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CAD of Colon Cancer on CT Colonography Cases without Cathartic Bowel Preparation

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Abstract

Computer-aided diagnosis (CAD) systems must show sufficient versatility to produce robust analysis on a large variety of data. In the case of colonography, CAD has not been designed to cope with the presence of stool, although labeling the stool with high contrast agents replaces the use of laxatives and reduces the patient discomfort. This procedure introduces additional challenges for the diagnosis, such as poorly tagged stool, stool sticking to colonic walls, and heterogeneous stool (tagged stool mixed with air or untagged stool). Our study proposes a robust algorithm for heterogeneous stool removal to be employed as a preprocessing module for CAD systems in colonic cancer detection. Colonoscopy data are automatically cleansed of residual stool to enhance the polyp appearance for improved diagnosis. The algorithm uses expectation-maximization, quadratic regression, level sets and minimum variance. Results show stool removal accuracy on polyps which are partially or fully covered by stool. The results are robust on stool lining and large pools of heterogeneous and weakly-tagged stool. The automatic detection of colon polyps using our CAD system on cathartic-free data improves considerably with the addition of the automatic stool removal module from 74% to 86% true positive (TP) rate at 6.4 false positives (FP)/case.

I. Introduction

In recent years, computed tomography colonography (CTC) has become a viable and noninvasive procedure for the detection of polyps [1,2]. Moreover, studies have shown that a large portion (72%) of the patients would prefer CTC to optical colonoscopy (OC) [3]. An additional factor of discomfort is the use of laxative for the preparation of the radiological exam; the diagnosis using cathartic-free bowel preparation is under investigation in clinical centers [4]. Very recent studies showed that non-cathartic-tagged CTC compares favorably with OC, with improved sensitivity when electronic stool subtraction is employed [5]. While computer-aided diagnosis (CAD) systems for colonography get increasing popularity and endorsement from the radiological community, they are not designed to cope with the presence of stool.

There has been little work on stool subtraction from cathartic-free colonic CTC data and it includes methods based on: eigenvalues of the Hessian matrix [6], polynomial fitting [7], and expectation maximization [8]. Although the reported results are adequate for the removal of fully tagged stool, a major challenge remains the ability to subtract stool that is not

homogeneously tagged, as seen in Fig. 1, without leaving residuals that increase the false positive (FP) polyp detections during diagnosis.

We propose an automatic method for heterogeneous stool removal that employs expectation maximization, polynomial regression, level-sets and minimum variance in a unique combination to achieve robust and accurate results. The algorithm is evaluated on cleansing colonic polyps partially or fully covered by tagged stool. The accuracy of this method is illustrated by the results of CAD of colon polyps

II. Methods

An outline of the methodology can be found in Fig 2.

A. Data and Materials

CTC data from cathartic-free bowel preparation were acquired at the Department of Radiology at the Mayo Clinic, Rochester MN: on Lightspeed Ultra scans for testing the stool removal algorithm, and Lightspeed Pro:16 scans for training the parameters, both from GE Healthcare.

Cases were selected from a polyp-enriched cohort and included cases in which at least 90% of the solid stool was visually estimated to be tagged and each colonic segment was distended in either the prone or supine view. Small untagged stool particles ≤ 5 mm and unlabeled colonic fluid were acceptable.

For the estimation of parameters during the development of the stool removal study, we used cases under various colonic preparations with barium and Gastroview and addressed as training data. For testing, data acquired at the same institution were used, and we ensured no overlap between training and testing.

The implementation used Visual C++ 8.0 (Microsoft) and the Insight Segmentation and Registration Toolkit (ITK) 2.4.

B. Classification via Expectation Maximization

The first step in our subtraction method utilizes expectation maximization (EM) [9,10] to divide the image into four separate classes: air, tissue, stool, and unclassified residuals. The goal is to adjust the variable intensities that might occur in different CT images. In order to initialize the EM, we separated the images into three classes that are easily distinguishable, with all remaining voxels set to the unclassified category. The hard thresholds for these classes are given in Table I. These values were determined through a conservative adaptation of the values presented in [7]. The classified voxels were assigned probabilities of 1 for their corresponding class, while no probability values were assigned to the unclassified voxels.

The EM's mean, variance and weight were initialized with the intensity from the solid partitions. The probability $P_{j,i}^{t+1}$ of voxel i being in class j at the $t+1$ time step is

$$P_{j,i}^{t+1} = \frac{W_j^t}{2\pi \sqrt{\sigma_j^t \cdot \rho_{j,i}^t}} \cdot e^{-\frac{(I_i - \mu_j^t)^2}{2\sigma_j^t} - \frac{(P_{j,i}^t - \lambda_{j,i}^t)^2}{2\rho_{j,i}^t}}$$

where I_i is the intensity for voxel i , μ_j^t, σ_j^t and W_j^t are the mean, variance and weight for class j at time step t , $P_{j,i}^t$ is the probability of class j for voxel i at time t , and lastly $\rho_{j,i}^t$ and $\lambda_{j,i}^t$ are

the mean and variance of the probability for class j on the first order neighbors around voxel i . We utilized the neighborhood values to reduce the effect of noise and discontinuities.

