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An Adaptive Paradigm for Computer-Aided Detection of Colonic Polyps

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Abstract

Most previous efforts in developing computer-aided detection (CAdE) of colonic polyps apply similar measures or parameters to detect polyps regardless their locations under an implicit assumption that all the polyps reside in a similar local environment, e.g., on a relatively flat colon wall. In reality, this implicit assumption is frequently invalid, because the haustral folds can have a very different local environment from that of the relatively flat colon wall. We conjecture that this assumption may be a major cause of missing detection of polyps, especially small polyps (<10mm linear size) located on the haustral folds. In this paper, we take the concept of adaptive-ness and present an adaptive paradigm for CAdE of colonic polyps. Firstly, we decompose the complicated colon structure into two simplified sub-structures, each of which has similar properties, of (1) relatively flat colon wall and (2) ridge-shaped haustral folds. Then we develop local environment descriptions to adaptively reflect each of these two simplified sub-structures. To show the impact of the adaptive-ness of the local environment descriptions upon the polyp detection task, we focus on the local geometrical measures of the volume data for both the detection of initial polyp candidates (IPCs) and the reduction of false positives (FPs) in the IPC pool. The experimental outcome using the local geometrical measures is very impressive such that not only the previously-missed small polyps on the folds are detected, but also the previously miss-removed small polyps on the folds during FP reduction are retained. It is expected that this adaptive paradigm will have a great impact on detecting the small polyps, measuring their volumes and volume changes over time, and optimizing their management plan.

Keywords

Colonic polyps; computed tomography colonography; computer-aided detection; colon structure decomposition

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I. Introduction

According to the American Cancer Society statistics, colorectal carcinoma (CRC) is the third most commonly diagnosed cancer and the second leading cause of death from cancers in the United States (American Cancer Society, 2013). It was estimated that 142,820 new cases will be diagnosed with 50,830 dying from the disease in 2013. Fortunately, most CRC arises from polyps, a process which can take 5–15 years for malignant transformation into cancer. Thus, early detection and removal of the polyps before or during the malignant transformation will effectively decrease the incidence rate of CRC (Muto *et al.* 1975; Winawer *et al.* 2000; Levin *et al.* 2008).

In general, a polyp is an abnormal growth of tissues on the inside lining of the large intestine (or the colon for simplicity), projecting from the mucosa of the colon and protruding into the intestinal canal (or the lumen for simplicity). Some polyps are flat; others have a stalk. Detecting the abnormal growth is routinely performed by clinical optical colonoscopy (OC). Because of its invasiveness and high cost, OC may not be an ideal choice for screening purposes (Liang *et al.* 2010). An alternative option is virtual colonoscopy (VC), which mimics the OC procedure of navigation inside the colon lumen, looking for polyps on the inner wall mucosa. Current practice of VC employs computed tomography (CT) imaging modality and, therefore, VC is also named CT colonography (CTC). For screening purpose, the navigation through the long “pipe-like” colon can be very user intensive and time consuming, thus computer-aided detection (CAdE) has been explored in the past decades for CTC.

While CAdE of large ($\geq 10\text{mm}$) polyps has been reported at an acceptance level with comparison to human experts’ or radiologists’ performance, the detection of small ($< 10\text{mm}$) polyps remains a challenging task for CAdE. Appendix I summarizes some typical CAdE examples with their reported results on polyps of variable sizes in a chronological order.

From typical CAdE examples in Appendix I, it is clearly seen that the results vary greatly among the reports even the data sample size goes up from over 100 to over 2,000, especially including the small polyps ($< 10\text{mm}$ linear size). Based on the reported results, we can conjecture that one major factor among others (such as oral contrast tagging, quality of bowel distension and catharsis, CT slice thickness, manually sampled sets of desirable cases, use of easy-to-detect polyps, different evaluation methodologies, etc.) contributing to the variation in detecting the small polyps is an implicit assumption, which was made by most above CAdE methods, that the polyp is growing out from a relatively flat surface environment. This implicit assumption may be acceptable for polyps on the relatively flat colon wall, but will be unlikely held for polyps on the ridge-shaped haustral folds. For example, Franaszek *et al.* (2006) observed that almost 90% of small and medium size polyps, missed by their CAdE program, were located on the haustral folds. This exploratory study aims to relieve the implicit assumption by an adaptive paradigm of (1) presenting a reasonable theoretical description of a more realistic polyp growing environment, (2) deriving the corresponding geometrical measures for the theoretical description, and (3) providing the associated experimental outcome to demonstrate the gain of the more realistic polyp growing environment model.

The remainder of this paper is organized as follows. In Section II, an outline of the proposed adaptive paradigm is presented, and then a methodology for extracting the colon mucosa layer from the CT abdominal volume image is reviewed for the purpose of constructing a patient-specific model of the colon, followed by description of the more realistic polyp-growing environment model. In Section III, experimental design and results are reported. Finally, discussion and conclusions are given in Section IV.

II. Methods

II.A. Outline of the Proposed New Paradigm

In general, polyp candidates can be detected based on their geometric features characterizing their differentiations from the prior knowledge about the normal colon wall and the true polyps (Bhotika *et al.* 2006). A desired CAdE pipeline would take into account not only the morphological structure of the polyp itself, but also its surrounding environment of the colon structure (Franaszek *et al.* (2006), because both the calculation of the geometrical measures and the classification of the measures for a polyp candidate are affected by the environment where the candidate resides. Such adaptive approach to polyp detection represents our proposed CAdE paradigm, called adaptive CAdE hereafter.

Figure 1 shows a flowchart of a typical adaptive CAdE pipeline. The three boxes of Stage I, Stage II and Stage III illustrate how we embed the polyp growth environment model into both the computation of geometrical measures and the classification of the measures for CAdE. The interpolation operation on the CTC volume image dataset may be needed because the original CTC dataset may not consist of isotropic image voxels (due to variable image slice thickness), and isotropic voxel arrays help post-image processing operations. In the presence of partial volume effect (PVE), the anatomical mucosa layer shall be a volumetric layer in the CTC image and, therefore, a volumetric mucosa (VM) shall be extracted. This task is performed automatically by a statistical image segmentation algorithm, which models the PVE in a maximum *a posteriori* expectation-maximization (MAP-EM) framework and was validated by experiments (Wang *et al.* 2008a; Liang *et al.* 2009). The three-stage (I, II and III) geometric analyses, which are the main theme of this work, are performed on the extracted VM layer for polyp detection. The details of the three-stage geometric analysis operations are reported below in Sections II.C–F.

