colon**

295 Despite adequate colonic insufflation, short segments of colonic collapse commonly occur, particularly when the
296 patient changes position from supine to prone. Furthermore, residual colonic fluid due to suboptimal bowel preparation
297 can occlude the colonic lumen, resulting in more than one colonic segment for 3D reconstruction. If the colon is locally
298 severely under-distended, the segmentation method described in section 2.1 can lead to disconnected colon segments.
299 Most 3D workstations allow the radiologist to manually choose the order in which the centerline connects these
300 disconnected colonic segmentations. Fig. 7 shows a patient's colon with a collapse in the descending colon (DC) in
301 the supine position. While some centerline-based methods can handle local colonic collapse, they only provide a 1D
302 correspondence along the centerline. To the best of our knowledge, only Suh et al.²⁰ have attempted a 3D registration

303 of images where the colon is collapsed in only one view but report limited accuracy.

304 If the collapsed segment is relatively straight, its length can be estimated as the Euclidean distance between the
305 centerlines of the well-distended segments. The length of each well-distended segment is estimated based on the
306 length of its centerline. We currently select the beginning and end points, as well as the correct order of each segment,
307 manually. The angular alignment between each segment was determined as the shift around the y -axis which minimizes
308 the 3D distance between points with the same angular orientation on either side of the collapse. The cylindrical images
309 I of such a case (patient 17) are shown in Fig. 8. It can be seen that despite the missing data in the collapsed section of
310 the descending colon, we can register both supine colon segments with the fully distended prone endoluminal colon
311 surface reasonably well.

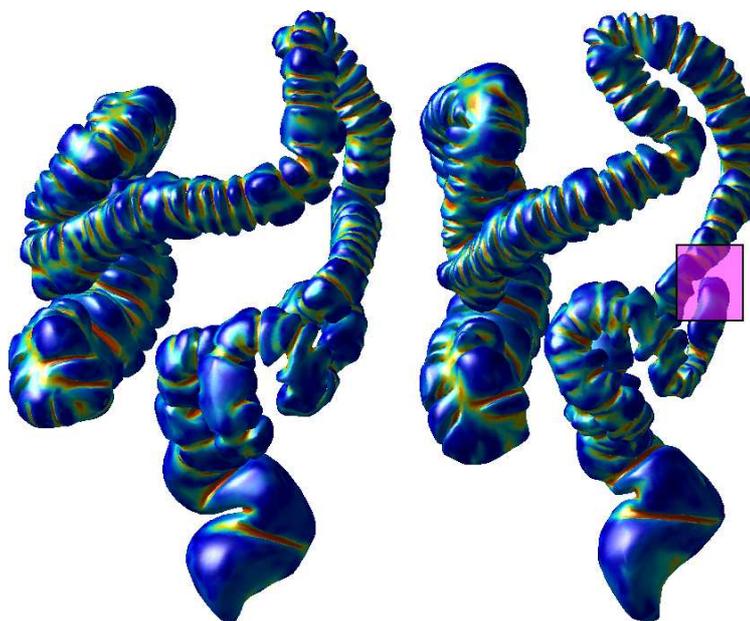


FIGURE 7. A case where the descending colon is collapsed in the supine position (marked, right image) but fully distended in the prone(left).

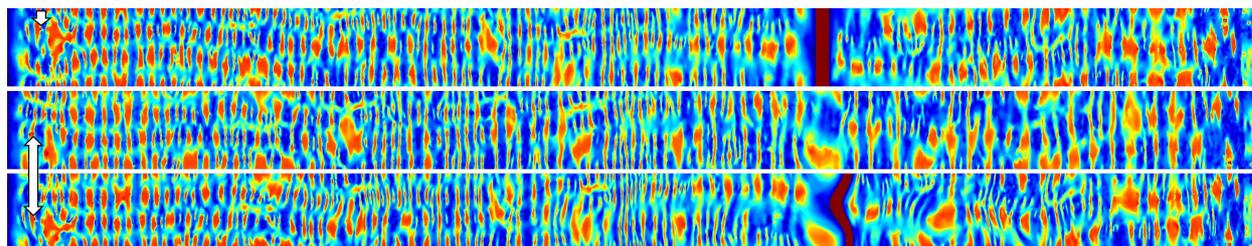


FIGURE 8. Cylindrical representation as raster images of the collapsed supine (top), prone (middle) and deformed supine (bottom) endoluminal colon surface of patient 17. The location of a polyp is marked before (top) and after registration (middle, bottom).

