Structure-analysis method for electronic cleansing in cathartic and noncathartic CT colonography

Wenli Cai,^{a)} Michael E. Zalis, Janne Näppi, Gordon J. Harris, and Hiroyuki Yoshida
Department of Radiology, Massachusetts General Hospital/Harvard Medical School,
Boston, Massachusetts 02114

(Received 17 December 2007; revised 22 April 2008; accepted for publication 30 April 2008;
published 24 June 2008)

Electronic cleansing (EC) is an emerging method for segmentation of fecal material in CT colonography (CTC) that is used for reducing or eliminating the requirement for cathartic bowel preparation and hence for improving patients' adherence to recommendations for colon cancer screening. In EC, feces tagged by an x-ray-opaque oral contrast agent are removed from the CTC images, effectively cleansing the colon after image acquisition. Existing EC approaches tend to suffer from the following cleansing artifacts: degradation of soft-tissue structures because of pseudo-enhancement caused by the surrounding tagged fecal materials, and pseudo soft-tissue structures and false fistulas caused by partial volume effects at the boundary between the air lumen and the tagged regions, called the *air-tagging boundary* (AT boundary). In this study, we developed a novel EC method, called *structure-analysis cleansing*, which effectively avoids these cleansing artifacts. In our method, submerged soft-tissue structures are recognized by their local morphologic signatures that are characterized based on the eigenvalues of a three-dimensional Hessian matrix. A structure-enhancement function is formulated for enhancing of the soft-tissue structures. In addition, thin folds sandwiched between the air lumen and tagged regions are enhanced by analysis of the local roughness based on multi-scale volumetric curvedness. Both values of the structure-enhancement function and the local roughness are integrated into the speed function of a level set method for delineating the tagged fecal materials. Thus, submerged soft-tissue structures as well as soft-tissue structures adhering to the tagged regions are preserved, whereas the tagged regions are removed along with the associated AT boundaries from CTC images. Evaluation of the quality of the cleansing based on polyps and folds in a colon phantom, as well as on polyps in clinical cathartic and noncathartic CTC cases with fluid and stool tagging, showed that our structure-analysis cleansing method is significantly superior to that of our previous thresholding-based EC method. It provides a cleansed colon with substantially reduced subtraction artifacts. © 2008 American Association of Physicists in Medicine. [DOI: [10.1118/1.2936413](https://doi.org/10.1118/1.2936413)]

Key words: electronic cleansing, CT colonography, virtual colonoscopy, fecal tagging, noncathartic preparation

I. INTRODUCTION

CT colonography (CTC), also known as *virtual colonoscopy*, is an emerging technique for screening for colon cancer,^{1,2} the second leading cause of cancer deaths among men and women in the United States.³ The images acquired by a CT scanner are reformatted into a simulated three-dimensional (3D) endoluminal view of the colon that is comparable to what is seen with optical colonoscopy (OC). Radiologists can “fly through” the virtual colon, from the rectum to the cecum and back, searching for polyps and masses. By virtual colonoscopy, therefore, one can noninvasively examine the interior of the colon.

One of the major obstacles to the wide acceptance of CTC is the need for a full cathartic colon cleansing,⁴ similar to that for conventional OC. The perceived discomfort and inconvenience associated with this process have been identified as a main barrier and as one of the major sources of poor patient adherence in colon cancer screening.^{5–8} Early investigations suggested that tagging stool with ingested contrast agents and digitally subtracting tagged fluid and stool from

the CT images, called *electronic cleansing* (EC)^{9–11} or *digital bowel cleansing* (DBC),^{12,13} may permit CTC examinations to be performed without the use of conventional bowel cleansing, thus providing the potential to make CTC a more “patient-friendly” examination.¹⁴

The early work on EC in CTC dates back to late 90s.^{9–11} However, published work on EC research has been limited. Chen *et al.*¹⁵ used a statistical model based on the Markov random field (MRF) for classification of each voxel by its local feature vector. Li *et al.*¹⁶ reported an improvement by using a hidden MRF to integrate the neighborhood information for removal of nonuniformly tagged fluid. Recently, Wang *et al.*¹⁷ presented a partial volume image segmentation method for classifying voxels in different material cases. Zalis *et al.*¹³ used the Sobel approximation of the image gradient, followed by a dilation operator, to identify the boundary between the air lumen and tagged regions. Serlie *et al.*¹⁸ employed a three-material (air, soft-tissue, and tagged material) transition model by using histogram analysis. They also used the CT values and their gradient to characterize the

boundary of tagged fluid. Lakare *et al.*¹⁹ used segment rays to analyze the intensity profile as they traverse through the images for removal of the boundary of tagged fluid.

The majority of the existing EC methods are designed to remove only tagged fluid resulting from rigorous cathartic bowel cleansing, with the following assumptions: (1) tagged fluid appears as a bowel-shaped liquid pool that has a large, horizontal, plain surface; and (2) its tagging is almost homogeneous, i.e., the CT values within the fluid pool are almost uniform. Thus, these EC methods may remain severely limited in removing semisolid stool that is the typical fecal residue in reduced- or noncathartic fecal-tagging CTC. Generally, existing EC approaches tend to suffer from the following artifacts, especially when 3D endoluminal views are used as the primary tool for interpretation:

- **Soft-tissue structure degradation** caused by the pseudo-enhancement effect: Folds and polyps submerged in the tagged materials may be erroneously cleansed as tagged materials because they have higher CT values than do normal soft-tissue structures.
- **Pseudo-soft-tissue structures and false fistulas** caused by the partial volume effect: Portions of the boundary between the air lumen and tagged regions, called the *air-tagging boundary* (AT boundary), may be uncleaned, and this may mimic the appearance of soft-tissue structures such as polyps or folds. Over-cleansing, in which folds are erroneously removed as AT boundary, occurs for the same reason, introducing false fistulas.

These artifacts in existing EC methods limit the usefulness of the fecal-tagging CTC in their diagnostic utility, as demonstrated by the artifacts and pitfalls observed by Pickhardt and Choi.²⁰ Few EC schemes that are designed for noncathartic bowel preparation have been reported. Novel EC methods for subtracting tagged fecal materials are indispensable for applying 3D visualization of virtual colonoscopy to fecal-tagging CTC examinations, especially to noncathartic fecal-tagging CTC examinations.

In this study, therefore, we developed a novel EC method, called a *structure-analysis cleansing* (SA-cleansing) method, which preserves the soft-tissue structures submerged in or partially covered by tagged fecal materials in CTC images, while removing tagged materials without generating spurious objects. In our method, submerged folds and polyps are differentiated from the neighboring tagged fecal materials by use of the local morphologic features that are computed from the eigenvalue signatures of a multiscale Hessian matrix. Structures with a rut-like shape (submerged fold) or cup-like shape (submerged polyp) are enhanced by the enhancement functions based on the eigenvalue signatures of the Hessian matrix. Other structures are de-enhanced and thus subtracted from CTC images. In addition, local roughness is introduced for determining whether a voxel is on a thin soft-tissue layer sandwiched between the air lumen and tagged regions, called an *air-tissue-tagging layer* (ATT layer), or on an AT boundary. The AT boundary appears similar to an ATT layer and is the main source of the artifact of pseudo-soft-tissue struc-

tures. The AT boundary needs to be removed along with the tagged regions, whereas the thin soft-tissue structure within an ATT layer needs to be preserved. A local roughness function measures the irregularity of the local iso-value structure based on the multiscale volumetric curvedness. The application of the local roughness function enhances the thin soft-tissue structures within an ATT layer and suppresses the AT boundary. The analyses of local structures based on eigenvalue signatures and local roughness are designed to reduce the artifacts of soft-tissue structure degradation and pseudo-soft-tissue structures.

The remainder of the paper is organized as follows: Section II describes the method of analysis of local structures based on eigenvalue signatures. Section III presents the method for analysis of local roughness. Section IV introduces the structure-analysis cleansing method. Section V describes the experimental results of our EC method for the CT images of a colon phantom, for clinical CTC images with manually cleansed colons, and some clinical examples of the cleansed CTC images with the noncathartic bowel preparation. Sections VI and VII present a discussion and conclusions, respectively.