II.B. Volumetric Mucosa Segmentation

For detection purpose, our first task is to focus attention on the mucosa or region of interest (ROI) in the acquired CTC volumetric image. This task is usually performed by image segmentation. Due to the PVE on the mucosa, a hard segmentation for a single-voxel layer is not recommended for the detection purpose (van Wijk *et al.* 2010). Considering the need of contrast tagging agents to opacify the residual fecal for differentiation of the residual materials from colon wall and polyps (Liang *et al.* 1997), it is desirable to preserve the original image content while obtaining the ROI. For the preservation purpose, we then developed the statistical MAP-EM image segmentation algorithm which simultaneously estimates tissue mixture percentages within each image voxel and statistical model

parameters for the tissue distribution on the mucosa layer (Wang *et al.* 2008a; Liang *et al.* 2009). Figure 2 illustrates an example how the segmentation algorithm works.

The algorithm takes the CTC image of Fig. 2(a) and electronically cleanses the tagged residual materials, as shown in Fig. 2(b), and simultaneously extracts the VM layer as the ROI, as shown in Fig. 2(d). Inside the VM layer is the colon lumen, as shown in Fig. 2(c), which is useful for navigation flight-path planning and user-interactive visualization. In the following, we will focus on the segmented VM layer. To facilitate numerical operation, a mask file is made to reflect the estimated colon wall tissue percentage in each voxel within the VM layer and is expressed mathematically as an image $\{O_i\}$, $0 < O_i < 1$, where an image voxel with value close to 0 indicates that the voxel is mostly filled of air, an image voxel with value close to 1 indicates that the voxel is mostly filled of colon wall tissue, and an image voxel with value of 0.5 indicates that the voxel is half air and half wall tissue.

II.C. Polyp Growth Environment Model

The VM layer or ROI contains the original image information about the colon mucosa in the presence of PVE. In addition, each voxel in the ROI is labeled as a mixel with three percentage values of air, tissue and tagged fecal materials. From the volumetric ROI, we can directly compute geometrical measures for a specific task (Wang *et al.* 2004, 2005). For the purpose of illustrating the proposed local environment model for polyps in a straightforward fashion, we shrink the multiple-voxel thick VM layer into a mathematical surface and generally divide the surface into two regions corresponding to their shapes: one region represents the relatively flat colon wall and the other represents the ridge-shaped haustral folds. Since the polyps on the relatively flat colon wall have been well described in the CADe examples in Appendix I, then we focus our attention on polyps on the ridge-shaped haustral folds.

In general, four possible polyp-growing local environments can be illustrated by Fig. 3, where a polyp growing on the relatively flat environment of colon wall is shown by Fig. 3(a) and on the ridge-shaped haustral fold by Fig. 3(b)–(d). From the simplified illustration of Fig. 3, it can be seen that the local geometrical environment of Fig. 3(a) is different from that of Fig. 3(b)–(d). To make a connection between the simplified model and the reality, a typical example of polyps on the wall and on the fold is shown in Fig. 3(e)–(f), where it is clear that the same geometry measures or parameters of successful detection for the polyp on the wall will likely generate several false positives (FPs) on the fold, i.e., detect the non-polyp areas as polyps. For the purpose of CADe of polyps on both the wall and folds, the local environment variations shall be considered. Adapting this more realistic polyp-growing environment model of Fig. 3 into computation of geometrical measures in volumetric data for CADe is described in the following sections.

II.D. Geometry Guided Colon Structure Decomposition

Given the extracted VM layer, our first stage geometric analysis is to (1) identify the landform geometries of Fig. 3, where polyps arise in the VM layer, and (2) label the landform geometries according to their geometrical shapes, e.g., the plain (or colon wall),

the base, hill or top of the mountain (or haustral fold) corresponding to Fig. 3(a), (b), (c) and (d), respectively. More detailed workflow for this stage analysis is shown in Fig. 4.

Given a 3D volumetric image $I(x, y, z)$ of the VM layer or ROI, the Euclidean differential invariants (i.e., the first or higher order derivatives) are considered for the purpose of calculating the geometric features in the image. The derivatives are usually calculated as convolutions of the image with predefined kernels or operators that approximate the derivatives. In the calculation, we adopt the widely-used Gaussian kernel in the convolution as $G_\sigma(x, y, z) = e^{-(x^2+y^2+z^2)/2\sigma^2} / (\sqrt{2\pi\sigma^2})^3$, where σ determines the width of the Gaussian kernel. Let $t = 2\sigma^2$ be a scale-parameter (to be determined later by experiments), then the first- and second-order derivatives are computed on the scale-space representation data and the forms of the first- and second-order derivatives are shown mathematically as follows:

$$L_x(t) = \partial_x G(t) * I, L_y(t) = \partial_y G(t) * I, L_z(t) = \partial_z G(t) * I, \quad (1)$$

$$L_{xy}(t) = \partial_{xy} G(t) * I, L_{xz}(t) = \partial_{xz} G(t) * I, L_{yz}(t) = \partial_{yz} G(t) * I,$$

$$L_{xx}(t) = \partial_{xx} G(t) * I, L_{zz}(t) = \partial_{zz} G(t) * I, L_{yy}(t) = \partial_{yy} G(t) * I.$$

The above second-order Gaussian derivatives are then used to build a 3×3 Hessian matrix,

$$H(t) = \begin{bmatrix} L_{xx} & L_{xy} & L_{xz} \\ L_{xy} & L_{yy} & L_{yz} \\ L_{xz} & L_{yz} & L_{zz} \end{bmatrix}.$$

