Semi-automatic Algorithm for Lumen Segmentation in Histological Images

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Abstract

In this paper we focus on a problem of lumen segmentation in histological images. A large number of annotated images are necessary for the development of diagnostic algorithms that can help to detect changes, such as lumen serration, indicating really serious health problems like cancer. We propose a semi-automatic interactive segmentation algorithm to accelerate the process of manual image annotation. The core of our annotation approach is a classical graph-cut algorithm that uses manually selected parameters. The user annotates an image with two types of scribbles corresponding to the gland lumen structure and the non-lumen area. After that, the model annotates all unlabeled pixels, providing the user with a fully annotated image based on the scribbled input data. The user can interact with the annotation algorithm and add new scribbles to adjust the result. The algorithm allows to reduce the annotation time of a typical histological image by 10 times for the PATH-DT-MSU dataset that can potentially seriously increase the number of fully annotated histological images.

Keywords

Graph-cut based segmentation, semi-automatic segmentation, lumen segmentation, medical images, histology.

1. Introduction

The use of digital images is becoming more and more popular in various areas of our lives, including medicine. Moreover, digital images are the basis of digital pathology - one of the most promising areas in diagnostic medicine. Digital pathology involves the collection, management, exchange and interpretation of pathological information, including slides and digital data.

The images obtained using a microscope slide scanner are used by histologists to carry out morphological diagnostics - analysis of cellular structures and identification of structural disorders, for example, a change in the shape of the lumen.

One of the important problems in the field of morphological diagnostics is the segmentation of glandular lumen in histological images and the lumen shape analysis. Automatic algorithms for segmentation of glandular lumen structures help histologists to detect disorders in the human body faster, as well as to confirm the assumptions of doctors about the clinical condition of the patient.

Neural network models are best suited for automatic segmentation, but they require a large amount of labelled data. Thus, semi-automatic methods of annotation, i.e. methods that use weak annotation from the user, are also relevant, but less time-consuming compared to the manual pixel-level annotation methods. Semi-automatic segmentation algorithms greatly simplify the task of data markup, so this work is devoted to the development of such an algorithm.

There is a number of semi-automatic segmentation algorithms. We carried out a comparative testing of several of these algorithms for the task of glandular lumen segmentation in histological images.

The first algorithm we tested was the Magic wand. The user should specify the pixel of the object and set a threshold value. The algorithm assigns to the object an area that includes the pixel marked by the user and pixels whose intensities differ from the intensity of the specified pixel by no more than the threshold. Below (Fig. 1(b)) is an example of usage Magic wand from Adobe Photoshop with a single threshold: some areas became undersegmented, some became oversegmented. This means that for the effective usage of this tool for lumen segmentation, the threshold value must be chosen independently for each lumen, which is very inconvenient in practice.

The second existing algorithm for segmentation that we tested was Intelligent scissors [1, 2]. A significant disadvantage of this tool is excessive user interaction with the program. For example, the segmentation result shown in Fig. 1(c) is satisfying, but in this case the user has to spend a significant amount of time on markup - about 10-15 minutes. This is due to the fact that the user needs to perform the mark-up very carefully: the mouse cursor has to be close enough to the contour of the gland lumen.
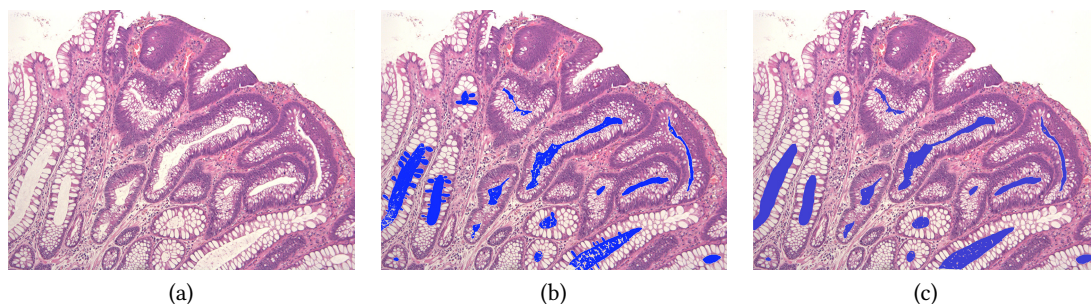

(a)	(b)	(c)

Figure 1: Results of various algorithms for the glandular lumen segmentation task. (a) the source histological image, (b) the segmentation result of the Magic wand algorithm, (c) the segmentation result of the Intelligent scissors algorithm. The blue color on the results indicates the gland lumen.