II. ANALYSIS OF SUBMERGED SOFT-TISSUE STRUCTURES

II.A. Eigenvalue signatures of folds and polyps

In this study, the EC algorithms were defined on CT volumetric data in 3D Euclidean space, R^3 . Let $I(\mathbf{x})$ denote the CT value at a point $\mathbf{x}=(x,y,z) \in R^3$ in a CT volume. The local structure of I in a neighborhood of $\mathbf{x}$ can be approximated by the Taylor expansion

$$I(\mathbf{x} + d\mathbf{x}) = I(\mathbf{x}) + g(\mathbf{x})d\mathbf{x} + \frac{1}{2}H(\mathbf{x})(d\mathbf{x})^2, \quad (1)$$

where g and H denote the gradient vector and the Hessian matrix, respectively:

$$g = (f_x, f_y, f_z), \quad H = \begin{pmatrix} f_{xx} & f_{xy} & f_{xz} \\ f_{yx} & f_{yy} & f_{yz} \\ f_{zx} & f_{zy} & f_{zz} \end{pmatrix}. \quad (2)$$

Here, f_a and f_{ab} are first and second partial second derivatives of $I(\mathbf{x})$, which can be calculated by the convolution of the partial first and second derivatives of a Gaussian function and I :

$$f_a = \frac{\partial I(\mathbf{x})}{\partial a} \equiv \left(\frac{\partial}{\partial a} G_{0;\sigma}(\mathbf{x}) \right) * I(\mathbf{x}), \quad (3)$$

$$f_{ab} = \frac{\partial^2 I(\mathbf{x})}{\partial a \partial b} \equiv \left(\frac{\partial^2}{\partial a \partial b} G_{0;\sigma}(\mathbf{x}) \right) * I(\mathbf{x}),$$

where $G_{0;\sigma}(\mathbf{x})$ is an isotropic Gaussian function with a mean value of 0 and a standard deviation of σ .

The variance of the Gaussian filter, σ^2 , is referred to as the *scale parameter* in the scale-space representation in computer vision.²¹ It represents an image as a one-parameter family of smoothed images parameterized by the size of the

FIG. 1. (a) Schematic illustration of a colonic polyp (a cap), a haustral hold (a ridge), and the colonic wall (a cylinder). (b) Planar map of the colon illustrates the morphologic shapes of the polyp and the fold. The polyp is depicted as a cap-like structure, whereas the fold is depicted as a ridge-like structure on the colonic planar surface. The three vectors e_1 , e_2 , and e_3 represent the eigenvectors of the Hessian matrix for the polyp and the fold.

smoothing kernel used for suppressing fine-scale structures. Image structures of spatial size smaller than σ are largely smoothed away in the scale-space level at scale σ^2 . The parameter σ^2 also serves as the scale parameter in the Hessian matrix, which is determined based on the size of the underlying structures in CTC images. In our study, we set σ to one voxel unit, μ , to smooth away structures smaller than one voxel; thus the examples in this section were generated by use of $\sigma = \mu$, if not specified otherwise. The multiscale Hessian matrix was calculated over two scales, i.e., μ and 2μ .

Let the eigenvalues of Hessian matrix H be λ_1 , λ_2 , and λ_3 ($|\lambda_1| \leq |\lambda_2| \leq |\lambda_3|$), and let their corresponding eigenvectors be e_1 , e_2 , and e_3 respectively. The local morphologic structure of an object can be characterized by use of a combination of the eigenvalues of the Hessian matrix, called *eigenvalue signatures*.^{22,23} In this section, we exploit the eigenvalue signatures of fold and polyp structures submerged in the tagged materials to preserve them in the cleansed images.

In the colonic lumen, polyps tend to appear as bulbous, cap-like structures that adhere to the colonic wall; folds appear as elongated, ridge-like structures; and the colonic wall appears as a large, nearly flat, cup-like structure,²⁴ as illustrated by the planar map in Fig. 1. Morphologically, when folds and polyps are submerged in the tagged materials, they present rut-like (concave ridge) and cup-like (concave cap) shapes, because the tagged materials usually have higher CT values than do those for soft-tissue structures.

Figures 2(a) and 2(b) show a fold in a phantom submerged in the tagged materials. The profiles in Fig. 2(e) show the change in CT values and eigenvalues of the Hessian matrix along the short axis on the cross-sectional image of a fold. Along the short axis, the CT values and the eigenvalues of the Hessian matrix were calculated and sampled by an interval of one voxel. The resulting CT profile demonstrates the pseudo-enhancement effect; the fold, for which the CT value is originally approximately 50 HU, is enhanced up to 600 HU. We observe that the maximum eigenvalue, λ_3 , changes from negative to positive, and then to negative again, i.e., the local structure in CT images changes from

convex to concave, and then to convex again, along the sampling line. The convex structure corresponds to the transition from the tagged materials (bright foreground) to the fold (dark background), whereas the concave structure corresponds to the transition from the fold (dark foreground) to the tagged materials (bright background). We are interested only in the latter shape, i.e., that of the local structures for which $\lambda_3 > 0$.

In the range of $\lambda_3 > 0$, we observe that the minimum eigenvalue λ_1 is close to zero; this indicates that there is no change in curvature along the central axis because the direction of the eigenvector e_1 corresponds to the central axis of the fold. Eigenvectors e_2 and e_3 , which are perpendicular to e_1 , are on the plane perpendicular to the central axis of the fold, and they correspond to the long and short axes, respectively. Suppose that the thickness of a fold is substantially smaller than its height. Then, λ_3 is inversely proportional to the thickness of the fold and λ_2 is inversely proportional to the height of the fold.

Figures 2(e) and 2(f) show the profiles along the short and long axes of the cross-sectional image of the fold in Fig. 2(a), respectively. As shown in these profiles, λ_1 is close to zero and λ_3 stays positive in the region of the axis in the fold area, whereas λ_2 changes from positive to negative. This change implies that the background structures changed from tagged materials to the colonic wall, i.e., λ_2 varies with the height of the fold relative to the background. Therefore, submerged folds are characterized by an eigenvalue signature of $\lambda_3 > 0$, $\lambda_1 \approx 0$, and $\lambda_2 \ll \lambda_3$.

Unlike a fold, a submerged polyp is a cup-like structure. Figure 2(g) shows the profiles for the CT values and the eigenvalues of a polyp along the sampling line in Figs. 2(c) and 2(d). The region with $\lambda_3 > 0$ indicates the polyp region. It should be noted that all eigenvalues are zero in the middle of the polyp (around point 15); in this region, the kernel for computing the second derivative of the CT values is located completely within the soft-tissue region, in which the CT profile varies very little. In the region where λ_3 is positive, λ_1 , λ_2 , and λ_3 are roughly linearly proportional, and they are

FIG. 2. Profiles of a submerged fold and a submerged polyp on a colon phantom. (a) Two sampling lines on the cross-sectional image of a fold. CT values and eigenvalues of the Hessian matrix are sampled along the short and long axes of the fold. (b) Coronal view of the fold in (a). (c) A sampling line on the cross-sectional image of a polyp. (d) Coronal view of the polyp in (c). (e) Plot of the change in CT values and eigenvalues of the Hessian matrix along the short axis in (a). (f) Plot of the change in CT values and eigenvalues of the Hessian matrix along the long axis in (a). (g) Plot of the change in CT values and eigenvalues of the Hessian matrix along the sampling line in (c).

comparable in magnitude. Therefore, polyps submerged in the tagged fecal materials are characterized by an eigenvalue signature of $\lambda_3 > 0$, $\lambda_1 \approx \lambda_2$, and $\lambda_2 \propto \lambda_3$.

These relationships among eigenvalues build up the eigenvalue signatures that are characteristic of folds and polyps submerged in tagged materials, as shown in Table I.

II.B. Structural enhancement functions for folds and polyps

Based on the eigenvalue signatures, we designed two structural enhancement functions, one to enhance the rut-like and the other, the cup-like structures. The first is the rut-enhancement function F_{rut} , defined as

$$F_{\text{rut}} = F_A \cdot F_B, \quad (4)$$

where F_A and F_B are discrimination functions to uplift rut-like structures.

The discrimination function F_A is designed to differentiate between an elongated object and a spherical object:

$$F_A = \exp\left(\frac{R_a^2}{2\alpha^2}\right), \quad R_a = \frac{|\lambda_1|}{\sqrt{|\lambda_2\lambda_3|}}. \quad (5)$$

This function reflects a part of the eigenvalue signature in Table I: $\lambda_1 \approx 0$ and $|\lambda_1| \ll |\lambda_2|$ and $|\lambda_1| \ll |\lambda_3|$. It takes a maximum value when λ_1 approaches zero, that is, when the underlying object has an elongated structure. It takes a minimum value when $\lambda_1 = \lambda_2 = \lambda_3$, that is, when the underlying object has a spherical structure. The range of the function is controlled by the parameter $\alpha < 1$.