In order to acquire the desired shape information by the above second-order derivatives or Hessian matrix, Frangi *et al.* (1998) suggested to calculate the three eigenvalues $|\lambda_1|$, $|\lambda_2|$, $|\lambda_3|$ and their corresponding eigenvectors $\mathbf{O}$, $\mathbf{P}$ and $\mathbf{Q}$ which form the orthonormal basis for a local Cartesian coordinate system, as shown by Fig. 5. Eigenvector $\mathbf{O}$ is aligned to the direction associated with the eigenvalue λ_1 (Medioni *et al.* 2000). Similarly eigenvectors $\mathbf{P}$ and $\mathbf{Q}$ are aligned to the directions associated with the eigenvalues λ_2 and λ_3 , respectively. The eigenvalue analysis of the Hessian matrix has a unique application in extracting the principal directions where the local second order structure of the image can be decomposed. This uniqueness serves our purpose of decomposing the colon structure. Several structure patterns can be measured by the eigenvalues, such as plate-like ($|\lambda_1| \approx |\lambda_2| < |\lambda_3|$), blob-like ($|\lambda_1| \approx |\lambda_2| \approx |\lambda_3|$) and tube-like ($|\lambda_1| < |\lambda_2| \approx |\lambda_3|$) structures, as shown in Fig. 5. Then our goal is to use these measures to decompose the VM layer into structures with desired geometries, such as colon wall or haustral folds. In this respect, we have the following definitions.

Definition #1

A measure of colon structural patterns for each voxel is defined as: (1) plate likeness LN_{pl} , if ($\lambda_1 > 0$ and $\lambda_2 > 0$ and $\lambda_3 < 0$); (2) colon wall likeness LN_{cw} , if ($\lambda_1 > 0$ and $\lambda_2 < 0$ and $\lambda_3 < 0$); (3) haustral fold likeness LN_{hf} , if ($\lambda_1 < 0$ and $\lambda_2 < 0$ and $\lambda_3 < 0$); and (4) blob likeness

LN_b ; if $(\lambda_1 < 0 \text{ and } \lambda_2 < 0 \text{ and } \lambda_3 < 0)$. Since both LN_{hf} and LN_b are protruding components adhered to the colon wall, we can define LN_{hfb} to describe the protruding likeness (LN_{hf} and LN_b) in the lumen space. (The opposite direction would indicate a depressed polyp candidate). For other patterns with combinations of $(\lambda_1, \lambda_2, \lambda_3)$ different from the above three cases of LN_{hfb} , LN_{cw} and LN_{pl} , such as the joint parts between two structures or other “noisy” patterns, we will define their measures as zero. These defined structure patterns are much like the structures of mountains and plains on an undulating terrain. For presentation purpose, we will use P_i to represent the four categories of patterns of $(LN_{hfb}, LN_{cw}, LN_{pl}, 0)$.

There may be many ways to group the three eigenvalues into a formula for quantitative computation. For example, Kim *et al.* (2007) proposed a calculation formula to utilize them to provide certain quantitative measures. We adopt this calculation strategy and derive a colon shape pattern measurement as follows:

$$T_t(\lambda) = \begin{cases} (1 - e^{-\frac{A^2}{2\alpha^2}}) \cdot (1 - e^{-\frac{S^2}{2\gamma^2}}) & \text{for pattern } LN_{hfb} \\ e^{-\frac{A^2}{2\alpha^2}} \cdot (1 - e^{-\frac{B^2}{2\beta^2}}) \cdot (1 - e^{-\frac{S^2}{2\gamma^2}}) & \text{for pattern } LN_{cw} \\ e^{-\frac{B^2}{2\beta^2}} \cdot (1 - e^{-\frac{S^2}{2\gamma^2}}) & \text{for pattern } LN_{pl} \\ 0 & \text{for other patterns} \end{cases}, \quad (2)$$

where $A = \frac{|\lambda_1|}{\sqrt{|\lambda_2\lambda_3|}}$, $B = \frac{|\lambda_2|}{|\lambda_3|}$, $S = \sqrt{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}$, α , β , and γ are user-defined parameters, and the eigenvalues $\lambda_1, \lambda_2, \lambda_3$ are ordered as $|\lambda_1| \geq |\lambda_2| \geq |\lambda_3|$ as defined above. In implementation, α and β are fixed to 0.5. The value of the threshold γ depends on the grey-scale range of the image and was selected as the half value of the maximum Hessian norm in our experiments, and the selection worked well. The subscript t of T_t indicates that the pattern likeness is calculated in the scale-space representation of the original image, see Eq. (1). Regarding the scale selection, Grin *et al.* (1992) proved that, for feature detection, those scale levels can be selected at which the normalized measures of feature strength achieve the local maxima over the scales. Based on this proof, the pattern likeness can be estimated in a multi-scale manner, thus the calculation algorithm of Eq.(2) becomes adaptive (a key point of our adaptive paradigm). Accordingly, the pattern likeness can be defined as,

$T_i(\lambda) = \max_{t \in [t_{\min}, t_{\max}]} T_t(\lambda)$, where $t_{\min}$ and $t_{\max}$ are the maximum and minimum scales at which the appropriate structures are expected to be extracted, as described below.

Definition #2

A shape decomposition descriptor for each voxel in a volume image is defined as a quintuple, which consists of a set of $\{P_i, T_i, \lambda_1, \lambda_2, \lambda_3\}$. Though P_i and T_i are computed from λ_s ($1 \leq s \leq 3$), where $\{\lambda_s\}$ contain basic geometric information about the concerned voxel, they provide an integrated or collective measure of the eigenvalues $\{\lambda_s\}$. Thus we introduce the quintuple for curvature analysis by the subsequent procedure.

According to the pattern likeness value T_i at each voxel, the entire VM layer can be described in tube-like (mostly the colon wall), blob-like (mostly the haustral folds or polyps) and other pattern likeness (mostly the connected or jointed areas with $T_i=0$). Based on this

mapping, the outcome was considered as the global geometric priority of the objects, i.e., the colon wall and the haustral folds. T_i and λ_s are then stored for all the following steps. Figure 6 illustrates an example of how the above described adaptive colon-decomposition approach works. Once the complicated colon structure is decomposed into two relatively simple objects of colon wall and haustral folds, then polyp detection can be performed adaptively on each of the object.