3. CLINICAL EVALUATION

312 Ethical permission was obtained to utilize anonymized CT colonography data acquired as part of normal day-to-day
313 clinical practice. CT colonography had been performed in accordance with current recommendations for good clinical
314 practice⁹ and any detected polyps subsequently validated via optical colonoscopy. For the purpose of establishing
315 spatial correspondence across complete endoluminal surfaces, we selected 24 patients where the colon was not under-
316 distended in both the prone or supine positions and who had either fluid ‘tagging’ (the increased radio-density allows
317 ‘digital cleansing’ of residual fluid) or little remaining fluid. This allowed a continuous segmentation over the full
318 length of the colon using the methods described in section 2.1.

319 The datasets were randomly allocated into development and validation sets (using random permutation), with 12
320 cases each. During the course of the development, we discovered that it is difficult to identify corresponding features
321 by eye in the cylindrical image representations for some cases. Closer examination revealed that this was due to
322 either large difference in distension of the colon in the prone and supine views or to insufficient fluid tagging.
323 Large differences in distension can lead to considerable local dissimilarity of surface features, such as folds. Fig.
324 9 and 10 show such a case with marked differences in cylindrical representations I_p and I_s (Fig. 9, top and bottom),
325 resulting from very different distensions (Fig. 10). These can occur only partially or over the full extent of the colon.
326 Furthermore, differences in the colon surface can occur due to insufficient fluid tagging for accurate digital cleansing.
327 This also leads to artifacts in the segmentation. We identified 4 development datasets with marked differences in
328 local distension, which therefore had different surface features and these were excluded from the study, leaving 8
329 development cases (patients 1 to 8). The development set was used to tune the registration algorithm parameters (as
330 described in section 2.5).

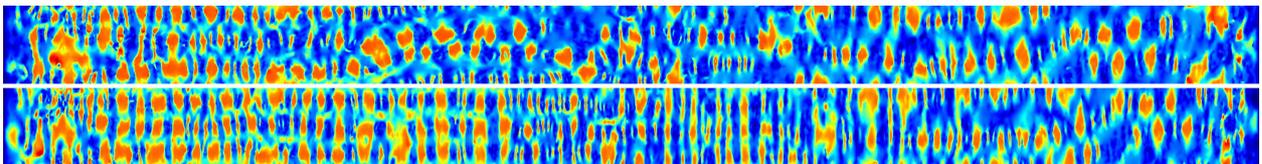


FIGURE 9. Widely different distension changes the shape index of the cylindrical representations in supine (top) and prone (bottom). 3D renderings are shown in Fig. 10

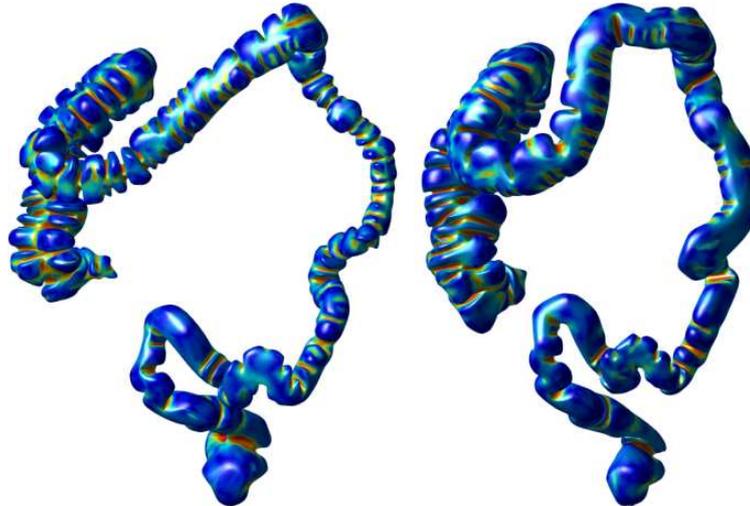


FIGURE 10. Different amounts of distension in prone and supine view cause differences of local features in the cylindrical images.