Changes in the value of the discrimination function F_A as a function of R_a at different values of α are shown in the curves in Fig. 3(a). Figure 3(b) shows a coronal image of the colonic phantom, in which all the voxels above 200 HU are shaded. (The details on the structure of the phantom are de-

TABLE I. Eigenvalue signatures of fold and polyp submerged in the tagged materials.

Anatomic example	Morphological category	Eigenvalue signature
Submerged fold	Rut	$\lambda_3 > 0$ and $\lambda_1 \approx 0$ and $\lambda_2 \ll \lambda_3$
Submerged polyp	Cup	$\lambda_3 > 0$ and $\lambda_1 \approx \lambda_2$ and $\lambda_2 \propto \lambda_3$

FIG. 3. Effect of discrimination function F_A on the differentiation of folds from other structures in the colon phantom. (a) Curves show the change in the values of F_A as a function of R_a at different values of α . (b) Coronal view of the CTC images of a colon phantom. All voxels above 200 HU are shaded. We observe that parts of the folds and polyps are pseudo-enhanced. (c) The response images of the phantom image in (b) resulting from the application of F_A at $\alpha=0.1, 0.25, 0.5$, and 1.0 .

scribed in Sec. V A) The response images of the phantom resulting from the application of the discrimination function F_A at different values of α are shown in Fig. 3(c). The submerged structures, especially the thin folds, are enhanced at different scales with different α values. A small value of α narrows the enhancement range of folds, whereas a large value of α enlarges the enhancement range. In order to balance the level of enhancement with noise and other structures, we selected $\alpha=0.5$ in our study.

The discrimination function F_B characterizes the cross-sectional structure of a rut, or the crest shape, on the plane perpendicular to the central axis of the rut, and thus it depends only on the ratio of λ_2 to λ_3 , as follows:

$$F_B = \exp\left(-\frac{(R_b - \gamma)^2}{2\beta^2}\right), \quad R_b = \frac{|\lambda_2|}{|\lambda_3|}. \quad (6)$$

The function F_B reflects the relationship between λ_2 and λ_3 . The curves in Figs. 4(a) and 4(c) show the change in the values of the discrimination function F_B with $\gamma=0.2$ and 0.3 , respectively. The range of the function is controlled by the parameter $\beta < 1$. $R_b=0.0$ represents a plate-like structure, whereas $R_b=1.0$ represents a structure with a circular section. Thus, the function F_B enhances structures between these two shapes. Figures 4(b) and 4(d) show the response images resulting from the application of F_B with $\gamma=0.2$ and

0.3 , respectively, to the colon phantom shown in Fig. 3(b). From left to right, the three figures in Figs. 4(b) and 4(d) show the response images resulting from the application of F_B with $\beta=0.1, 0.3$, and 0.5 . To balance the side effect from the enhancement of plate and sphere, we selected the values $\gamma=0.3$ and $\beta=0.3$ in our study.

The second structural enhancement function is a cup-enhancement function, F_{cup} , to uplift the cup-like structure, i.e., the submerged polyp structure, defined by

$$F_{\text{cup}} = F_C(\lambda_1, \lambda_2) \cdot F_C(\lambda_2, \lambda_3), \quad (7)$$

where

$$F_C(\lambda_i, \lambda_j) = 1.0 - \exp\left(-\frac{R_c^2}{2\eta^2}\right), \quad R_c = \frac{|\lambda_i|}{|\lambda_j|}. \quad (8)$$

The parameter η controls the range of the enhancement function F_C , as illustrated in Fig. 5(a). The enhancement results of F_C with $\eta=0.1, 0.2$, and 0.5 are shown in Fig. 5(b). Because most polyps are not strictly spherical in shape, we selected $\eta=0.2$ in this study.

We calculate the values of the rut- and cup-enhancement functions on each of the voxels in the tagged regions that satisfy $\lambda_3 > 0$; thus, the structures exposed in the air lumen are excluded, as demonstrated in Figs. 6(c) and 6(d). The

FIG. 4. Effect of the discrimination function F_B on the differentiation of folds from other structures in the colon phantom. (a) Curves show the change in the values of F_B as a function of R_b at a fixed value of $\gamma=0.2$ and at different values of β . (b) The response images of F_B from the application of $\gamma=0.2$ and $\beta=0.1, 0.3$, and 0.5 . (c) Curves show the change in the values of F_a as a function of R_b at a fixed value of $\gamma=0.3$ and at different values of β . (d) The response images of F_B from the application of $\gamma=0.3$ and $\beta=0.1, 0.3$, and 0.5 .

maximum value of the two enhancement functions is assigned as a structurally enhanced value H_Λ at point $\mathbf{x}$:

$$H_\Lambda(\mathbf{X}) = \max\{F_{\text{rut}}(\mathbf{x}), F_{\text{cup}}(\mathbf{x})\}. \quad (9)$$

Figure 6(e) illustrates the responses of F_{rut} , F_{cup} , and the structurally enhanced value H_Λ .

Because both F_{rut} and F_{cup} are scale-dependent functions, the final Hessian response field, $\mathcal{H}$, is thus defined as the maximum response of the structural enhancement function H_Λ across scales:

$$\mathcal{H}(\mathbf{x}) = \max_{\sigma=\sigma_1}^{\sigma_n} (H_\Lambda(\mathbf{x}; \sigma)) = \max_{\sigma=\sigma_1}^{\sigma_n} \{F_{\text{rut}}(\mathbf{x}; \sigma), F_{\text{cup}}(\mathbf{x}; \sigma)\}, \quad (10)$$

where the range of scale is $[\mu, 2\mu]$ in voxel units.

Figure 7 shows images of the Hessian response field of a colon resulting from the application of the structural enhancement functions of folds and polyps to a clinical CTC case. We observe that the submerged folds and polyps are well enhanced, whereas the other structures, such as tagged materials, air bubbles, folds in the lumen, and the colonic wall, are de-enhanced.

III. ANALYSIS OF LOCAL ROUGHNESS

III.A. Similarity between AT boundary and thin soft-tissue structures

A CT value at an AT boundary is a mixture of the CT values from two materials, air and tagged material, because of the partial volume effect (PVE).²⁵ Thus, the CT value at the AT boundary, I_{AT} , takes on a wide spectrum of values, ranging from that of air to that of tagged materials. Typically, the lumen air, soft-tissue, and tagged material in CTC images have CT values in the range of $[-1000 \text{ HU}, -800 \text{ HU}]$, $[-100 \text{ HU}, 100 \text{ HU}]$, and $[200 \text{ HU}, 1400 \text{ HU}]$, respectively, I_{AT} typically ranges from -800 HU to 600 HU , and thus it overlaps significantly with that of the soft-tissue structures. Therefore, when a thin soft-tissue structure is sandwiched between the air lumen and a tagged region, i.e., the ATT layer, the CT values and their gradients of the sandwiched thin soft-tissue structure become very similar to those of the AT boundary. For example, Series 1 in the plots in Fig. 8(c) shows the change in the gradient of CT values along the profile across the thin fold as shown by a gray arrow in Fig. 8(a), whereas Series 2 and 3 are those along the AT boundary profiles as shown by gray arrows in Fig. 8(b). As shown in the figure, these three profiles show very similar patterns for the change in CT values and the gradient magnitudes; there-

FIG. 5. Effect of the discrimination function F_C on the differentiation of polyps from other structures in the colon phantom. (a) Curves show the change in the values of F_C as a function of R_C at different values of η . (b) The response images resulting from the application of F_C to the phantom image in Fig. 3(b), when η was set to 0.1, 0.2, and 0.5.

fore, determination of whether a voxel belongs to an AT boundary based only on the gradient may be difficult.

III.B. Local roughness

We therefore developed a method of analyzing the local roughness in the neighborhood of a voxel to determine whether the voxel is on an AT boundary or on a thin soft-tissue structure in an ATT layer.

This method is based on the observation that the CT values in an interface generated by an AT boundary are often more irregular than that of soft-tissue structures because of the local nonlinear volume averaging caused by the PVE between air and tagged materials. Such image irregularity is reduced when a thin soft-tissue structure is located in the middle of the air lumen and tagged regions because of the smoothness caused by the narrow range of CT values of soft-tissue structures. This image irregularity is illustrated by the iso-value voxels shaded in Figs. 8(a) and 8(b). We observe that the iso-value voxels on the AT boundaries are often disconnected, whereas those of thin soft-tissue

structures are connected, indicating that the image intensity of an AT boundary is more irregular than the thin soft-tissue structures sandwiched within an ATT layer. We thus used the local roughness to measure this irregularity.