II.E. Shape Feature-Based Suspicious Polyp Detection

After the above first stage geometric analysis for colon structure decomposition, our second stage geometric analysis is to develop adaptive geometry measures for efficient detection of suspicious polyps. At this stage, our focus is to quickly find those concerned voxels from the entire VM layer and then group them into patches, which mimic the colonic polyps. By this strategy, we will reduce our targeted space from the entire VM volume, which consists of several hundred thousands of voxels, to a small number of patches (e.g., around one hundred), so that more sophisticated features can be extracted from the patch volumes to reduce the FPs in the patches for final detection. The procedure for getting the suspicious patches is detailed in Fig. 7.

To facilitate the separation of the haustral folds from the colon wall using the pattern likeness value T_i at each voxel, a new mask file is generated from the original mask file $\{O_i\}$ as:

$$NewS_i = \begin{cases} 0 & \text{If } 0 < O_i < 1 \text{ and } T_i \text{ equals to } 0 \\ O_i & \text{Others} \end{cases} \quad (3)$$

where $NewS_i$ stands for the value of voxel i in the new mask file, and $0 < O_i < 1$ indicates the region of mucosa. In this new mask file, the boundaries between the two simplified shape components can be distinguished as shown in Fig. 6(b) and 6(e), because the voxel values, $NewS_i$, in the connected or jointed areas are usually *zero* as seen in our experiments. Using the new mask file, all the image voxels in the VM layer will be labeled as wall voxels and fold voxels. Various geometric measures can then be efficiently calculated from all the labeled voxels within the VM layer for the task of adaptive detection of suspicious patches. Most geometric measures are based on the well-established shape index (SI),

$SI = \frac{1}{2} - \frac{1}{\pi} \arctan \frac{k_1 + k_2}{k_1 - k_2}$, and curvedness (CV), $CV = \sqrt{\frac{k_1^2 + k_2^2}{2}}$, where k_1 and k_2 represent the maximum and minimum curvatures, respectively.

In implementing our detection task in the 3D VM layer, both SI and CV values are calculated by taking the principal curvatures (the second order derivatives in the 3D image) as the only input. To compute the principal curvatures for implicit surfaces (e.g., iso-surfaces) embedded in the 3D VM layer image, we adapt the kernel method (Wang *et al.* 2004; 2005), which employs special local and global geometrical information for identifying suspicious patches on the colon wall or haustral folds. More details on the calculations in the 3D space are given below.

Given a volume data $I(x,y,z)$, the curvature information can be represented by k_T , where k_T is calculated, as detailed in Appendix II, by (Monga *et al.* 1995),

$k_T = k_1, k_2 = \frac{-\text{roots} \left\{ \begin{array}{cc} H - \lambda I & g^T \\ g & 0 \end{array} \right\}}{|g|}$, where $I(\cdot)$ represents the image intensity, H is the above mentioned Hessian matrix, and g is the gradient of $I(\cdot)$. The principal curvatures and their directions are expressed as functions of the first and second derivatives of the volume image.

The above geometrical calculation is performed on each voxel in the 3D VM layer space (not on a surface). For the detection purpose, it is needed to consider the voxel neighborhood and extract the features of a group of voxels or a patch. Different from sheer surfaces, the correlation between neighboring voxels in the VM layer not only exists in the first- or second-order derivatives spatial domain, but also appears along the path that is determined by normal directions across multiple “iso-surfaces” in the volumetric or VM layer. In order to have a robust estimate on the curvature of each voxel and also a voxel neighborhood in the VM layer, an isotropic smoothing operator, such as a window or Gaussian kernel, is routinely used (Sundaram *et al.* 2008). By experiments, Wang *et al.* (2005, 2008b) and Zhu *et al.* (2010a) found that an integral curvature calculation is superior to the routine operator in consideration of all the neighboring voxels in the volume data for polyp detection. However, in their integral calculations, they treat all the structures equally (as the routine operator does) without considering where the polyps are located. In such case, the difference of the curvature values obtained from different colon structures is not effectively considered as shown in Fig. 8(a). This phenomenon is usually observed when a polyp is growing on a haustral fold, explaining the cause of frequent miss detection of small polyps there. In our adaptive approach, the new mask file $NewS_i$ of Eq.(3) specifies the integral path along the decomposed colon structure. The adaptive manner not only facilitates the integration process but also avoids the above over-smoothed (p, q) by constraining the integral paths to the calculated edge or iso-surface of the mucosa (p_1, q_1) as shown in Fig. 8(b). An adaptive integral path will also retain the local environment or geometric characteristics of the decomposed objects, reduce the noise effect on the geometry measure calculation, and improve the subsequent IPC detection.

After the integration of the local curvature along the path, we can calculate an adaptive SI and CV by substituting the principal curvatures (k_1, k_2) by (K_{L1}, K_{L2}):

$$K_{L1,2}(x_i, y_i, z_i) = \frac{\sum_j^{\vec{p}} w_j k_j}{\sum_j^{\vec{p}} w_j}, \quad (4)$$

where $\vec{p}$ is the path, along which the local curvature is integrated, and w_j is the weight, which is determined by the relative distance between point (x_i, y_i, z_i) and all the points on the integration path and is normalized to 1. Because of the weighting, the resulted value $K(K_{L1}, K_{L2})$ of Eq.(4) is expected to be smaller than the previously reported ones (Yoshida *et al.*

2001). The adaptive SI and CV from $K(K_{L1}, K_{L2})$ of Eq.(4) are then used to detect the IPCs. For comparison purpose, the same SI and CV definitions will be used in the calculation of the geometry measures without consideration of the local environment variation and the outcome will be set as the baseline. As an example, Appendix III illustrates the difference of the calculated adaptive SI distributions with and without consideration of the local environment when a polyp is on the haustral fold and the similarity when a polyp is on the colon wall. Since both SI and CV are derived from the same Eq.(4), the calculated adaptive CV distributions have the similar characteristics as that of the adaptive SI. It is expected that the adaptive geometry measures will improve the detection of polyps on the haustral folds where the previous implicit assumption on the polyp growing environment may fail, while retaining the detection on the colon wall where the previous implicit assumption may be acceptable. In addition to this expectation, we would further expect a gain on the reduction of the FPs in the IPC pool by the adaptive strategy. This is the third stage geometric analysis of our adaptive CAdE pipeline of Fig. 1, as detailed below.