The above examples demonstrate that existing solutions are not suitable for solving the problem of semi-automatic glandular lumen segmentation in histological images. Therefore a new tool for this task is in demand. At the same time, the main feature of the developed tool should be interactivity, i.e. the ability of the program to instantly display the result during interaction with the user. In this case, it will be possible to conveniently mark-up a large number of images and, next, develop more precise deep learning methods for the glandular lumen segmentation.

2. Proposed method

In this work we propose an interactive method for glandular lumen segmentation based on a graph-cut algorithm [3] since this algorithm uses both regional image information and boundary information. In other words, the graph-cut algorithm combines the approaches used in the Magic wand and Intelligent scissors segmentation algorithms, which significantly improves the algorithm and makes it perfect for semi-supervised learning in histology.

2.1. Graph-cut algorithm for image segmentation

Let us consider the concept of the graph-cut algorithm and how it can be used for image segmentation.

Let $G = <V, E>$ be an undirected graph, where V are vertices and E are edges of the graph. Vertices can be of two types:

1. vertices corresponding to pixels;
2. two terminal vertices: s denotes the object, t denotes the background.

Edges can also be of two types:

1. connecting neighboring vertices-pixels in the image;
2. connecting terminal vertices to vertices-pixels.

Each edge is assigned a non-negative weight w. Initialization of these weights will be discussed further. The cut is a subset of the edges of E. Let us denote it by C, then $C \subset E$. The cost of the cut $|C|$ is the sum of the weights on the edges C:

$$|C| = \sum_{e \in C} w_e, \tag{1}$$

where $e \in C$ is the edge belonging to the detected cut, w_e is the weight of the edge e.

The algorithm consists in finding the minimum cut, i.e., the cut with the minimum cost. Finding the minimum cut is equivalent to finding the maximum flow, which is proved in [4, 5]. Therefore, the maximum flow algorithm [6] can be used to obtain the minimum cut of the graph. The algorithm result is two disjoint subsets S and T, where $s \in S$, $t \in T$ and $S \cup T = V$. In terms of segmenting an image, these two subsets represent the object and background pixels, respectively.

Image segmentation can be considered as a pixel labeling task: let the object label be 1 and the background be 0. For reasonable segmentation, the minimum cut should occur at the boundary between the object and the background. Next, obj will denote the object, and bkg - the background.

Let $L = \{l_1, l_2, \ldots, l_p\}$ be the set of labels, where p is the number of pixels in the image and $l_i \in \{0, 1\}$, $i = \overline{1, p}$.

Finding the minimum cut is equivalent to minimizing the energy function defined as follows:

$$E(L) = \alpha R(L) + B(L) \longrightarrow \min, \tag{2}$$

where $R(L)$ is the regional term, $B(L)$ is the boundary term, and α is the importance of the regional term.

The regional term controls how similar the pixels of the object are to the intensity of the object, and is determined as follows:

$$R(L) = \sum_{p \in P} R_p(l_p),\tag{3}$$

where $R_p(l_p)$ is the penalty for assigning a label l to a pixel p.

This penalty can be obtained by comparing the pixel intensity p with the histograms of the object and background:

$$R_p(1) = -\ln \Pr(I_p \,|\, 'obj'),\tag{4}$$

$$R_p(0) = -\ln \Pr(I_p \,|\, 'bkg'),\tag{5}$$

where $\Pr(I_p \,|\, 'obj')$ and $\Pr(I_p \,|\, 'bkg')$ are the probabilities of belonging a pixel p with intensity I_p to the object and background, respectively.

We can see from the equations (4) and (5) that if the probability $\Pr(I_p \,|\, 'obj')$ is larger than $\Pr(I_p \,|\, 'bkg')$, then the penalty $R_p(1)$ is less than $R_p(0)$, i.e., if a pixel intensity is more similar to an object, then the penalty for assigning this pixel to an object is small, which implies a decrease in the energy function (2) with correct segmentation.