The local roughness at point $\mathbf{x}$ is defined as the cumulative difference of the local volume curvedness, $CV_\sigma(\mathbf{x})$, between adjacent scales as follows:

$$R(\mathbf{x}) = \sum_{i=1}^n (B_i \cdot \Delta CV_i(\mathbf{x})^2), \quad (11)$$

where $\Delta CV_i(\mathbf{x}) = CV_{\sigma_i}(\mathbf{x}) - CV_{\sigma_{i-1}}(\mathbf{x})$ represents the difference in the curvedness values at scales i and $i-1$, n is the number of scales, and B_i is a scale-dependent basis function that weights the difference of the curvedness values at each scale. Here, the volumetric curvedness at voxel $\mathbf{x}$ is defined as

$$CV_\sigma(\mathbf{x}) = \sqrt{\frac{1}{2}(\kappa_1^\sigma(\mathbf{x})^2 + \kappa_2^\sigma(\mathbf{x})^2)}, \quad (12)$$

where κ_1^σ and κ_2^σ are the two principal curvatures at scale σ .^{26,27} The principal curvature can be calculated by

FIG. 6. Hessian response of submerged colonic structures: (a) and (c) show coronal and axial images of the colon phantom, respectively: all voxels above 200 HU are shaded. (b) and (d) are the Hessian response field of (a) and (c), respectively, in which the corresponding voxels above 200 HU are shaded. (e) Response images resulting from application of the rut-enhanced function F_{rut} , the cup-enhancement function F_{cup} , and structural enhancement function H_A .

$$\kappa_1^\sigma = H \pm \sqrt{H^2 - k}, \quad i = 1, 2, \quad (13)$$

where K and H are the Gaussian curvature and mean curvature, respectively. They are calculated by

$$K = \frac{1}{h^2} [f_x^2(f_{yy}f_{zz} - f_{yz}^2) + 2f_yf_z(f_{xz}f_{xy} - f_{xx}f_{yx}) + f_y^2(f_{xx}f_{zz} - f_{xz}^2) + 2f_xf_z(f_{yz}f_{xy} - f_{yy}f_{xz}) + f_z^2(f_{xx}f_{yy} - f_{xy}^2) + 2f_xf_y(f_{xz}f_{yz} - f_{zz}f_{xy})], \quad (14)$$

$$H = \frac{1}{2h^{3/2}} [f_x^2(f_{yy} + f_{zz}) - 2f_yf_zf_{yz}) + f_y^2(f_{xx} + f_{zz}) - 2f_xf_zf_{xy}) + f_z^2(f_{xx} + f_{yy}) - 2f_xf_yf_{xy}), \quad (15)$$

where $h = f_x^2 + f_y^2 + f_z^2$, $f_a = \partial I(\mathbf{x}) / \partial a$, $f_{ab} = \partial^2 I(\mathbf{x}) / \partial a \partial b$.

Both f_a and f_{ab} can be calculated by a convolution of the

FIG. 7. Demonstration of the effect of the structural enhancement functions on folds and polyps. (a) Portion of the colonic lumen filled with tagged materials. (b) Result of the Hessian response field to the lumen in (a). The folds submerged in the tagging materials are well enhanced. (c) Portion of the colonic lumen that is half filled with tagged materials. A submerged thin fold and a small polyp are indicated by black arrows. (d) Result of the Hessian response field to the lumen in (c). The submerged folds and polyps are well enhanced, as indicated by the white arrows.

FIG. 8. Similarity between an AT boundary and the soft-tissue structure sandwiched between the air lumen and a tagged region. (a) The profile across the thin fold is shown by a gray arrow. (b) Two AT boundary profiles are shown by gray arrows. In both images (a) and (b), voxels of which the CT value is between -200 HU and 200 HU are shaded. Three profiles including the CT value and gradient value were sampled along the lines, from the filled circle to the arrow point. (c) Plot of the change in the gradient of CT values along the profiles in (a) and (b). Series 1 shows the change in the gradient along the profile in (a), whereas Series 2 and 3 show the change in the gradient along the profiles in (b). The three profiles show a very similar pattern of change in the CT values and gradient values.

partial first and second derivatives of a Gaussian function and I , as shown in Eq. (3). Similar to the computation of the Hessian matrix, the value of the volumetric curvedness is related to the scale of σ .

The curvedness, CV_{σ} , is computed by filtering of images with increasing scale, from scale 0 (σ_0) to scale n (σ_n), and then, at each scale i , by application of the first and second derivative filters of scale σ_i to the image.

FIG. 9. (a) Image of a large block of tagged fecal material that has an AT boundary (top dots) and a thin fold sandwiched between the air lumen and the tagged region (bottom triangles). (b) Local roughness images generated from the image in (a). Here, a bright pixel represents a low roughness value. (c) Plots of the curvedness values across the scales. The dotted curves show the change in the curvedness values at the voxels along the AT boundary, as represented by circles in (a). The solid curves show the change in the curvedness values at the voxels, represented by triangles in (a), along the thin haustral fold sandwiched between the tagged region and the air lumen.

FIG. 10. Local roughness of the iso-value voxels at $[-200 \text{ HU}, 200 \text{ HU}]$ distinguishes the AT boundaries and the thin folds within the ATT layer. (a) and (b) show CTC images in which arrows indicate either the AT boundaries or thin folds sandwiched between lumen air and tagged materials. (c) and (d) show the roughness response fields corresponding to (a) and (b). In (c), the thin fold [white arrow in (a)] is enhanced, whereas the AT boundary [black arrow in (a)], which has the same profile as the thin fold, is de-enhanced. The image in (d) demonstrates that the local roughness enhances the folds that are buried underneath the tagged objects [white arrows in (b)], whereas the AT boundary against gravity [black arrow in (b)] is de-enhanced.

The dotted curves in the plot in Fig. 9(c), show the change in curvedness values across scales at voxels along the AT boundary, as represented by circles in Fig. 9(a). The solid curves in the plot show the change in curvedness values at voxels represented by triangles in Fig. 9(a) along the thin haustral fold sandwiched within the ATT layer. At small scales, the AT boundary has high curvedness values; however, they quickly decrease to become as small as those for the thin fold. The curvedness values stay almost the same across the scales for the thin fold. Therefore, the local roughness defined by Eq. (11), which reflects the relative change in curvedness, can be used effectively for differentiation between an AT boundary and a thin fold sandwiched within an ATT layer. Because the roughness value varies in different images, we used arctan function to compare the roughness values in a normalized range. Thus, the roughness response field, $\mathcal{R}$, is defined by

$$\mathcal{R} = 1.0 - \tan^{-1}(\mathcal{R})/(0.5\pi). \quad (16)$$

Figure 9(b) shows the roughness response field $\mathcal{R}$ of the image in Fig. 9(a), in which a bright pixel represents a low roughness value. As shown in this image, thin soft-tissue structures show the minimum roughness, i.e., the highest smoothness. The fold at the bottom of the tagged region in Figure 9(b) shows less roughness than that of the AT boundary on the top of the tagged fecal material in Figure 9(a). This demonstrates that we can use the local roughness to differentiate between an AT boundary and a thin fold sandwiched in an ATT layer, and thus to preserve the thin folds adhering to the tagged region.

Figure 10 shows another example of the relationship between roughness and the AT boundary. Comparing images

(a) and (b) with images (c) and (d), we observe that the thin folds that are sandwiched between the air and the tagged materials (white arrows) are enhanced, whereas the AT boundaries (black arrows), especially that of the tagged stools against gravity [black arrow in Fig. 10(b)], are de-enhanced.

IV. STRUCTURE-ANALYSIS (SA) CLEANSING METHOD

Our cleansing method uses a level set model,²⁸ which combined with the structural response from the eigenvalue signatures and the local roughness described in the previous sections. The structure analysis (SA) cleansing method consists of the following five steps: (1) initial segmentation of the colon, (2) computation of the Hessian response field $\mathcal{H}$, (3) computation of the local roughness response field $\mathcal{R}$, (4) segmentation of tagged regions based on the level set method, and (5) replacement of the tagged regions that are segmented in step (4) with air, followed by reconstruction of the colonic wall submerged in tagged regions.