The EM was run for 5 iterations and upon its completion, the unclassified voxels with $P_{tissue} \geq 0.8$, $GM \leq 300 * P_{tissue}$, and $I \leq 600$ were classified as tissue. Tissue voxels with $P_{tissue} \leq 0.1$ are assigned to the unclassified category. These cutoffs were determined utilizing a set of training data. During this first step of the algorithm, we only reclassified tissue voxels, because air and stool are easily distinguishable, while the boundaries and heterogeneous stool were addressed at a later step. Fig. 3 presents the normalized histogram of the intensity distributions of the four classes: air, tissue, stool and unclassified residuals.

C. Boundary Correction via Quadratic Regression

During this second step, we followed the method by Carston et al [7], with additional changes, as described below. The proposed detection of boundaries, or unclassified regions, is based on a quadratic regression of gradient magnitude versus intensity. This was done by comparing the distance deviation from a set of empirical curves found to describe uniquely each of the three transition boundaries (air-tissue, tissue-stool and air-stool). The initial classifications were obtained from our EM algorithm and the output of this step gives the probabilities for the method presented in [7]. We did not utilize any morphological operators, as in [7] the authors did not demonstrate substantial benefit from them.

In addition, instead of comparing the raw distance from the regressed curves, we biased the curve toward tissue-stool and air-tissue rather than stool-air by a factor of 1.5, as to retain more tissue. This step is justified by the existing overlaps between tissue-stool and stool-air, as well as air-tissue and stool-air. Lastly, we stipulated that a thin stool voxel that was originally classified as a tissue-stool boundary may not be marked as full stool because that seemed to erode folds that were surrounded by stool.

D. Removal of Heterogeneous Stool via Minimum Variance and Level Sets

The last step in our digital stool subtraction algorithm is a novel method to detect and subtract heterogeneous stool, which can be separated into three stages: detect regions connected to full tissue, detect boundaries by using level sets, and eliminate regions classified as thick tissue, but not connected to full tissue. The image shown in Fig. 1 exemplifies the rationale behind this method. Note in this typical example that regions of heterogeneous stool have a large body, but relatively few connections to the colon walls, as they are separated by thick well-tagged stool.

In order to determine the connectedness of a tissue voxel to the colon body, we used a chamfer distance map from known tissue ($I * P_{tissue} \geq 300$). The voxels with chamfer values greater than 20 are classified as full tissue. In addition, we computed the minimum 2D variance for each voxel across the 9 distinctive planes that can be used to cut a $5 \times 5 \times 5$ neighboring volume, without doing interpolation. Voxels connected to full tissue with a minimum variance less than 500 are set to full tissue. The empirical value of 500 allowed the good segmentation of heterogeneous stool on the training data.

Next, we employed a curved level set [11], with the input being the binary image resulting from thresholding at $I = -700$, and an edge potential map that was constructed using

$1 - \frac{\lambda_1^i / \lambda_2^i}{\max_i (\lambda_1^i / \lambda_2^i)}$, where λ_1^i and λ_2^i are the first and second largest eigenvalues of the Hessian matrix at voxel i . The level set algorithm was run for 50 iterations with propagation, curvature, and advection scaling being 0.4, 0.1, and 0.4 respectively. Utilizing the level set output we

assigned any voxel that is attached to a full tissue voxel to also be a tissue-boundary voxel, if it met one of the criteria in the first two rows of Table II.

The criteria in the first two rows of Table II stipulate that full tissue voxels can propagate into boundaries, but boundaries cannot become full tissue. This condition connects areas on the colon folds that were previously erroneously labeled as stool, while isolating regions containing heterogeneous stool, which have similar characteristics to full tissue.

The last step eliminates the heterogeneous stool voxels connected to the boundary regions. We assumed that any voxel having a chamfer distance greater than 8 and was not marked as tissue must be heterogeneous stool. In addition, any voxel connected to heterogeneous stool was also a heterogeneous stool voxel if it met the criteria in the last two rows of Table II, which works similarly to propagating tissue, except that it is tuned to propagate heterogeneous stool. The values shown in Tables II are empirical and were determined by using only the laxative-free cases in the training data.

III. Results

A. Automatic Stool Removal

The stool subtraction algorithm was tested on 43 CTC scans from prone and/or supine scans of 22 patients containing 42 polyps larger than 10mm (21 unique polyps, if matched between prone and supine scans). Eleven polyps (6 matched polyps) were partially or fully covered by stool and 9 (5 matched polyps) of them were correctly cleansed, as exemplified in Fig. 4. The algorithm was able to remove heterogeneous stool (the polyps in Fig. 4.a and 4.b), stool linings (the polyp in Fig 4.b), and weakly tagged stool (the polyp in Fig. 4.c), while preserving the polyps and the colonic tissue. Two polyps (1 matched polyp) were not satisfactorily cleansed, as shown in Fig. 5; note the large air bubble in the middle of the heterogeneous stool, which contradicts the assumption in the algorithm that heterogeneous stool forms pools with centers that have characteristic similar to those of tissue, rather than of air.