The boundary term $B(L)$ in the function (2) controls how contrast the detected boundary between the object and the background is, and is defined as follows:

$$B(L) = \sum_{\{p,q\} \in N} B_{<p,q>} \cdot \delta(l_p, l_q),\tag{6}$$

where p, q are neighboring pixels and

$$\delta(l_p, l_q) = \begin{cases} 1, & \text{if } l_p = l_q, \\ 0, & \text{if } l_p \neq l_q, \end{cases}\tag{7}$$

$$B_{<p,q>} = \exp\left(-\frac{|I_p - I_q|}{2\sigma^2}\right),\tag{8}$$

where σ can be viewed as camera noise.

This means that if neighboring pixels have the same labels, then the penalty will be 0. If they are different, then the pixels belong to the segmented boundary and the penalty (8) is defined to be a non-increasing function of $|I_p - I_q|$.

Thus, when the intensities of two neighboring pixels with different labels on the predicted boundary are similar, the penalty is large. The reduction of the penalty is achieved by finding the boundary with the largest possible difference in pixel intensities on it. Therefore, the energy function (2) is minimal at the real boundary of the object.

So, when the intensity of a pixel is more like an object, the weight between this pixel and the terminal vertex s responsible for the object is larger than between this pixel and the terminal vertex t, which means that the minimum cut is likely to pass along the edge with less weight and the segmentation will be correct. For neighboring pixels with a similar intensity, the weight is large, which means that the cut is unlikely to pass between these pixels. Thus, the minimum cut of the graph is close to the boundary of the object.

Fig. 2 shows an example of a graph cut for image segmentation 3×3, the thickness of the edges denotes the value of weight.
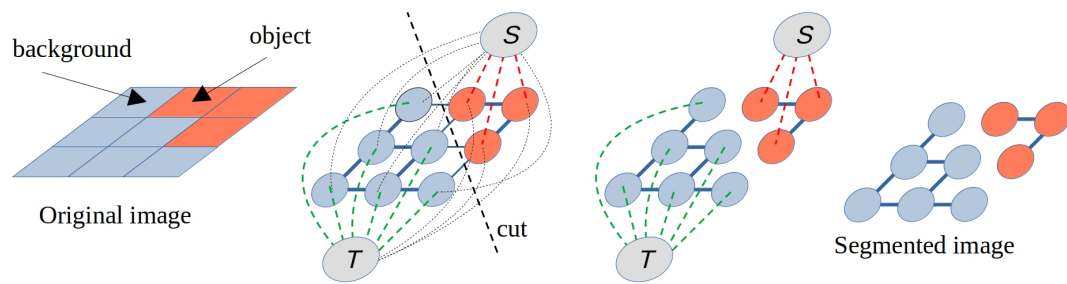
Figure 2: An illustration of the graph-cut algorithm. The cut corresponds to the minimum energy (2).

2.2. Used dataset and user interaction details

The testing and evaluation of the proposed interactive segmentation method was performed on a S1 subset of a histological medical imaging dataset PATH-DT-MSU [7, 8]. S1 subset of PATH-DT-MSU dataset (http://imaging.cs.msu.ru/en/research/histology/path-dt-msu) consists of 60 images obtained from hematoxylin and eosin staining of paraffin sections of colon biopsy material. It contains images of hyperplastic polyps (HP), sessile serrated adenomas (SSA/P) and normal colon mucous glands.

The user annotates an image with two types of scribbles: red and blue, corresponding to the gland lumen structure and the non-lumen area, respectively. After that, the model annotates all unlabeled pixels according to the above described algorithm, providing the user with a fully annotated image based on the scribbled input data. The user can interact with the annotation algorithm and add new scribbles to adjust the result until he is satisfied with it.

2.3. Applying the graph-cut algorithm for lumen segmentation

The above algorithm was implemented, and initially the algorithm parameters were set as follows: $\sigma = 3$ as the average of the most commonly used camera noise values and $\alpha = 1$, which means the same influence of both regional and boundary terms.

The implemented algorithm was tested on the open dataset PATH-DT-MSU S1 [7, 8]. Examples of the algorithm application results with these parameters are shown in Fig. 3(b). It can be seen that the algorithm did not work as required in the task: the image was oversegmented. Thus, we decided to modify the algorithm.