331 Furthermore, this observation led us to exclude another 4 cases of the validation set which showed large differences
332 in the cylindrical images. Of those, 2 showed marked differences in distension, 1 case showed insufficient fluid tagging
333 and 1 case showed both problems. This resulted in a total of 8 data sets with fully connected colon segmentations in
334 both views for validation (patients 9 to 16).

335 Recognizing the problems introduced by cases with marked differences in distension, we selected another 5 cases
336 for validation of the method on cases with local colonic collapse (patients 17 to 21). Here, the distension and surface
337 features of the 3D endoluminal surfaces S were judged by eye to be sufficiently similar in the well-distended segments
338 before execution of the registration algorithm. This selection process results in a total of 13 cases used for validation,
339 as described in the following sections: 8 fully connected sets and 5 with local colonic collapse. In order to assess the
340 spatial accuracy of the proposed registration method, we use clinically validated polyps and haustral folds to measure
341 the registration error.

342

3.1. Validation using polyps

343 Experienced radiologists identified polyps in both prone and supine CT colonography scans using 2D multi-
344 planar reformats and endoscopy data for guidance. The polyps' endoluminal extent was labeled to provide reference
345 coordinates for validation. Polyp labels were checked and corrected if necessary and then matched by eye between the
346 prone and supine view by an experienced colonography radiologist (DJB).

347 The cases were selected to present a widespread distribution of polyps throughout the colonic length so that
348 registration accuracy could be investigated over the entire endoluminal surface. Crucially however, any polyps were
349 masked in the 2D cylindrical images I such that those pixels lying on or close to the polyp were ignored during

350 registration when computing the similarity measure $C_{\text{similarity}}$. Thus, it was impossible for the polyps used for validation
 351 to bias the registration results. Fig. 11 illustrates masking of polyps.

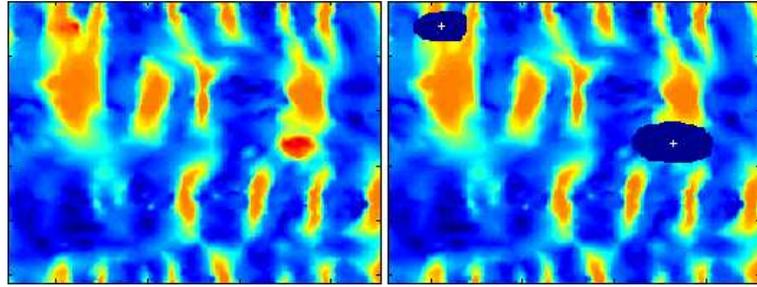


FIGURE 11. Masking of polyps to ensure they do not influence subsequent registration: polyps in unfolded view (left). Masked polyps (right) to be ignored in registration. The center of mass c which is used as a reference point is marked with a cross.

352 In order to determine registration error, we identified a pair of reference points for each manually matched polyp in
 353 the prone and supine views. The reference points were defined as the points at the center of the intersecting surface
 354 between the extracted endoluminal colon surfaces S and the segmented polyps. Therefore, these points lie on the
 355 surfaces S_p and S_s respectively. The center point $c(x, y)$ is computed as the center of mass of the intersecting pixels in
 356 the 2D images I , as indicated in Fig. 11 (right). Each 2D reference point $c(x, y)$ corresponds to a 3D point $c'_i(x, y, z)$ on
 357 the surfaces S which lies inside the polyp's volume. We then determined the registration error in mm by transforming
 358 each reference point c'_s on S_s using the 3D mapping T_{ps} to find $T_{ps}(c'_s)$, which lies on surface S_p , and computing the
 359 3D Euclidean distance to c'_p , which also lies on surface S_p .