B. CAD on Cathartic-free Data

A database of cases without cathartic bowel preparation was employed to analyze the performance of the CAD system for colonic cancer detection. The system was run on the testing database presented in Section III.A with and without the new module of stool subtraction. The comparative free-response receiver operating characteristic (FROC) curves are presented in Fig. 6.

As expected, the automatic detection of colon polyps using our CAD system is hampered by the presence of stool in the scans, as heterogeneous stool represents a prevailing source of FP. However, as illustrated in Fig. 6, the sensitivity of the CAD system is of 81% detected polyps at a rate of 9.7 FP/case without using the stool subtraction module. The evolution of the FROC curve improves considerably after stool subtraction on cathartic-free data from 74% to 86% true positive (TP) rate at 6.4 FP/case. The p-value of the Fisher exact test at this point on the FROC curve is 0.08.

IV. Discussion

We presented a method to remove tagged stool from cathartic-free bowel preparation CT data to assist with the diagnosis of colonic cancer. Unlike previously published algorithms [6,7,8], the method was designed to remove well tagged, heterogeneous, as well as weakly tagged stool. The results are robust on fine grain details around folds, stool lining on polyps and large pools of stool. The method allows for variability in the input data set, as well as decreases the effect

of noise with the introduction of expectation maximization, implementation of robust edge detection, and a novel level set-based heterogeneous stool subtraction algorithm.

The stool subtraction algorithm failed to cleanse a polyp (both in the supine and prone scans) due to the assumption that large air pockets do not exist in stool fragments, which occurs, in our experience, in a small number of cases and can lead to erroneous cleansing and an increase of the number of false positives. Future work will include increasing the robustness of our algorithm to accommodate complex cases of heterogeneously-tagged stool.

The CAD system [2] can detect colonic cancer with fine accuracy on data with cathartic-free bowel preparation, without employing the new algorithm for heterogeneous stool removal. Moreover, the performance of the CAD system showed a significant improvement on stool-tagged data when the stool removal module was used, with sensitivity and specificity appropriate for routine clinical use.

The runtime for our digital stool subtraction on a typical patient varies from one to two hours, depending on the size of the data and complexity of the cases for convergence. However, from tests on colon CAD using the stool subtraction algorithm, we noted that the large number of false positives generated without stool subtraction can cause the support vector machine (SVM) to have a running time of two hours, and on average, the amounts of time required to run a case with or without stool subtraction are similar.

A prerequisite of the method is to not affect the performance of CAD systems on a mixed database of cases using laxative and cathartic-free preparation and provided by various institutions [2]. More results of embedding the stool removal method into a CAD system will be reported in the near future.

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Fig. 1.
A typical example of cathartic-free tagged CT of the colon.

Fig. 2.
Diagram of the stool subtraction algorithm flow.

Fig. 3.

A typical distribution of the classes after expectation maximization. The distributions are normalized by their maximum value.

Fig. 4.

Three polyps under tagged stool in uncleansed images (top row) and the results of our stool removal algorithm (bottom row). The arrows point at the stool areas and ellipses indicate the polyps.

Fig. 5.
An example of erroneous stool removal. The arrow points to the air bubble in the middle of the heterogeneous tagged stool and the ellipsis indicates the polyp.

Fig. 6.

FROC curves of the performance of the CAD system on cathartic-free CTC data; we present comparative performances with and without the use of the stool subtraction module.

TABLE I

Initialization of EM

Classes	Threshold Values
Stool	$I \geq 800$ and $GM \leq 0.8 \cdot I$ or $I \geq 1000$
Tissue	$I \geq -250$ and $I \leq 150$ and $GM \leq 300$
Air	$I \leq -800$ and $GM \leq 250$

The initial thresholds for initializing EM, with I being intensity and GM being gradient magnitude.

TABLE II

Tissue boundary propagation criteria

Case Type	Criteria
Continued Propagation of Full Tissue	<ul style="list-style-type: none"> • $-2 < CVLS < -1$ • $PVLS < -1$
Boundary of Tissue	<ul style="list-style-type: none"> • $CVLS - PVLS > -0.5$ • $CVLS < 1$ • $PVLS > -1$
Full Heterogeneous Stool	<ul style="list-style-type: none"> • $CVLS < 0.1$
Boundary of Heterogeneous Stool	<ul style="list-style-type: none"> • $CVLS - PVLS > -0.1$ • $CVLS > 0$ • $PVLS > -0.5$

CVLS represents the level set value of the current voxel, while PVLS represents the level set value of the voxel to propagate to.