In the step of initial colon segmentation, first, the air-filled colonic lumen is detected by thresholding. Then, each voxel on the surface of the thresholded colonic lumen is used as a seed for region growing in order to segment the entire colonic lumen, including fecal-tagging regions and the colonic wall. Then, in the second step of computing the Hessian response field, eigenvalues of the Hessian matrix are calculated at each voxel in the initial segmented colon region to characterize the representative soft-tissue structures such as rut-like and cup-like objects. Equations (4) and (7) compute the response value for rut-like and cup-like structures, respectively. The maximum of these two response values is used as the Hessian response field, $\mathcal{H}$, of submerged structures in tagged regions, as shown in Eq. (10). In the third step of computing the roughness response field, the local roughness of the boundary of tagged regions is quantified by the cumulative difference in the local volumetric curvedness by using Eq. (11). The result is the local roughness response field, $\mathcal{R}$, around the tagged regions, as shown in Eq. (16). In the fourth step, segmentation of tagged regions is performed by initializing of the level set front with the tagged regions segmented in the first step, i.e., the colonic lumen above 200 HU. The level set front is then evolved through the partial differential equation in Eq. (17) that controls the evolution of the level set front. The evolution function has three speed functions from images: the speed function of image gradients, $F(g(\mathbf{x}))$, the speed function of the Hessian response field, $F(\mathcal{H}(\mathbf{x}))$, and the speed function of the roughness response field, $F(\mathcal{R}(\mathbf{x}))$. Here, $\mathbf{x}$ represents a point on the level set front. These three speed functions are balanced with a mean curvature smoothing constraint, shown in the last term in Eq. (17), where $C_{\text{Curvature}}$ is a parameter controlling the strength of the constraint. We used $C_{\text{Curvature}}=0.2$ in our study.

$$\begin{aligned} \frac{\partial \phi}{\partial t} = & \{F(g(\mathbf{x})) - F(\mathcal{H}(\mathbf{x})) - F(\mathcal{R}(\mathbf{x}))\} |\nabla \phi| \\ & + C_{\text{Curvature}} \nabla \cdot \left(\frac{\nabla \phi}{|\nabla \phi|} \right) |\nabla \phi|, \end{aligned} \quad (17)$$

where F is a speed function, for which we employed the following threshold speed function:

$$\begin{aligned} F(x) = & \text{sign}(t(x)) \cdot |t(x)|^n, \quad \text{where} \\ t(x) = & \begin{cases} -1 & \text{if } x < T - \Delta \\ (x - T)/\Delta & \text{otherwise} \\ 1 & \text{if } x > T + \Delta \end{cases}, \end{aligned} \quad (18)$$

where $\text{sign}(t)$ is a sign function (a.k.a. an indicator), i.e., 1 if t is positive and -1 if t is negative; n is an integer factor that controls the smoothness of the speed of the level set front. In this study, we used $n=2$. T is a threshold value that is determined by Otsu's thresholding method.²⁹ This threshold separates the enhanced and nonenhanced objects in the histogram calculated from the shell, which is a thick 3D region encompassing the level set front.³⁰ The range in the speed function, Δ , will be set to a half of the difference between the threshold and the peak value of the histogram of the enhanced objects.

With use of the gradient speed function to segment the AT boundary and the two counter forces from the Hessian response field and roughness response field, the level set front becomes insensitive to the AT boundary and thus can remove the tagged regions, whereas it can preserve the colonic structures that are submerged in the tagged regions.

Finally, in the last step, also called reconstruction of the transition layer, the tagged regions that are segmented in step four are replaced with air, and an artificial transition boundary between the colonic walls and the subtracted tagged regions are reconstructed by the mucosa reconstruction method that we developed earlier.¹³

V. EXPERIMENTAL RESULTS

To evaluate the quality of cleansing in our SA-cleansing method, we designed two experiments: a phantom experiment and a manual cleansing experiment. In each experiment, the results of the new SA-cleansing method were compared with those of our previous threshold-based cleansing method¹³ that is referred to as *T cleansing* hereafter. In addition, we demonstrated some artifact-free cleansed cases examined by the noncathartic bowel preparation. The subtraction threshold was set to 200 HU in all experiments.

The SA-cleansing method was implemented by using C++ in Microsoft.NET environment. The software runs on a Window XP platform. All experiments were conducted on an Intel Pentium-based 2.8 GHz computer with 2 GB of memory.

FIG. 11. Comparison of coronal images between the original phantom and the phantom cleansed by use of the SA- and T-cleansing methods. (a) Coronal image without tagged materials. (b) Coronal images after being filled with tagged materials. (c) and (d) show the coronal view of the cleansed images of (b) by use of the SA- and T-cleansing methods, respectively.

V.A. Phantom experiment

In the phantom experiment, our method was evaluated by use of a colon phantom made of material that had an x-ray attenuation coefficient similar to those of soft-tissue (Phantom Laboratory, Salem, NY).³¹ Twenty-one phantom polyps and 11 phantom folds were embedded in the colon phantom. The colon phantom was scanned by a multi-detector CT scanner (LightSpeed; GE Medical Systems, Milwaukee, WI) twice, once in a native, cleansed state without tagging material and once with a contrast solution simulating the observed attenuation of tagging materials used in human CTC images. The phantom was scanned by use of the following scanning parameters: 3.5 mm collimation, 1.6 mm reconstruction interval, tube current of 50 mA, and voltage of 140 kVp. CT images obtained for the native, cleansed state served as a reference standard, and those with a contrast solution were subjected to the SA- and T-cleansing methods. The cleansing quality was assessed by comparison of the cleansed image with the reference standard for each colonic feature. The tagging material in the phantom for the experimental conditions demonstrated a mean attenuation of 870 ± 91 HU and consisted of a 1:30 dilution of 300 mg/ml organically bound nonionic iodine contrast agent (Omnipaque iohexol 300, GE Healthcare, Princeton, NJ), the same contrast agent we employ for clinical fecal tagging in CTC.

Each of the submerged soft-tissue structures (polyps and folds) was located visually both in the cleansed and in the original colon phantom, and a 64^3 voxel volume of interest (VOI) centered at each soft-tissue structure was extracted for comparison to the reference standard. Because the phantom was removed from the CT table while the phantom was filled with tagged material, each VOI extracted from the cleansed colon phantom was registered rigidly to the corresponding VOI in the reference standard by use of a 3D affine

FIG. 12. Evaluation results of EC on polyps in a colon phantom. (a)–(d) Examples of the cleansing results of a submerged phantom polyp by use of SA- and T-cleansing methods. (a) Detailed view of the original phantom polyp. (b) Detailed view of the polyp in (a) after SA cleansing. (c) Detailed view of the polyp in (a) after T cleansing. (d) 3D view of the original phantom polyp before the colon phantom was filled with tagged materials. (e) MIP image of the difference between (a) and (b). (f) MIP image of the difference between (a) and (c). (g), (h) Results for the 11 submerged polyps. (g) RMSE values of the difference VOIs for individual submerged polyps. (h) The difference in the number of soft-tissue voxels, defined as those with CT values higher than -600 HU, in the resulting VOIs from SA and T cleansing with respect to the reference standard. The t -test showed that both RMSE and the difference in the number of soft-tissue voxels were significantly lower for SA cleansing than for T cleansing ($p=0.0003$ and 0.0001 , respectively).

transformation,³² and the difference between the two VOIs was calculated. The root-mean-square error (RMSE) of the difference VOI was used as a measure of the goodness of cleansing.

We used 11 submerged phantom polyps and seven submerged folds for evaluation of the quality of cleansing. Figure 11 demonstrates EC on 2D images. Figure 11(a) shows the original phantom image without tagging, and Fig. 11(b) shows the phantom image filled with tagged materials. Figures 11(c) and 11(d) show the cleansed images by the SA-cleansing and the T-cleansing method, respectively. 3D cleansing images are demonstrated in Fig. 12. Figures 12(a)–12(d) show an example of the cleansing results of a submerged phantom polyp by use of the SA- and T-cleansing methods. We observe that the SA-cleansing method cleanses the tagged materials and preserves the polyp shape more precisely than does the T-cleansing method. Figures 12(e) and 12(f) show the maximum intensity projection (MIP) images of the difference VOI between the cleansed polyp and the reference standard. These images also demonstrate that the SA-cleansing method produced less error than did the T-cleansing method.

Figure 12(g) shows the RMSE values of the difference VOIs for individual submerged polyps. The average RMSE value for the 11 different VOIs was 48.9 HU for the SA-cleansing method, whereas it was 71.2 HU for the T-cleansing method. A paired t -test showed that the differ-

ence between these RMSE values was statistically significant ($p=0.0003$). Figure 12(h) shows the difference in the number of soft-tissue voxels, defined as those with CT values higher than -600 HU (voxels lower than -600 HU were regarded as air), in the VOIs resulting from SA cleansing and T cleansing with respect to the reference standard. The average number of voxels in SA cleansing was 134.6 voxels, whereas it was 659.9 voxels in T cleansing ($p=0.0001$), indicating that T cleansing may lose five times more voxels than does SA cleansing.