II.F. A Priori Knowledge-Based False Positive Reduction

It has been realized that the SI and CV measures are very sensitive to small variations on the colon wall (Yoshida *et al.* 2001; Wang *et al.* 2005). Because of their computational efficiency, they can be used to detect the IPCs in a relatively effective manner in terms of maximizing the detection rate with reasonable number of FPs. Subsequently, the attention shall be focused on the IPCs, whose space is much smaller than that of the VM layer. In other words, we have reduced the space from the whole abdomen to the VM layer (by the image segmentation) and then to the IPCs (by the sensitive geometrical measures). In the reduced space or the IPC pool, more sophisticated features from each IPC volume can be extracted and used for FP reduction in the IPC pool. By the adaptive idea above, we can compute the more sophisticated features in a similar manner adaptive to the local environment for the task of FP reduction. The pipeline for FP reduction is shown in Fig. 9.

In order to extract more sophisticated features from each detected IPC for FP reduction, we adapt the strategy of Zhu *et al.* (2009) to obtain a volume of interest (VOI), which has a convex surface enclosure for the concerned IPC. From the VOI, both morphological and textural features can be computed. Similar to their feature extraction procedures (Yoshida *et al.* 2001; Näppi *et al.* 2002; Wang *et al.* 2005; Zhu *et al.* 2009), we introduce an object likeness distribution analysis (OLDA) to calculate new features (both geometrical and textural) for FP reduction. Because the object likeness on each voxel has been obtained already in our IPC detection above, then the OLDA-derived features can be straightforwardly computed by the already available adaptive object likeness measures for each IPC by

$$OLDA_{mean} = \frac{1}{n} \sum_{i=1}^n T_i, \text{ and } OLDA_{std} = \sqrt{\frac{1}{n-1} \sum_{i=1}^n (T_i - OLDA_{mean})^2} \quad (5)$$

where $OLDA_{mean}$ is the mean of likeness value T_i , notation $OLDA_{std}$ indicates the standard deviation, and n is the total number of voxels in the concerned IPC's VOI.

Note that the above *OLDA* measures are directly derived from the local environment description of object likeness and reflect mainly the local environment information. They may not cover the whole picture of the polyp. Thus, they will be added to the previously established common features, such as the mean and variance of SI, the variance of CV and the variance of CT image intensity (Summers *et al.* 2000; Näppi *et al.* 2002). Then a feature vector for each IPC's VOI is obtained. The feature vectors will be fed into the well-known support vector machine (SVM) classifier with the widely-used nonlinear RBF (radial basis function) (Chang *et al.* 2001; 2010). A half of the entire IPC dataset is randomly selected as the training subset with the portion of true polyps unchanged, and the other half is treated as the testing dataset. Following the guideline of LIBSVM, the two parameters (cost: the model slack variable and gamma: the parameter in the RBF kernel) are determined by a ten-fold cross-validation in the training step. The outcome of the SVM classification on the previous established common features only will be set as the baseline for comparison purpose. The improvement on the SVM outcome by the addition of the newly developed *OLDA* features will reflect the gain by the new adaptive features.

II.G. Experimental Design

The experimental design of this study aims to show the gain of the above presented adaptive approach for CAdE with special focus on the detection of the small polyps. Based on the report of Summers *et al.* (2010) that polyp size measurements at CTC tend to be 1~2mm larger than the pathological measurements, then the polyps ranged from 5~8mm would be selected by the pathological measurement, corresponding to 6 to 9mm by CTC measurements.

Under the above condition, a total of 60 patient datasets with the desired polyp size range were selected, and each dataset includes two scans at supine and prone positions respectively, resulting in 120 CT scans. For the purpose of demonstrating the difference of prior and post colon structure decomposition, one polyp in the two different scans at supine and prone positions was counted as different polyps, thus there were 130 polyps in the desired size range from 5 to 8mm, confirmed by both CTC and OC. The size distribution of the polyps is shown in Table I, and the shape distribution is listed in Table II. In corresponding to the polyp selection from the supine and prone scans of each patient, the evaluation results will be presented in terms of by-polyp detection sensitivity and number of FPs per dataset. In other words, the terms "sensitivity" and "FP rate" in the following text will mean the by-polyp sensitivity and the number of FPs per dataset.

To show the gain by the above presented adaptive approach with consideration of the local environment, the baseline reference was made using the similar geometry analysis without consideration of the local variable environment, i.e., assuming all polyps residing on a same environment or relatively flat wall. In other words, the well-known geometry merits of SI and CV and the associated calculations in volumetric data (Monga *et al.* 1995; Yoshida *et al.* 2001; Näppi *et al.* 2002; Wang *et al.* 2005, 2008b; Sundaram *et al.* 2008; Zhu *et al.* 2009) were utilized in this study to set up the baseline in order to show the gain of the presented adaptive approach.

III. Results

III.A. Detection of Initial Polyp Candidates

It has been recognized in the literature that the parameters' configuration in a CADe pipeline has a noticeable impact on the experimental results (Summers *et al.* 2000; Yoshida *et al.* 2001; Franaszek *et al.* 2006). Similar to other CADe systems, the presented adaptive CADe pipeline also has several empirical parameters as listed in Table III. Parameters α and β were determined above after Eq.(2). γ was determined dynamically by maximizing the value of

$\sqrt{\lambda_1^2 + \lambda_2^2 + \lambda_3^2} / 2$. t may vary, depending on image noise and voxel size, and was determined experimentally. The SI seed and CV seed control the thresholds for selecting the candidate voxels, while the corresponding growing seed is responsible for growing a suspicious patch. Regarding the growth of the patch, one of the most significant prior knowledge is that the value of growing seed adaptively relies on the labels established by the pattern likeness measure P_i . When P_i indicates a blob-like structure, then the value of growing seed will be set to a relatively narrow and low value range (0~0.10) for the blob-like structure; otherwise it will grow according to a relatively wide range of value (0~0.25). However, there will be no difference for the CV measure.