360 All 8 datasets used to fine-tune the algorithm had clearly corresponding features in both prone and supine 2D
 361 representations, such as patient 7 in Fig. 5 (top, middle). It can be seen that after cylindrical B-spline registration, the
 362 corresponding features are well aligned (Fig. 5, bottom). The corresponding 3D renderings are illustrated in Fig. 1.
 363 Polyps of the same case and corresponding virtual endoscopic views after their prone and supine views were aligned
 364 using the registration result are shown in Fig. 12 and Fig. 13.

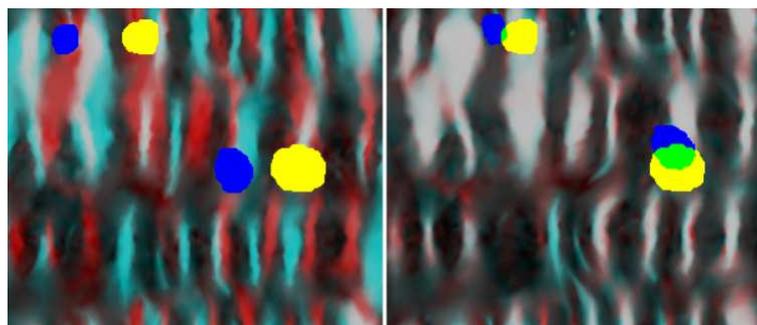


FIGURE 12. Overlay of masked out polyps before (left) and after (right) establishing spatial correspondence. The prone image is colored red with a yellow polyp mask, and the prone is colored cyan with a blue polyp mask. After establishing spatial correspondence, aligned features display gray and the overlapping region of polyp masks in green.

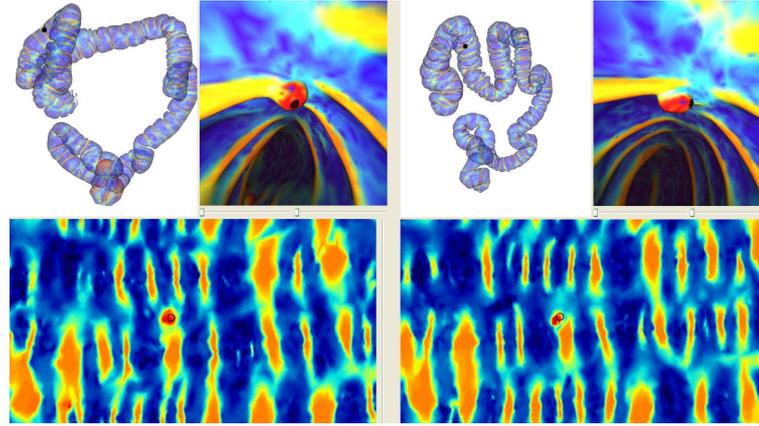


FIGURE 13. Polyp localization for patient 7 after registration using the prone (left) and supine (right) virtual endoscopic views. The black dot shows the resulting correspondence in the 2D (bottom) and 3D (top) renderings.

365 We used the same registration parameters as optimized using the development set (patient 1 to 8) on the validation set
 366 (patients 9 to 21). Table 1 shows the results of assessing the registrations using the polyps of the 13 validation sets. The
 367 error after the cylindrical parameterization but before the B-spline registration is denoted Polyp Parameterization Error
 368 (*PPE*), and the error after the B-spline registration is denoted Polyp Registration Error (*PRE*). Before calculating
 369 *PPE* the images are translated in the *y*-direction (around the colon) to minimize the *SSD* between the images, as the 0
 370 degrees position is arbitrarily assigned by the cylindrical parameterization.