2.4. Improvements of the base algorithm

2.4.1. Parameters revision

First of all, we decided to revise the parameters of the graph-cut algorithm. The parameter σ has not been changed, only the parameter α was reconsidered. To make the segmentation algorithm more suitable for histological images, more attention should be paid to the lumen
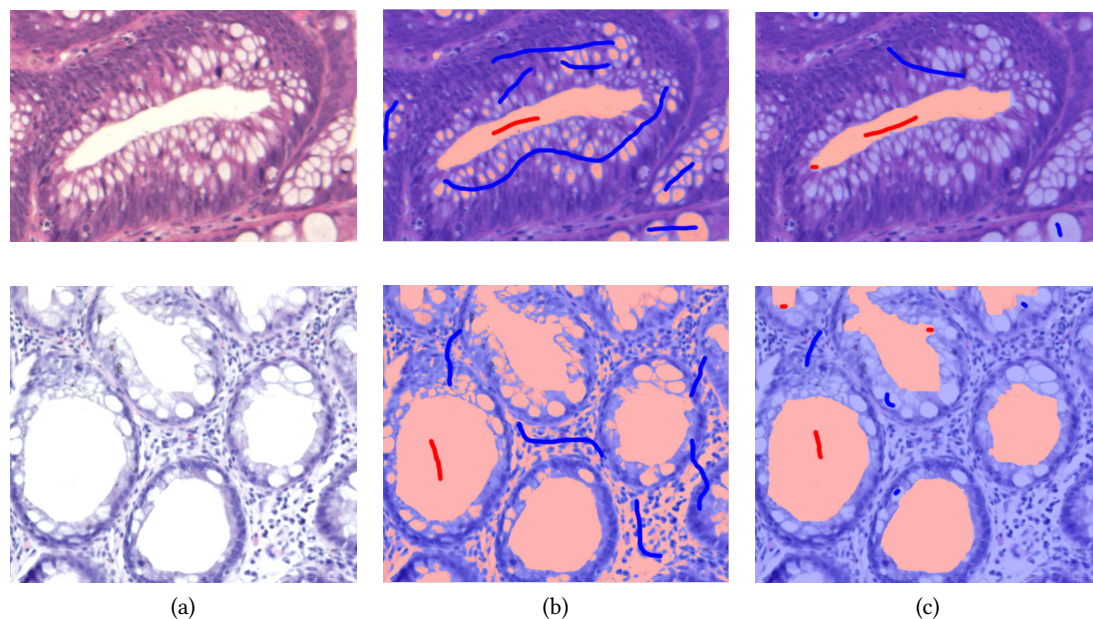
| (a) | (b) | (c) |

Figure 3: Results of applying the graph-cut algorithm for lumen segmentation in histological images. (a) source image, (b) the user's mark-up and segmentation result with $\alpha = 1$, $\sigma = 3$, (c) the user's mark-up and segmentation result with $\alpha = 0.05$, $\sigma = 3$. The scribbles are bolded for better visualization.

boundary than to the intensity of the lumen pixels. Otherwise, the image will be oversegmented as was shown in Fig. 3(b).

In order to achieve required segmentation accuracy and performance of lumen gland segmentation in histological images we selected $\alpha = 0.05$. Examples of segmentation with this parameter are shown in Fig. 3(c).

2.4.2. Rethinking the distance function

In our initial implementation, the image was converted from RGB format to grayscale, as is usually done when applying graph-cut algorithm. The used formula was

$$L = R \cdot 0.299 + G \cdot 0.587 + B \cdot 0.114, \tag{9}$$

where L is the intensity in grayscale and R, G, B are the intensities of the red, green and blue components, respectively.

Function (8) can be rewritten as:

$$B_{<p,q>} = \exp\left(-\frac{\rho}{2\sigma^2}\right). \tag{10}$$

Then in the initial implementation ρ was defined as:

$$\rho = |I_p - I_q|, \tag{11}$$

where I_i is the intensity of pixel i in the range from 0 to 255 in grayscale.

To compare the efficiency of the algorithm, the distance function was also calculated as the Euclidean distance:

$$\rho = \sqrt{(I_p^r - I_q^r)^2 + (I_p^g - I_q^g)^2 + (I_p^b - I_q^b)^2}, \qquad (12)$$

where I_i^r, I_i^g, I_i^b are the intensities of the red, green and blue components of the pixel i, respectively.