After a preliminary candidate voxel selection and patch growing by the geometrical measures with the associated parameters, suspicious patches were obtained. These suspicious patches were fed to a filter which is based on voxels' feature values, including SI, CV, magnitude of the gradient, CT intensity value, sphericity, compactness, wall/region density and spatial coordinates, for the purpose of removing noise-induced patches (Summers *et al.* 2000; Yoshida *et al.* 2001; Wang *et al.* 2005, 2008). After the filtration, the survived patches grew into the colon tissue area to form the IPCs.

A comparison study was conducted between the presented adaptive CADe scheme and the baseline reference, which is similar to the presented one but does not consider the local environment variation. As a result, the average FP number per dataset, as shown in Table IV, is 15.3/dataset for the baseline reference, and 17.2/dataset for the presented adaptive IPC detection. For their FP rates, the baseline detected 124; and the presented adaptive CADe identified 128 from the total of 130 polyps or true positives (TPs). The gain in detection sensitivity by the presented adaptive geometrical measures is very obvious while retaining a similar FP rate as compared to the baseline which uses the same common geometry merits of SI and CV over the entire colon without consideration of the local environment variation.

In order to get insight into the gain by the presented adaptive IPC detection, we reviewed both the successful cases and the failed cases. All the successful detections by the baseline were detected by the presented adaptive method. All the four new successful detections by the adaptive method (vs. the baseline) reside on the haustral folds, as shown by Fig. 10, where the case of Fig. 10(c) is the case of Fig. 3(f). The baseline failed to detect these four small polyps because of its invalid implicit assumption that these polyps reside on a similar flat local environment.

The two FPs of the baseline and the adaptive method are flat growths of 6mm size. Figure 11 shows the details on their CTC image slices. In the first miss-detection case, the small flat polyp resides on the side of a haustral fold and is covered by tagged fecal material, as shown by Fig. 11(a). The electronic cleansing operation uncovered it (Liang *et al.* 1997) as seen in Fig. 9(b). While the electronic cleansing operation seems successful, it does not help the detection in this case. In the second miss-detection case, the small flat polyp resides on the colon wall, as seen in Fig. 11(c). The electronic cleansing operation does not affect this case since there is no tagged fecal material on this polyp, as seen in Fig. 11(d). These two miss-detection cases are mainly due to the flatness of the small polyps. Resolving this kind of miss detections needs more sensitive geometrical measures and/or texture information on the small area and its nearby surroundings.

III.B. False Positive Reduction

To show the discrimination capability of the presented adaptive OLDA measures of the local environment for FP reduction, firstly we compared the new OLDA features with the common intensity-based features used in the previous work (Näppi *et al.* 2002; Wang *et al.* 2005; Zhu *et al.* 2009) for distinguishing polyps from non-polyp patches. (It is noted that the SI and CV geometry-related features had been used in the IPC detection above, and there is no reason to consider them again in FP reduction.) Both the intensity-based and the OLDA-derived features were first extracted from all the TPs and the FPs in the IPC pool. Then all these extracted features were divided into two groups or operators: intensity-based operator (INO) and OLDA-based operator (OLO). Figure 12 illustrates the clustering results, where OLO showed a more cohesive polyp group versus non-polyp patches as compared to the result of INO. For quantitative comparison, the class distance between polyps and non-polyps was calculated and normalized, and the resulted value is 0.42 in INO and 0.60 in OLO, while the standard deviation is 0.75 for INO and 0.57 for OLO. It is obvious that OLO is more discriminative than INO by both visual judgment on Fig. 12 and quantitative measures in terms of the mean and standard deviation of the distances between each point and their center on the plots of Fig. 12.

To further demonstrate the efficiency of the OLDA features for FP reduction, we conducted another experiment with and without the new OLDA features. In this experiment, we aimed to show the gain by adding the adaptive new measures for FP reduction. For each patient dataset, all IPCs of the presented adaptive method above were chosen as a set of samples. The extracted common intensity-based features above were set as the baseline reference (i.e., the case without the new OLDA features). Then the above extracted OLDA features were added to the baseline (i.e., the case with the new OLDA features). During FP reduction process, feature vectors (with or without the OLDA measures) of all IPCs were randomly separated into two groups with the same number of TPs, serving as training and testing datasets respectively. To increase the statistical power, we conducted 50 random tests. To see how much the gain is for OLDA features, we took the IPCs with or without OLDA features as the inputs to train and test IPCs using a ten-fold cross-validation strategy. The free-response receiver operating characteristics (FROC) was employed to evaluate the FP reduction process. The FROC is defined as a plot of the TP number/total number of the polyps vs. the FP number/total number of the datasets. Note that the FP number here stands

for the resulted number after the FP reduction. Further note that FPs/dataset is used as the x coordinate, and it reflects the average FP rate for all the 50 random input datasets. Figure 13 shows the FP reduction performance with and without the OLDA features. A statistical significance test was performed with a p value of $1.03\text{E-}4 < 0.05$, indicating a significant difference.

In addition to the experiment on the discriminative measure of Fig. 12 and the experiment on the gain of adding the new adaptive OLDA features of Fig. 13, we further evaluated the overall CADe performance of the presented adaptive method with comparison to the baseline (without consideration of the local environment variation) using the 60 patient datasets. In this experiment, both the IPC detection and FP reduction in the IPC pool were considered together in the CADe pipeline of Fig. 1. The overall performance includes both the IPC detection and the following FP reduction. To verify the effectiveness of the presented adaptive method over the baseline, the well-known leave-one-out strategy was applied in this experiment. For each patient dataset, all IPCs from other patient datasets were selected as the training samples. The results are shown by Fig. 14, where the improvement on FP reduction by the presented adaptive approach is so obvious with comparison to the baseline (i.e., without consideration of the local environment variation). By the presented adaptive paradigm, the FROC analysis yielded 2.2 FPs per dataset at 98% sensitivity with a standard error of 5.63%. With respect to the area under the ROC curve or the AUC value, the baseline has an AUC value of 0.76, while the presented adaptive method has a value of 0.87. Regarding to the curves in Fig. 14, the standard deviations for the baseline and the presented adaptive method are 0.244 and 0.211, respectively. The obvious gain in the overall CADe performance by the presented adaptive paradigm is clearly due to the consideration of the more realistic polyp growing local environment.