TABLE 1. Registration error in mm for 13 polyps in the 13 patients used for validation of the registration method. These included 8 fully connected cases (patients 9 to 16) and 5 cases with local colonic collapse (patients 17 to 19). The Polyp Parameterization Error (*PPE*) gives the error in aligning the polyps after cylindrical parameterization but before registration, the Polyp Registration Error (*PRE*) gives the error after cylindrical registration.

Patient	Polyp location	Collapsed location in prone	Collapsed location in supine	<i>PPE</i> [mm]	<i>PRE</i> [mm]
9	AC	none	none	32.4	3.0
10	Cecum	none	none	13.7	6.0
11	Cecum	none	none	30.2	3.1
12	Cecum	none	none	41.9	2.4
13	DC	none	none	15.7	6.8
14	AC	none	none	11.8	4.6
15	DC	none	none	23.9	3.6
16	AC	none	none	18.5	11.1
17	Cecum	none	1 x DC	24.8	9.4
18	AC	none	1 x SC	62.6	3.9
19	Rectum	1 x DC	1 x DC	55.9	6.0
20	Cecum	3 x (DC, SC)	none	13.3	12.4
21	AC	1 x DC	1 x DC	39.0	1.5
Mean [mm]				29.5	5.7
σ [mm]				16.4	3.4

371 The *PRE* had a mean (\pm std. dev.) of 5.7 (\pm 3.4) mm for 13 validation patients with a single polyp each, and all 13
 372 polyps were well aligned. The *PPE* results show that cylindrical parameterization on its own is not enough to align the

373 datasets – the cylindrical non-rigid B-spline registration is required for accurate alignment. This result is sufficiently
374 accurate to direct the radiologist to an area of the endoluminal surface, which is close to the suspected lesion in both
375 views, even in the case of local colonic collapse (patients 17 to 21).

376 The hepatic flexure were not used to initialize the registration for patient 12 and patients 18-20, as the distances
377 along the centerline between prone and supine varied more than t_{var} (here, 5%). However, the cylindrical registration
378 was still able to align features well.

379 The resulting error for 9 polyps in the 8 development cases was $6.6 (\pm 4.2)$ mm after non-rigid registration (*PRE*)
380 and therefore slightly higher than *PRE* of the validation set. The polyps for development of the registration method
381 occurred in the ascending colon (AC), transverse colon (TC), descending colon (DC) and sigmoid colon (SC).

382 **3.2. Validation of spatial correspondence along the entire length of the colon**

383 Polyps can give definite points of correspondence on the colon surface and give a good estimate of the registration
384 performance. However, their number is limited to only one polyp per case in our validation set. In order to assess
385 the registration quality over the entire endoluminal colon surface, corresponding haustral folds were chosen from the
386 prone and supine datasets. Reference point coordinates were provided to lie centrally on the fold in both views; the
387 haustral fold centers were automatically calculated by first segmenting each fold on the colon surfaces S using a graph-
388 cut method⁴⁴ based on the principal curvatures κ_1 and κ_2 . Then, the center of each fold was computed as the vertex
389 which has the lowest maximum distance to any vertex on the border of the segmented fold.

390 Using the cylindrical representations to establish regions of likely correspondence and virtual colonoscopic views
391 for assurance, a radiologist (DJB, with experience in over 500 validated colonography studies) then manually identified
392 corresponding folds from the prone and supine views. Any folds where the radiologist could not be certain of
393 correspondence were not used for validation, but this still provided an average of 90 pairs of corresponding folds per
394 patient, with a total of 1175 pairs over all 13 validation cases (patients 9 to 21). The center points of the corresponding
395 folds were then used as corresponding reference points for assessing the registration.

396 Fig. 14 shows the normalized distributions of reference points versus a normalized position along the centerline
397 from cecum (0.0) to rectum (1.0) for 8 un-collapsed and 5 cases exhibiting local colonic collapse. The decline in
398 number of reference points is due to the fact that there are naturally fewer folds in the left hemi-colon.