Figures 13(a)–13(c) show the cleansing results for a submerged phantom fold by use of the SA- and T-cleansing methods. We observe that the submerged fold was recovered well in SA cleansing, whereas it was somewhat degraded in T cleansing. Figure 13(d) shows the RMSE values of the difference VOIs for individual submerged folds. The average RMSE value for the seven difference VOIs was 67.4 HU for the SA-cleansing method, whereas it was 89.9 HU for the T-cleansing method. A paired t -test showed that the difference between these RMSE values was statistically significant ($p=0.0007$). Figure 13(e) shows the difference in the number of soft-tissue voxels, defined as those with CT values higher than -600 HU, in the resulting VOIs from SA cleansing and T cleansing with respect to the reference standard. The average numbers of voxels for the SA-cleansing method and the

FIG. 13. Evaluation results of EC on folds in a colon phantom. (a)–(c) Examples of the cleansing results of a submerged phantom fold by use of SA- and T-cleansing methods. (a) Detailed view of the phantom fold before the colon phantom was filled with tagged materials. (b) Detailed view of the fold in (a) after SA cleansing. (c) Detailed view of the fold in (a) after T cleansing. (d), (e) Results for the seven submerged folds. (d) RMSE values of the difference VOIs for individual submerged folds. (e) The difference in the number of soft-tissue voxels, defined as those with CT values higher than -600 HU, in the resulting VOIs from SA and T cleansing with respect to the reference standard. The t -test showed that both RMSE and the difference in the number of soft-tissue voxels were significantly lower for SA cleansing than for T cleansing ($p=0.0007$ and 0.0003 , respectively).

T-cleansing method were 251.3 and 2567.4 ($p=0.0003$), respectively, indicating that SA cleansing is substantially closer to the reference standard than is T cleansing.

V.B. Manual cleansing experiment

In this experiment, we used 16 fecal-tagging CTC cases, which were selected from the CTC cases obtained in the study by Pickhardt *et al.*,³³ (Courtesy of Dr. J. Richard Choi, Center for Virtual Colonoscopy, Walter Reed Army Medical Center) for evaluation of the quality of cleansing. In this study, patients underwent a standard 24 h colonic preparation with oral administration of 90 ml of sodium phosphate and 10 mg of bisacodyl. Fecal tagging was performed with 500 ml of barium for solid-stool tagging and 120 ml of diatrizoate meglumine and diatrizoate sodium for colonic fluid tagging. Multidetector CT scanning was performed in both supine and prone positions with the following scanning parameters: 1.25–2.5 mm collimation, a table speed of 15 mm/s a reconstruction interval of 1 mm, a tube current of 100 mA, and a voltage of 120 kVp.

Among these 16 cases, ten contained one polyp larger than 8 mm submerged in tagged fecal materials. These ten submerged polyps were located visually with a VOI size of 64^3 voxels, the same size as in the phantom experiment. An experienced radiologist manually cleansed the VOIs to establish the reference standard. The manual cleansing was finished on an Amira workstation (Mercury Computer Systems, Berlin, Germany). The tagged regions were contoured manu-

ally, and the contoured regions were filled by the CT value of air (-1000 HU). Ten VOIs were also subjected to the SA- and T-cleansing methods. Similar to the phantom experiment in Sec. V A, we used the RMSE as the measure of the quality of cleansing.

Figure 14(a) shows an example of the manual cleansing of a 9 mm submerged polyp, and Figs. 14(b) and 14(c) show the cleansing results for the polyp by use of the SA- and T-cleansing methods, respectively. Visual comparison indicates that no severe degradation was observed in the shape of the polyp obtained by the SA-cleansing method; however, severe polyp degradation as well as a false fistula were observed in the images resulting from T cleansing.

Figure 14(d) shows RMSE values of the difference VOIs for the ten polyps resulting from the SA- and T-cleansing methods. The mean RMSE for the ten polyps from SA cleansing was 45.9 HU, and was 75.4 HU for T cleansing ($p=0.0005$). It should be noted that the absolute value of the RMSE varies substantially among the polyps because of their local structures and the tagging conditions. We observe that, for polyp 10, both T cleansing and SA cleansing matched the manual-cleansing results very well because the tagging material around this polyp had relatively low CT values (around 300–400 HU), and thus no pseudo-enhancement effect was observed on this polyp.

Figure 14(e) shows the difference in the number of voxels higher than -600 HU in the VOIs resulting from SA cleansing and T cleansing with respect to the reference standard.

FIG. 14. Evaluation results from the manual cleansing experiment. (a)–(c) Examples of the cleansing results of a 9 mm polyp submerged in tagged fluid in clinical CTC cases by use of the SA- and T-cleansing methods. (a) Detailed view of the polyp in (a) after SA cleansing. (c) Detailed view of the polyp in (a) after T cleansing. We observe the fold and polyp degradation as well as a false fistula in (c). (d),(e) Results for the ten submerged polyps. (d) RMSE values of the difference VOIs for ten individual submerged polyps. (e) The difference in the number of soft-tissue voxels, defined as those with CT values higher than -600 HU, in the resulting VOIs from SA and T cleansing with respect to the reference standard. The t -test showed that both MSE and the difference in the number of soft-tissue voxels were significantly lower for SA cleansing than for T cleansing ($p = 0.0005$ and 0.0012 , respectively).

The average number of voxels in SA cleansing was 383, whereas it was 2,351 in T cleansing ($p = 0.0012$), indicating that T cleansing inappropriately removes, on average, six times more voxels than does SA cleansing.

V.C. Cleansing effect on noncathartic CTC cases

To demonstrate the effect of SA cleansing in clinical CTC cases with a large amount of semisolid residual fecal materials, we applied the SA cleansing to the fecal-tagging CTC cases prepared with noncathartic bowel cleansing. Patients underwent a 48 h colonic preparation with a low-fiber, low-residue diet, oral administration of 7.5 ml nonionic iodine diluted in 300 ml water at each of six meals, and 30 ml Omnipaque diluted in 960 ml water on the morning of the CTC examination. No catharsis was used in the bowel preparation. Multidetector CT scanning (LightSpeed; GE Medical Systems, Milwaukee, WI) was performed in both supine and prone positions, with the following scanning parameters: 2.5 mm collimation, 1.25 mm reconstruction interval, a tube current of 70 mA, and a voltage of 140 kVp. It should be noted that, unlike the CTC cases in Sec. V B, most of the tagged materials in these cases were semisolid rather than fluid, and thus they were difficult cases for EC. The SA-cleansing method took, on average, approximately 30 min for processing of one scan based on our test machine.

Soft-tissue structures submerged in the tagged materials, such as the submerged fold in Fig. 15(a) and the submerged polyp in Fig. 15(d), often suffer from the artifact of degradation of the soft-tissue structures due to the pseudo-enhancement effect; after the application of T cleansing, the enhanced portion of soft tissues was erroneously cleansed as tagged materials, resulting in degraded folds [Fig. 15(c)] or in degraded polyps [Fig. 15(f)]. Figures 15(b) and 15(e) show the results of SA cleansing. Both fold and polyp are successfully preserved, demonstrating the effect of SA cleansing in obviating the artifact of degradation of the soft-tissue structures.

As described in Sec. III, pseudo-soft-tissue structures caused by under cleansing or over cleansing of the AT boundary are a major source of artifacts in existing EC methods. In noncathartic CTC cases, the semisolid tagged stool made the detection of the AT boundary more difficult than that of fluid, as demonstrated by the pseudo-polyp or fold in Fig. 16(c) compared with Fig. 16(a), as well as the false fistulas shown in Fig. 16(f) compared with Fig. 16(d). Figures 16(b) and 16(e) demonstrate the effect of the local roughness function in SA cleansing. The semisolid tagged stool is well cleansed while the thin colonic fold is well preserved.

FIG. 15. Illustration of the reduction in the artifact of the degradation of the soft-tissue structures in SA cleansing. (a) A thin haustral fold (white arrow) is submerged in the tagged semisolid stool. (b) The thin fold is preserved in the SA-cleansing method. (c) The thin fold in (a) was erroneously removed after application of the T-cleansing method. (d) A small polyp (white arrow) is submerged in the tagged materials. (e) The submerged polyp is preserved in the SA-cleansing method. (f) The polyp in (d) was erroneously removed by the T-cleansing method.