The results of this transition to a new distance function are shown in Fig. 4.
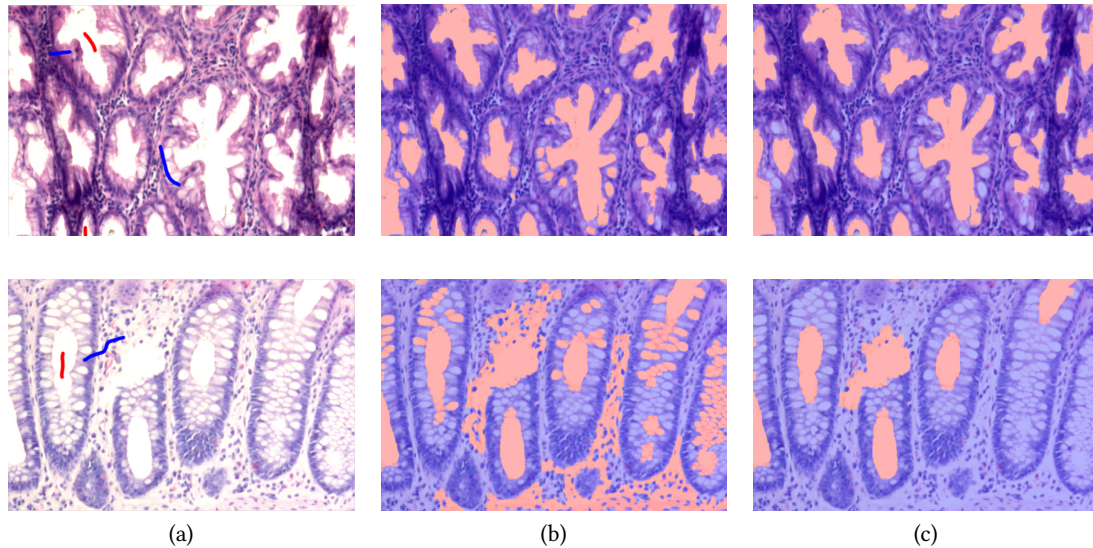

| (a) | (b) | (c) |

Figure 4: Examples of the algorithm application results at $\alpha = 0.05$, $\sigma = 3$ and various distance functions. (a) source image, (b) segmentation result with distance function (11), (c) segmentation result with distance function (12). The scribbles are bolded for better visualization.

Based on the above results, it can be noted that with the same user mark-up, the algorithm with the distance (12) calculated in RGB format gave a more accurate segmentation and did not oversegmented the image compared to the algorithm with the distance (11).

Thus, it can be concluded that the adjustment of parameters and rethinking of the distance function (8) allows to increase the accuracy of the method, thereby reducing the user's contribution to the markup.

3. Results

In this work we developed and implemented a method of semi-automatic interactive segmentation of the gland lumens in histological images.

The results of the algorithm application are presented in Fig. 5.

This algorithm is developed for mark-up, and the quality of mark-up is measured by the user and depends on a particular histologist, so it is difficult to compare the proposed algorithm with another algorithm by any metric of segmentation quality. A reasonable option is to compare
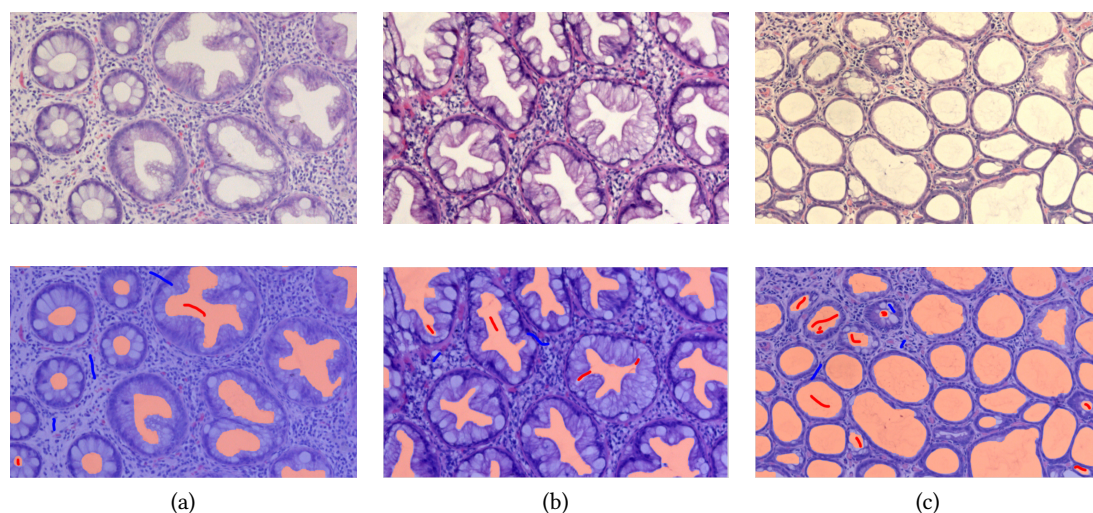
(a)	(b)	(c)