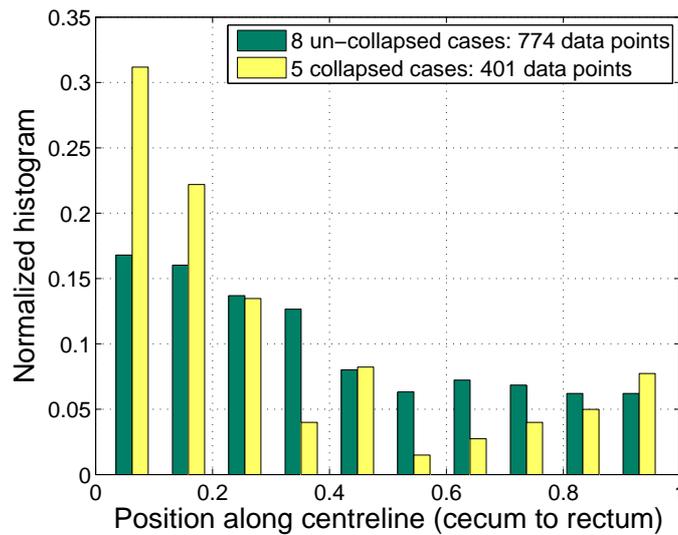


FIGURE 14. Normalized distributions of reference points normalized along the centerline from cecum to rectum for un-collapsed and collapsed cases.

399 We assess the Fold Registration Error (FRE) in the same way as described in section 3.1 but using the haustral
 400 fold centers as reference points. Using this large set of reference points, the FRE was $7.7 (\pm 7.4)$ mm for a total
 401 of 1175 points distributed over all 13 validation patients. In comparison, just using the cylindrical parameterization
 402 on its own (before B-spline registration) a Fold Parameterization Error (FPE) results in an error of $23.4 (\pm 12.3)$
 403 mm. A histogram of the registration error (FRE) is shown in Fig. 15. Here, the normalized distributions of FRE for
 404 un-collapsed and collapsed cases are colored differently and displayed next to each other for comparison. It can be
 405 seen that the majority of points (95%) lie below an error of 22.8 mm, with a maximum error of 44.1 mm. However,
 406 the FRE is slightly higher for the 5 collapsed cases with $9.7 (\pm 8.7)$ mm as opposed to the 8 un-collapsed cases with
 407 FRE of $6.6 (\pm 6.3)$ mm.

408 Using our method haustral folds are almost always aligned with another haustral fold in the other image, but this is
 409 not always the correct corresponding fold. Using the segmented haustral folds we could analyze how many of the folds
 410 were aligned with the correct corresponding fold, and how many were misaligned by one or more fold. 82% of all 1175
 411 reference points were assigned to the correct corresponding fold. 15% of reference points were misaligned by just one
 412 fold and 3% misaligned between two and three folds. This assumes that the radiologist correctly labeled corresponding
 413 haustral folds. We have no way to assess this but it is likely that at least some of the apparently misregistered data is
 414 due to this observer error. Nevertheless the identification of corresponding haustral folds is high.

415 In agreement with the FRE results, 71 % of haustral folds were correctly matched in the 5 cases with local colonic
 416 collapse. Whereas 88% of haustral folds in the 8 un-collapsed cases were assigned to the correct corresponding fold.
 417 The slight decline in registration quality of cases exhibiting local colonic collapse is due to the fact that, typically, the
 418 colon distension varies in the areas close to the collapse, e. g. the surface area of the descending colon in Fig. 7. Again,

419 this introduces marked difference in the local surface features which degrades the registration accuracy in these areas.