Figure 17 shows two examples of the preservation (recovery) of soft-tissue structures, submerged folds, and thin folds within ATT layers, in SA cleansing. The semisolid tagged stool is cleansed, whereas the submerged folds and the folds within the ATT layers indicated by the black arrows are well preserved in the cleansed images.

VI. DISCUSSION

Some parameters in the SA-cleansing method were set empirically. It is possible that they could be optimized further. We did not explore this possibility in this study because

an optimal setting of the parameters requires the availability of a large number of fecal-tagging CTC cases to cover the entire range of bowel preparation and tagging methods. However, we chose the parameters to be general, rather than optimized for our specific preparation and tagging cases. A summary of the major parameters follows.

Scale parameter σ is the fundamental parameter for the multiscale Hessian filter. We examined the change in the value of the Hessian response field H_{Λ} in Eq. (9) at different values of σ in the range of 0.5–8 voxel units by using our phantom images in Fig. 18. When σ was small, such as 0.5,

FIG. 16. Illustration of the reduction of an artifact of pseudo soft-tissue structures and false fistulas in SA cleansing. (a) The boundary between the lumen air and tagging stool (AT boundaries) is indicated by the white and black arrows. (b) Application of SA cleansing to the image in (a) generates no pseudo-soft-tissue structures. (c) Application of T cleansing to the image in (a) generates pseudo-soft-tissue structures as indicated by the white and black arrows. (d) A thin colonic wall sandwiched between the tagged regions and the lumen air is indicated by the white arrow. (e) The colonic wall in (d) is preserved by use of the SA-cleansing method. (f) The colonic wall in (d) is erroneously removed by T cleansing as the boundaries between the lumen and tagged materials, creating a false fistula, as indicated by the white arrow.

FIG. 17. Examples of the preservation of soft-tissue structures in SA cleansing. (a) and (c): Original CTC images with semisolid tagged stool. (b) and (d): Images after SA cleansing of the CTC images in (a) and (c), respectively. Both images demonstrate the soft-tissue preservation of submerged folds and thin folds within ATT layers (arrows) in the SA-cleansing method.

the folds and polyps were enhanced; however, noise was also enhanced. Soft-tissue structures became smoother as σ increased. When σ was large, such as 8, both soft-tissue structures and noise were smoothed away and the resulting images became fuzzy. To balance the enhancement between colonic structures and noise, we set the scale parameter σ to 1 and 2 in our study. It should be noted that the voxel unit is related to the scanning protocol, which was 0.648 mm in our phantom study. Thus, for optimal results, the scale parameter σ might need to be adjusted when a different image acquisition protocol is used.

The parameter values in the structural enhancement functions, i.e., α in F_A , β and γ in F_B , and η in F_C , were chosen based on our discussion in Sec. II by use of the phantom data. We chose the parameter values based on visual comparison of the enhancement of the structures at several discrete values. Thus, these parameters were not optimized. Nevertheless, the degree of enhancement was not very sensitive to the change in the parameter values, as demonstrated in Figs. 3–5. In addition, considering the variance of the colonic structures, change in these parameter values is expected to have an insignificant impact on the enhancement results as well as on the cleansing results.

In addition, the structural enhancement functions in Sec. II were designed to enhance the submerged fold and polyp, i.e., rut-like (concave ridge) and cup-like (concave cap) structures. For a partially submerged fold or polyp [Figs. 19(a) and 19(d)], the above enhancement functions might enhance only the submerged part of the fold or the polyp. Thus, it might create a disconnection at the interface between the submerged and nonsubmerged parts in the cleansed images. The solution that we employed was to enhance both submerged and nonsubmerged structures, i.e., rut-like and

ridge-like structures (folds) and cup-like and cap-like structures (polyps), as shown in Figs. 19(b) and 19(e). At the transition point between a concave and a convex structure, the enhancement value had a slight disconnection. However, the smoothing term in the level set evolution equation successfully recovered the soft-tissue structures in the cleansed images, as demonstrated in Figs. 19(c) and 19(f).

The iso-value range of $[-200 \text{ HU}, 200 \text{ HU}]$ in the local roughness analysis was determined based on the range of CT values of the soft-tissue structures. To calculate the roughness response in our experiments, we generated the scale space by changing the standard deviation of the Gaussian filter, σ_i , from 0.5 to 6.0 in voxel units. We did not explore the optimal base term for the accumulation of roughness in Eq. (11); instead, we used a constant base term, $B_i = 1$, for all i . The value of the parameter $C_{\text{Curvature}}$ in the level set front evolution equation, Eq. (17), was determined empirically based on our visual assessment of the results of the SA cleansing. A change in the parameter value did not significantly affect the results of the SA-cleansing method because most submerged structures were well enhanced by the cup- and rut-enhancement functions, and the enhancement results were smoothed by Gaussian smoothing.

Although the AT boundary between the tagged fluid and the colonic lumen is flat, the local roughness response is high at the boundary. This is because the CT value on the flat AT boundary of the fluid changes rapidly due to the large gradient and the volume averaging. Thus, the iso-value voxels on a flat AT boundary are not well connected, as shown in Fig. 8(a): the left part of the AT boundary is shaded, whereas the right part was out of the range of the iso-value. Therefore, the flat AT boundary can be detected by use of roughness analysis in a manner similar to the AT boundary of the semi-solid stool.

A limitation of the SA-cleansing method is its high computational cost. It takes approximately 30 min for electronically cleansing the CTC images from a scan of a patient on a standard PC. Optimization and parallelization of the EC code remain as future work.

In this article, the artifacts of soft-tissue structure degradation and pseudo-soft-tissue structures have been addressed by Hessian analysis and local roughness analysis, respectively, because these two types of artifacts are commonly seen in a wide spectrum of tagging regimens and preparations, including cathartic and noncathartic preparations. The artifact of incomplete cleansing, which is caused by inhomogeneity in tagging, is seen less commonly with cathartic preparations, but is seen with reduced and noncathartic preparations. Li *et al.*¹⁶ suggested using a hidden Markov random field (MRF) to integrate the neighborhood information for overcoming the nonuniformity problems. The hidden MRF was designed to solve the nonuniformity caused by random noise. However, artifacts of incomplete cleansing are caused mainly by structural noise such as air bubbles, fats, and undigested foodstuffs, which are a different type of inhomogeneity from that of the nonuniform distribution of the contrast agent. The proposed method of Li *et al.* was not

FIG. 18. Comparison of scale parameter σ in Hessian response fields. (a) CTC phantom image. (b)–(g) Hessian response fields are calculated with different scales ranging from $\sigma=0.5$ to 8 in voxel units.

FIG. 19. Illustration of cleansing of a fold (a–c) and a polyp (d–f) partially submerged in tagged semisolid stool in SA cleansing. (a) Fold indicated by the arrow is partially submerged in the tagged stool. (b) Response image of the structural enhancement function for both the submerged and nonsubmerged parts of the fold. (c) Fold cleansed by SA cleansing. (d) The polyp indicated by the arrow is partially submerged in the tagged stool. (e) Response image of the structural enhancement function for both the submerged and nonsubmerged parts of the polyp. (f) Polyp cleansed by SA cleansing.

designed for removal of this type of artifact. Indeed, the structure analysis method tends to detect structural noise in the inhomogeneously tagged region such as small foodstuff or air bubbles that have rut-like and cup-like shapes. Removal of the structural noise in inhomogeneous tagging for cleansing of the inhomogeneously tagged regions remains a subject for future research.

VII. CONCLUSION

In this study, we have developed a novel EC method called structure analysis cleansing. Unlike existing EC methods, our method subtracts a tagging region by use of the local morphologic information on the submerged soft-tissue structures and the local roughness of the volumetric curvedness at the boundary of tagged regions. Evaluation of results based on phantom and clinical cases showed that the SA-cleansing method delineated polyps and folds submerged in the tagged material better than was possible with our previously reported cleansing method based on thresholding, and thus the SA-cleansing method was able effectively to remove the artifacts of soft-tissue structure degradation. Moreover, our EC method was shown successfully to preserve the thin haustral folds adhering to tagged regions while removing the artifacts of pseudo soft-tissue structures.

ACKNOWLEDGMENTS

This work was partly supported by the Cancer Research and Prevention Foundation, USPHS Grant No. CA095279, and American Cancer Society Research Scholar Grant No. RSG-05-088-01-CCE. The authors thank Dr. J. Richard Choi, Center for Virtual Colonoscopy, Walter Reed Army Medical Center, for providing us with the CTC cases that were used for a part of the evaluation in this study.