In comparison to the previous CADe results in Appendix I, we have the following observations. For those studies with polyps of size 5mm and larger, the sensitivity varied from 90.5% to 100% with the number of polyps ranging from 43 to 246. With polyps of size range from 5mm to 9mm, the sensitivity varied from 80.6% to 83.0% with the number of polyps ranging from 325 to 1,186. In this study, we achieved a sensitivity of 98% with polyp size range from 5mm to 8mm and the number of polyps of 130. The performance of this presented adaptive CADe showed comparable to the best one in Appendix I.

IV. Discussion and Conclusion

In this paper, we presented an adaptive paradigm for CADe, which relieves an implicit assumption that all polyps reside on a relatively flat colon wall and presents a reasonable theoretical description of a more realistic polyp growing environment due to the complexity of colon structure. By decomposing the complicated structure into simpler ones, we can make the descriptive measures adaptive to each simplified structure and, therefore, expect an improved performance from the adaptive descriptive measures. More specifically, we can make the geometrical descriptive measures on small polyps more sensitive if the whole colon structure is decomposed into (1) relatively flat colon wall and (2) ridge-shaped haustral folds. We embedded this polyp growth environment model into the IPC detection stage, the FP reduction stage and the entire CADe pipeline. Because the implicit assumption

may be valid for the relatively flat colon wall structure, we do not expect noticeable gain in detecting polyps on the wall. However, the implicit assumption would frequently be invalid for the ridge-shaped haustral folds, where we expect to see a noticeable improvement in the detection by the presented adaptive new CADe paradigm.

We performed several experiments to show the sensitivity of the adaptive measures for IPC detection and FP reduction. The gain in IPC detection, FP reduction and combination of the two (i.e., IPC detection and FP reduction in the IPC pool) is noticeable. Most strikingly, the outcome from the detection on the haustral folds meets our expectation according our theoretical model.

While 128 out of 130 small polyps were successfully detected by the presented adaptive paradigm with 98% sensitivity and 2.2 FPs per dataset, the challenge in detecting small flat polyps still remains. Because the presented adaptive method focuses on the geometry measures and the flat polyps have very little geometry variation, so the failure in detecting the flat polyps is understandable. The ultimate solution to resolve this challenge is to acquire image contrast and texture differentiation between the polyps and their surroundings. This is our on-going research interest (Zhang *et al.* 2012, 2012a; Song *et al.* 2013, 2014).

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Appendix I: Some examples of CADe research progress during the past decades

Authors	Polyp Size	Sensitivity(FPs)	Dataset size	Category
Summers et al. 2000	10 mm	71% (3.5 per/patient)	50 polyps	surface
Yoshida et al. 2001	5 mm	95% (1.2/patient), or 100% (2/patient)	43	surface
Nappi et al. 2002	n/a	100% (2.4/patient)	43	volume
Pickhardt et al. 2003	6 mm	93.8% (< 10 mm), 93.9% (< 8 mm), & 88.7% (< 6 mm)	1,233	n/a
Paik et al. 2004	10 mm	100% (7/patient)	116	surface
Wang et al. 2005	10 mm	100% (2/patient)	153	volume
Suzuki et al. 2006	5 mm	96.4% (3.1/patient)	73	volume
Kim et al. 2007	6 mm	92.5% on per-polyp (5.5/patient) and 91.7% per-patient (3.1/dataset)	35	volume
Sundaram et al. 2008	5 mm	(>10 mm; 100%; 17.5/patient), (5–10 mm; 89.7%, 21.23/patient), (<5 mm; 59.1%; 23.9/patient) and (overall; 80.3%; 23.9/patient)	35	surface
Wang et al. 2008	6~9 mm	83% (p < 0.001)	1,186	volume
Yao et al. 2009	10 mm	95% (2.4/patient)	1,186	surface
Van Wijk et al. 2010	6 mm	95%(4/dataset)	57	volume

Authors	Polyp Size	Sensitivity(FPs)	Dataset size	Category
Zhu et al. 2010	5~9 mm	80.6% (5.23/patient)	325	volume
Liu et al. 2011	6 mm	66% (10/patient)	1,186	volume
Mang et al. 2012	6 mm	86.9% (p = 0.353)	2,063	surface

Appendix II: Implicit Curvature Calculation

Given an adequate volume data $L(x, y, z; t) = G * I$, where (x, y, z) is the Cartesian coordinates, t is the scale, G is a Gaussian kernel and I is the CTC image, we adopt the following notation for the curvature calculation in the volume data. The gradient of L ,

$$g = \nabla L = (L_x, L_y, L_z)^T, \quad (\text{A.1})$$

The Hessian matrix H , and the adjoint of the Hessian H^* are expressed as:

$$H = \begin{Bmatrix} L_{xx} & L_{xy} & L_{xz} \\ L_{yx} & L_{yy} & L_{yz} \\ L_{zx} & L_{zy} & L_{zz} \end{Bmatrix}, \quad (\text{A.2})$$

$$H^* = \begin{Bmatrix} L_{yy}L_{zz} - L_{yz}L_{zy} & L_{yz}L_{zx} - L_{yx}L_{zz} & L_{yx}L_{zy} - L_{yy}L_{zx} \\ L_{xz}L_{zy} - L_{xy}L_{zz} & L_{xx}L_{zz} - L_{xz}L_{zx} & L_{xy}L_{zx} - L_{xx}L_{zy} \\ L_{xy}L_{yz} - L_{xz}L_{yy} & L_{yx}L_{xz} - L_{xx}L_{yz} & L_{xx}L_{yy} - L_{xy}L_{yx} \end{Bmatrix}, \quad (\text{A.3})$$

Then the Gaussian curvature is defined by (Monga *et al.*, 1995):

$$K_G = \frac{g^* H^* g}{|g|^4} = \frac{\begin{vmatrix} H & g \\ g^T & 0 \end{vmatrix}}{|g|^4}. \quad (\text{A.4})$$

And the mean curvature is calculated by (Goldman, 2005),

$$K_M = \frac{g^* H g}{2|g|^3} = \frac{-\text{coeff}(\lambda) \text{in} \begin{vmatrix} H & g \\ g^T & 0 \end{vmatrix}}{2|g|^3}. \quad (\text{A.5})$$

The principal curvatures (k_1, k_2) can be computed from the mean and Gaussian curvatures (K_M, K_G) by the standard formula:

$$k_1, k_2 = K_M \pm \sqrt{K_M^2 - K_G}. \quad (\text{A.6})$$

According to Eqs. (A.4) and (A.5), then Eq. (A.6) is equivalent to:

$$k_1, k_2 = \frac{-\text{roots} \left\{ \begin{array}{cc} H - \lambda I & g^T \\ g & 0 \end{array} \right\}}{|g|}. \quad (\text{A.7})$$

Appendix III: Graphical Illustration of the Adaptive SI Distribution

To show the calculated adaptive SI distributions with and without consideration of the local environment, one polyp on the fold and another polyp on the wall were arbitrarily chosen from the database of Table I. The results are shown by Fig. 15 below.