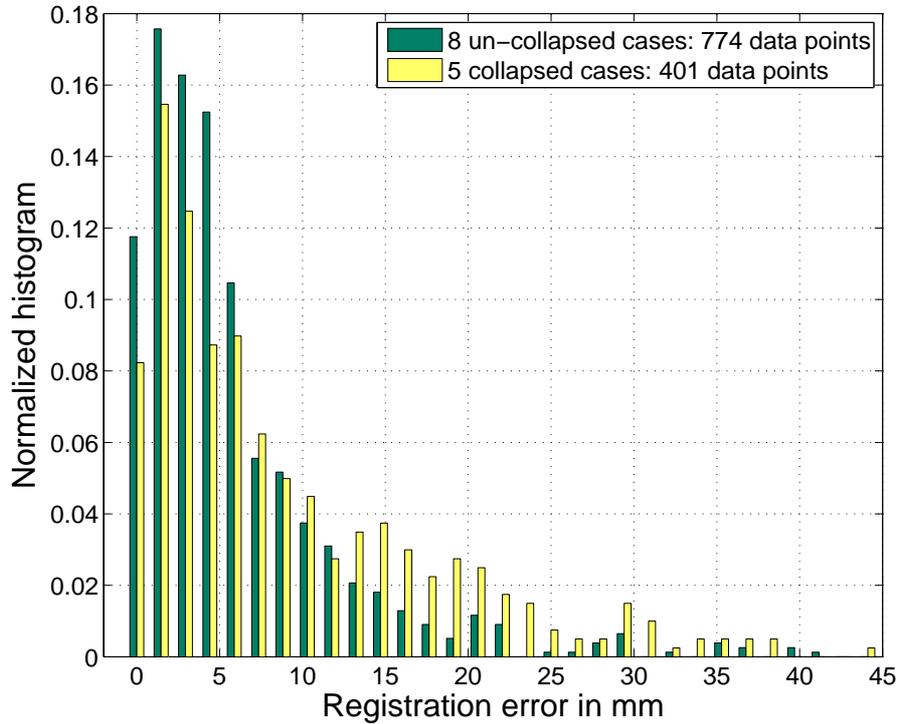


FIGURE 15. Normalized histograms of the Fold Registration Error (FRE) distributions in mm using reference points spread over the endoluminal colon surface for un-collapsed and collapsed cases.

4. DISCUSSION

420 We have presented a novel method for establishing spatial correspondence between endoluminal colonic surfaces ex-
421 tracted from prone and supine CT colonography data. Our method simplifies the problem of aligning the prone and
422 supine surfaces from a 3D to a 2D task. This is achieved by mapping the full endoluminal surface to a cylindrical
423 parameterization using a conformal mapping. The novel contribution of this work is that we use these cylindrical
424 parameterizations in order to align the endoluminal colon surface using non-rigid B-spline registrations. Cylindrical
425 raster-images with shape index values derived from the initial 3D surfaces are used to drive the registration. This
426 process can establish accurate correspondence between the 2D cylindrical parameterizations, and hence give corre-
427 spondence over the full 3D colonic surfaces which is able to recover the large colonic deformations and torsion that
428 occurs between the two acquisition positions.

429 Our approach is motivated by the assumption that the overall shape of the colon can undergo large deformations
430 when the patient changes position, but that the local shape of surface structures, such as haustral folds, remains similar

431 enough between scans to align the surfaces. During the development of our method we discovered that for 8 of the
432 24 un-collapsed cases there were large regions where the surfaces structures appeared markedly different between the
433 two scans. These were due to large differences in the distension of the colon or insufficient fluid tagging. We decided
434 to exclude these cases from this study as we expect our current method to fail for such cases. However, we strongly
435 suspect that most other methods presented in the literature that aim to generate accurate correspondence over the
436 colonic surface (i. e. the feature based methods²² and the voxel based methods^{19,20}) will also experience difficulties
437 with cases where the surface features appear differently in the two scans. The number of such cases observed in this
438 study indicates that these cases are not infrequent, and methods that can address these cases must be developed to
439 achieve maximum clinical benefit.