Figure 5: The results of the algorithm at $\alpha = 0.05$, $\sigma = 3$ and the distance function (12). The red color on the received masks indicates the gland lumens, blue indicates the background. Here the first row shows source images, the second row shows the user's mark-up and segmentation result. The scribbles are bolded for better visualization.

the time spent when the same user marks up. Here, our algorithm on the S1 subset of PATH-DT-MSU reduces the annotation time of a typical histological image by ~10 times compared to the manual segmentation in combination with intelligent scissors algorithm.

For images with a resolution of 1150 pixels by 700 pixels, the average time spent on the lumen segmentation performed upon user's mark-up is 700-800 milliseconds. Due to the low response time of the developed algorithm, it can be used for real-time segmentation of glands' lumen in histological images.

4. Implementation details

The proposed interactive segmentation algorithm is implemented using Python 3.5. As the part of this algorithm we used pymaxflow (https://github.com/Rhoana/pymaxflow) [6] implemented in C++ and later wrapped in Python using vectorized functions, to achieve real-time operation of the algorithm.

The graphical user interface for the proposed interactive segmentation algorithm is implemented with Tkinter framework.

The core part of the proposed algorithm and the graphical interface are implemented as separate modules that allows to integrate the proposed algorithm of lumen gland segmentation into specific histological software in the future.

5. Conclusion

In this paper we proposed a method for interactive image segmentation with scribble input and demonstrated its applicability for the problem of lumen segmentation considering the annotation of PATH-DT-MSU histological dataset. The proposed method allows to reduce the annotation time of a typical histological image by 10 times for PATH-DT-MSU dataset, which potentially will help a lot in extending and developing similar datasets and, as a consequence, can help in implementing real diagnostic algorithms.

Acknowledgments

References

[1] E. N. Mortensen, W. A. Barrett, Interactive segmentation with intelligent scissors, Graphical models and image processing 60 (1998) 349–384.

[2] E. N. Mortensen, W. A. Barrett, Intelligent scissors for image composition, in: Proceedings of the 22nd annual conference on Computer graphics and interactive techniques, 1995, pp. 191–198.

[3] F. Yi, I. Moon, Image segmentation: A survey of graph-cut methods, in: 2012 international conference on systems and informatics (ICSAI2012), IEEE, 2012, pp. 1936–1941.

[4] Y. Boykov, G. Funka-Lea, Graph cuts and efficient nd image segmentation, International journal of computer vision 70 (2006) 109–131.

[5] Y. Y. Boykov, M.-P. Jolly, Interactive graph cuts for optimal boundary & region segmentation of objects in nd images, in: Proceedings eighth IEEE international conference on computer vision. ICCV 2001, volume 1, IEEE, 2001, pp. 105–112.

[6] Y. Boykov, V. Kolmogorov, An experimental comparison of min-cut/max-flow algorithms for energy minimization in vision, IEEE transactions on pattern analysis and machine intelligence 26 (2004) 1124–1137.

[7] A. Khvostikov, A. Krylov, I. Mikhailov, O. Kharlova, N. Oleynikova, P. Malkov, Automatic mucous glands segmentation in histological images., International Archives of the Photogrammetry, Remote Sensing & Spatial Information Sciences (2019).

[8] N. Oleynikova, A. Khvostikov, A. Krylov, I. Mikhailov, O. Kharlova, N. Danilova, P. Malkov, N. Ageykina, E. Fedorov, Automatic glands segmentation in histological images obtained by endoscopic biopsy from various parts of the colon, Endoscopy 51 (2019) OP9.