^{a)} Author to whom correspondence should be addressed. Electronic mail: cai.wenli@mgh.harvard.edu

¹ M. Morrin and L. LaMont, "Screening virtual colonoscopy—ready for prime time?," *N. Engl. J. Med.* **349**(23), 2261–2264 (2003).

² B. Levin, D. Brooks, R. A. Smith, and A. Stone, "Emerging technologies in screening for colorectal cancer: CT colonography, immunochemical fecal occult blood tests, and stool screening using molecular markers," *Ca-Cancer J. Clin.* **53**(1), 44–55 (2003).

³ ACS, "Cancer facts and figures," American Cancer Society (2004).

⁴ J. M. Elwood, G. Ali, M. M. Schlup, B. McNoe, G. O. Barbezat, F. North, K. Sutton, B. Parry, and V. S. Chadwick, "Flexible sigmoidoscopy or colonoscopy for colorectal screening: A randomized trial of performance and acceptability," *Cancer Detect. Prev.* **19**(4), 337–347 (1995).

⁵ S. L. Ristvedt, E. G. McFarland, L. B. Weinstock, and E. P. Thyssen, "Patient preferences for CT colonography, conventional colonoscopy, and bowel preparation," *Am. J. Gastroenterol.* **98**(3), 578–585 (2003).

⁶ J. Wardle, S. Sutton, S. Williamson, T. Taylor, K. McCaffery, J. Cuzick, A. Hart, and W. Atkin, "Psychosocial influences on older adults' interest in participating in bowel cancer screening," *Prev. Med.* **31**(4), 323–334 (2000).

⁷ E. R. Weitzman, J. Zapka, B. Estabrook, and K. V. Goins, "Risk and reluctance: Understanding impediments to colorectal cancer screening," *Prev. Med.* **32**(6), 502–513 (2001).

⁸ T. M. Gluecker, C. D. Johnson, W. S. Harmsen, K. P. Offord, A. M. Harris, L. A. Wilson, and D. A. Ahlquist, "Colorectal cancer screening with CT colonography, colonoscopy, and double-contrast barium enema examination: Prospective assessment of patient perceptions and preferences," *Radiology* **227**(2), 378–384 (2003).

⁹ Z. Liang, F. Yang, M. Wax, J. Li, J. You, A. Kaufman, L. Hong, H. Li, and A. Viswambharan, "Inclusion of a priori information in segmentation of colon lumen for 3D virtual colonoscopy," presented at the *IEEE Nuclear Science Society-Medical Imaging Conference*, Albuquerque, NM, 1997.

¹⁰ M. Wax, Z. Liang, R. Chiou, A. Kaufman, and A. Viswambharan, "Electronic colon cleansing for virtual colonoscopy," presented at the *1st Int. Symposium on Virtual Colonoscopy*, Boston, MA, 1998.

¹¹ Z. Liang, D. Chen, R. Chiou, B. Li, A. Kaufman, M. Wax, and A. Viswambharan, "On segmentation of colon lumen for virtual colonoscopy," presented at the *SPIE Medical Imaging Conference*, San Diego, 1999.

¹² M. E. Zalis and P. F. Hahn, "Digital subtraction bowel cleansing in CT colonography," *AJR, Am. J. Roentgenol.* **176**(3), 646–648 (2001).

¹³ M. E. Zalis, J. Perumpillichira, and P. F. Hahn, "Digital subtraction bowel cleansing for CT colonography using morphological and linear filtration methods," *IEEE Trans. Med. Imaging* **23**(11), 1335–1343 (2004).

¹⁴ M. R. Callstrom, C. D. Johnson, J. G. Fletcher, J. E. Reed, D. A. Ahlquist, W. S. Harmsen, K. Tait, L. A. Wilson, and K. E. Corcoran, "CT colonography without cathartic preparation: Feasibility study," *Radiology* **219**(3), 693–698 (2001).

¹⁵ D. Chen, Z. Liang, M. R. Wax, L. Li, B. Li, and A. E. Kaufman, "A novel approach to extract colon lumen from CT images for virtual colonoscopy," *IEEE Trans. Med. Imaging* **19**(12), 1220–1226 (2000).

¹⁶ L. Li, D. Chen, S. Lakare, K. Kreeger, I. Bitter, A. Kaufman, M. Wax, P. Djuric, and Z. Liang, "An image segmentation approach to extract colon lumen through colonic material tagging and hidden Markov random field model for virtual colonoscopy," presented at the *SPIE Medical Imaging Conference*, San Diego, 2002.

¹⁷ Z. Wang, Z. Liang, X. Li, L. Li, B. Li, D. Eremina, and H. Lu, "An Improved Electronic Colon Cleansing Method for Detection of Colonic Polyps by Virtual Colonoscopy," *IEEE Trans. Biomed. Eng.* **53**(8), 1635–1646 (2006).

¹⁸ I. Serlie, R. Truyen, J. Florie, F. Post, Lucas van Vliet, and F. Vos, "Computed cleansing for virtual colonoscopy using a three-material transition model," presented at the *MICCAI*, Montreal, Canada, 2003.

¹⁹ S. Lakare, D. Chen, L. Li, A. Kaufman, and Z. Liang, "Electronic colon cleansing using segmentation rays for virtual colonoscopy," presented at the *SPIE Medical Imaging Conference*, San Diego, 2002.

²⁰ P. J. Pidehardt and J. H. Choi, "Electronic cleansing and stool tagging in CT colonography: Advantages and pitfalls with primary three-dimensional evaluation," *AJR, Am. J. Roentgenol.* **181**(3), 799–805 (2003).

²¹ T. Lindeberg, *Scale-Space Theory in Computer Vision* (Kluwer, Dordrecht, The Netherlands, 1994).

²² A. F. Frangi, W. J. Niessen, R. M. Hoogeveen, T. van Walsum, and M. A. Viergever, "Model-based quantitation of 3-D magnetic resonance angiographic images," *IEEE Trans. Med. Imaging* **18**(10), 946–956 (1999).

²³ Y. Sato, S. Nakajima, N. Shiraga, H. Atsumi, S. Yoshida, T. Koller, G. Gerig, and R. Kikinis, "Three-dimensional multi-scale line filter for segmentation and visualization of curvilinear structures in medical images," *Med. Image Anal.* **2**(2), 143–168 (1998).

²⁴ H. Yoshida and J. Näppi, "Three-dimensional computer-aided diagnosis scheme for detection of colonic polyps," *IEEE Trans. Med. Imaging* **20**(12), 1261–1274 (2001).

²⁵ M. Prokop and M. Galanski, *Spiral and Multislice Computed Tomography of the Body* (Thieme, New York, 2003).

²⁶ J. J. Koenderink, *Solid Shape* (MIT Press, Cambridge, 1990).

²⁷ Gabriele Lohmann, *Volumetric Image Analysis* (Wiley, New York, 1998).

²⁸ S. Ho, E. Bullitt, and G. Gerig, "Level set evolution with region competition: automatic 3D segmentation of brain tumors," presented at the *International Conference on Pattern Recognition*, Quebec City, Canada, 2002.

²⁹ N. Otsu, "A threshold selection method from gray level histograms," *IEEE Trans. Syst. Man Cybern.* **9**, 62–66 (1979).

³⁰ W. Cai, N. Holalkere, G. Harris, D. Sahani, and H. Yoshida, "Dynamic-threshold level set method for volumetry of porcine kidney in CT images: In-vivo and ex-vivo assessment of the accuracy of volume measurement," *Acad. Radiol.* **14**(7), 890–896 (2007).

³¹ M. E. Zalis, J. J. Perumpillichira, J. Y. Kim, C. Del Frate, C. Magee, and P. F. Hahn, "Polyp size at CT colonography after electronic subtraction cleansing in an anthropomorphic colon phantom," *Radiology* **236**(1), 118–124 (2005).

- ³²P. Thévenaz and M. Unser, "A pyramid approach to subpixel registration based on intensity," *IEEE Trans. Image Process.* **7**(1), 27–41 (1998).
- ³³P. J. Pickhardt, J. R. Choi, I. Hwang, J. A. Butler, M. L. Puckett, H. A.

Hildebrandt, R. K. Wong, P. A. Nugent, P. A. Mysliwiec, and W. R. Schindler, "Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults," *N. Engl. J. Med.* **349**(23), 2191–2200 (2003).