440 Another common occurrence is for there to be some regions of local colon collapse in one or both scans. Validation
441 of our proposed registration method on 5 cases where there was a collapse in at least one view showed promising
442 performance. It shows that the method is able to handle cases with multiple collapses in both views. Some of the
443 centreline based approaches can handle regions of local collapse, but these only give approximate correspondence
444 based on the shape of the centreline, and do not attempt to provide accurate correspondence over the colon surface.
445 To the best of our knowledge there has only been one other method proposed to date that attempts to provide accurate
446 correspondence over the colon surface (as opposed to just at the centreline) and to handle regions of local colon
447 collapse²⁰. However, this method has not yet been validated on cases with multiple collapses in both views as we
448 have. Furthermore, their results show limited accuracy.

449 The method presented here relies on extracted colon surfaces of good quality. Therefore, pre-processing steps of
450 segmentation (which involved manual interaction) and automated topological correction were necessary to extract
451 topologically correct surfaces for the patient data used here. It is clear that obtaining good quality segmentations of the
452 intraluminal colon surface reliably and robustly is a significant impediment to the clinical adoption of our method. We
453 will therefore be devoting more resources to improving and automating our segmentations, both at the image analysis
454 stage but also during patient preparation and data acquisition. Future work will extend the concepts described in this
455 paper to cases of markedly different distensions between prone and supine colonography, insufficient tagging and
456 automatically handling regions of local under-distension with more complex collapses. Although quality control of
457 CT colonography is improving, these remain common problems in routine clinical practice.

458 The current method requires some manual interaction. These are: 1) choosing the structure element sizes inter-
459 actively in order to correct the colon segmentations and include the the rectal insufflation catheter while visually
460 inspecting the segmentation quality. 2) We selected the start and end-point as well as the correct order of each well-
461 distended colon segment. Standard commercial 3D workstations already require the radiologist to manually choose the
462 order of each colon segment. These steps are relatively quick to perform and require minimal manual input. Therefore
463 we did not consider these few manual interactions to be a major impediment to our proposed method. However, We

464 will further investigate how individual colon segments can be arranged automatically in the case of colonic collapse.
465 This will also incorporate methods of detecting two corresponding points at each segment which defined the start and
466 end of each parameterized cylinder.

467 Given topologically correct surface meshes of the size used in this study, our single processor implementation of
468 the Ricci flow conformal mapping (using the steepest gradient descent minimization) currently takes several hours
469 to achieve sufficient convergence. However, faster solvers such as the Newton method³⁶ or a GPU-based implemen-
470 tation³⁷ can speed up the computation considerably. Alternatively, other conformal mapping methods could be used,
471 e.g.⁴⁵ which require less computation time. It should be made clear that obtaining the cylindrical parameterization was
472 not the focus of this study. There have been a number of parameterization methods presented in the literature, some
473 based on conformal mappings^{26,45,39} and some on other techniques⁴⁶, and we simply chose one that would generate an
474 appropriate mapping for us to use. Future work will investigate faster implementation of the Ricci flow as well as alter-
475 native techniques for generating the cylindrical parameterizations, in order to produce appropriate parameterizations
476 in a clinically feasible time frame.

477 In contrast to the cylindrical parameterization, the cylindrical B-spline registration, provides a result within a few
478 minutes, which is fast enough to be clinically useful. A multi-resolution-level registration approach was used in order
479 to help the registration optimization avoid getting stuck in local minima and to reduce the computation time. However,
480 our validation shows that some haustral folds were misaligned by one or more folds indicating that the registrations
481 were occasionally still getting trapped in local minima. Future research will investigate how better initialization of the
482 cylindrical registration and/or a better choice of registration parameters could solve this problem.

483 In conclusion we have provided a framework for the alignment of information from prone and supine CT colonog-
484 raphy; a very challenging registration problem. The method comprises conformal mapping of CT derived features onto
485 a cylindrical surface, followed by a cylindrical registration of these features. This establishes an estimate of a dense
486 correspondence throughout the derived colon surface. The results show promise, not only for polyp detection but also
487 for establishing correspondence between corresponding haustral folds on a limited set of colonography datasets.

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