Fig. 15: (a) – A polyp of 7mm on the fold. (b) – A polyp of 6mm on the wall. (c) – An image slice showing the 7mm polyp with the arrow indication. (d) – The image slice showing the segmented VM layer, where the enclosed VM layer including the polyp is our focus for this graphical illustration. All the voxels inside the enclosed VM layer are used for calculation of the principal curvatures (Monga *et al.*, 1995). (e) – The corresponding segmented image slice after applying the colon structure decomposition method where the different gray scales reflect different geometrical components such as “volley”, “plane” and “hill”. (f) – The plot (x,y,SI) without consideration of the local environment (i.e. the baseline), where (x,y) is the spatial coordinate and the objects outside the enclosed VM layer are ignored for illustration purpose. (g) – The plot (x,y,SI) with consideration of the local environment. (h) – The distribution (n,SI) without consideration of the local environment, where n (or horizontal axis) indicates the count of voxels inside the rectangular box in (d) or (e). (i) – The distribution (n,SI) with consideration of the local environment. Graphs (j)–(p) show the results of the 6mm polyp on the wall.

This graphical illustration clearly shows the difference, (f) vs. (g) and (h) vs. (i), when the polyp is on the fold (because of the different environment) and the similarity, (m) vs. (n) and (o) vs. (p), when the polyp is on the wall (because of the similar environment), concurring with the common expectation and reflecting the impact of considering the local environment for detection of small polyps on the fold.

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Fig. 1.

A flowchart of the proposed adaptive paradigm for CADE, where the three-stage geometric analyses are the major contribution of this work. It is noted that only geometrical analysis is considered here for the purpose of demonstrating the impact of the local geometrical environment variation to the detection task.

Fig. 2.

Illustration of a tissue-mixture MAP-EM segmentation of the colon mucosa in the presence of PVE. (a) A slice of abdominal CT image with the tagged fecal materials. (b) The corresponding slice where the tagged materials have been electronically cleansed. (c) The cleansed colon lumen on the same slice. (d) The corresponding VM regions. It is noted that the determination of the two borders of the VM layer is not critical once the VM layer is sufficiently thick to enclose the true mucosa.

Fig. 3. Illustration of possible growth morphology of polyps under different landform surfaces, where the arrows in (a)–(d) indicate the polyps' growing position: (a) on the plate of the colon wall; (b) near the bottom of the haustral fold; (c) on the slope of the haustral fold; and (d) on the top of the haustral fold. Pictures (e) and (f) show the virtual endoscopic reviews of a polyp on the colon wall and on the haustral fold.

Fig. 4.
The colon structure decomposition flowchart.

Fig. 5.
An illustration of three typical colonic structure patterns: plate-like (the second display from left), blob-like (the third display from the left) and tube-like (the right display). The first display is to illustrate the eigenvectors (O , P , Q) for the colon-like object in a local Cartesian coordinate system. The large eigenvalues are in red and small ones in blue.

Fig. 6.

An illustrative representation of the presented adaptive colon decomposition approach. Top row shows the 2D displays of the measurements on colon wall and haustral folds: (a) one slice of the partial volume segmentation results on the colon wall; (b) one slice of the decomposition result. Bottom row shows the corresponding 3D displays via a volume rendering: (c) shows the 3D segmentation results; (d) shows the decomposition results, where the red circle indicates a region of the demonstration and its zoom-view is shown by (e) to see more details on the demonstration of colon wall and haustral folds.

Fig. 7.
The flowchart for shape feature-based suspicious polyp detection.

Fig. 8.
Illustration of the integral curvature calculation on (a) the iso-surfaces in the original VM layer and (b) the new local environment geometry in the VM layer, where the integral path is adaptively specified for different local environment.

Fig. 9.
The illustration of our *a priori* knowledge-based false positive reduction.

Fig. 10.

The detected polyps at various locations on the haustral folds as indicated by yellow arrow.

Fig. 11.

Two failed detection cases. Slice (a) and (b) show one case where a small flat polyp resides on a side of a haustral fold; (a) shows the image slice prior to electronic cleansing and (b) after the cleansing; the arrow indicates the polyp location. Slice (c) and (d) show the other case where a small polyp resides on a colon wall; (c) shows the image slice prior to electronic cleansing and (d) after the cleansing; the arrow indicates the polyp location.

Fig. 12.

The discriminative distribution of INO (left) and OLO (right) measures.

Fig. 13.
The comparison study with and without OLDA features.

Fig. 14.
A comparison of FROC curves from different methods.

Table I

Size distribution of the polyps.

5mm	6mm	7mm	8mm
10 (7.7%)	54 (41.6%)	39 (30%)	27 (20.7%)

Table II

Shape distribution of the polyps.

Sessile	Peduncated	Flat
111 (85.4%)	9 (7%)	10 (7.6%)

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Table III

Actual parameters applied to patient study.

$t = 2\sigma^2$ first order	$t = 2\sigma^2$ second order	α, β	γ	SI seed range	SI growing seed range	CV seed range	CV growing seed range
1	0.1~4	0.5, 0.5	dynamic	0~0.06	0~0.25	0.05~0.14	0.02~0.5

Table IV

Average FP number per dataset and total TP detection of the comparison study.

	FP number per dataset	TP detection vs. total polyp number
Baseline	15.3	124/130
New Method	17.2	128/130