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Image processing methods for the structural detection and gradation of placental villi

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ABSTRACT

The context-based examination of stained tissue specimens is one of the most important procedures in histopathological practice. The development of image processing methods allows for the automation of this process. We propose a method of automatic segmentation of placental structures and assessment of edema present in placental structures from a spontaneous miscarriage. The presented method is based on texture analysis, mathematical morphology, and region growing operations that are applicable to the heterogeneous microscopic images representing histological slides of the placenta. The results presented in this study were obtained using a set of 50 images of single villi originating from 13 histological slides and was compared with the manual evaluation of the pathologist.

In the presented experiments, various structures, such as villi, villous mesenchyme, trophoblast, collagen, and vessels have been recognized. Moreover, the gradation of villous edema for three classes (no villous edema, moderate villous edema, and massive villous edema) has been conducted. Villi images were correctly identified in 98.21%, villous mesenchyme was correctly identified in 83.95%, and the villi evaluation was correct in 74% for the edema degree and 86% for the number of vessels. The presented segmentation method may serve as a support for current manual diagnosis methods and reduce the bias related to individual, subjective assessment of experts.

1. Introduction

Spontaneous miscarriage is the pregnancy that ends on its own within the first 20 weeks of gestation. The average risk of miscarrying is between 10% and 25% [1–4], and about 80% of miscarriages happen in the first trimester. The causes of spontaneous miscarriage are poorly understood. A woman who has had a previous miscarriage has a 25% chance of having another. A woman with two previous miscarriages has a 28% risk of another miscarriage, and for three previous miscarriages, the risk increases to 43% [1–4]. Therefore, correct diagnosis as well as effective treatment are important.

The analysis of the placental structures in spontaneous miscarriages (in the first trimesters of pregnancy) is complex [5–7], and it involves qualitative histological assessment of placental tissue under the microscope. The placenta is formed and it keeps changing during pregnancy. Abnormalities in placental structure and function may be critical for the fetus, and can lead to spontaneous miscarriage [8]. Microscopic analysis of the placenta can provide valuable information related to the causes of the spontaneous miscarriage [9]. Placental pathologies are associated with infarction (25% of cases), chorioamnionitis (12.5% of cases), molar changes (9% of cases), hypervascularization and avascularization according to [10]. The latest methods for qualitative and quantitative assessments of placenta from miscarriages include: determining the presence of villi, counting of vessels inside of villi, and evaluation of villi edema. According to [9,10]:

- If villi are not established, the fetus cannot develop properly;
- The insufficient number of blood vessels (avascularization) can be an effect of inadequate angiogenesis of the fetus;
- Too many blood vessels (hypervascularization) can result from the disorders in the osmotic transfer between the fetus and the mother;
- The edema (storage of excessive fluid inside the villi) is a response to the hydropic problem;
- The occurrence of hemorrhages on the images of placenta suggests coagulation-related disorders.

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The histological evaluation of the placental specimen provides information that helps to identify the causes of spontaneous miscarriages and it may subsequently help to avoid the next miscarriage.

The complexity of placental tissue is difficult to assess manually. In the literature, several studies propose methods for the automatic recognition of villi structures in the placenta [11–17]. The aim of the research performed in Refs. [12–14] was the radiological evaluation of placenta during pregnancy. Alansary et al. [13] have presented methods to delineate the human placenta in MRI scans. Stevenson et al. [14] have described a method for placenta segmentation in 3D ultrasound images, while Ayache et al. [12] have proposed a method for automatic recognition of placental tissues and staging of its development. Placental development was assigned to four classes, based on features extracted by discrete wavelet transform (DWT) and further classified by a multilayer perceptron (MLP). Under the microscope, the villi are evaluated based on the number of blood vessels and the degree of edema. Almoussa et al. [11] have presented a method of automatic detection and extraction of blood vessels from a histological image of placenta by using image processing techniques and neural networks. In our previous work [15–17], we have presented algorithms that can recognize individual structures (villi, trophoblast, and vessels) on the histopathological images of placenta. In this work, we have presented an automatic system for the villi detection and evaluation (based on edema degree and vessels number). To the best of our knowledge, no existing solutions can automatically support the pathological diagnosis of spontaneous miscarriages.

The aim of present work is to evaluate villi after spontaneous miscarriage by using microscopic image analysis and to supplement the manual slide reading with a quantitative readout. To the best of our knowledge, no work presenting the automatic system of recognition and evaluation of placental structures has been reported until now. The novelty of the presented work is the automatic detection and analysis of placental villi on the images, as well as the automatic evaluation of edema degree.

The proposed algorithm is based on texture techniques [19,20], color normalization [18,21], mathematical morphology [22], and region growing [23]. Our method that can segment out villi, villi edema, villous mesenchyme, trophoblast, collagen, and villi vessels were quantitatively evaluated using manual delineation of these tissue components by a pathologist. The results have been compared with the medical expert annotations.

In Section 2 we describe the materials used in this study, in section 3 we present the proposed methods and algorithms. The summarized results and conclusions are shown in sections 4 and 5, respectively.

2. Materials

Thirteen histological slides of the placenta stained with hematoxylin and eosin (H&E) were retrieved from the archives of the Department of Pathology, Military Institute of Medicine, Warsaw, Poland. The slides were digitized using 3DHistech Pannoramic 250 Flash II scanner with 20 × lens magnification—the effective resolution was 0.389 μm per pixel. Digital slides of whole slides (WSI) were encoded as 24 bit RGB matrices and saved in *mrxs* format. The data of the patient were removed from glass slides. This research project was approved by the Research Ethics Board of the Military Institute of Medicine.

In our experiments, we analyzed those parts of WSIs that contained villi. Therefore 27 different images from 13 WSIs were selected and marked by the pathologist. Fig. 1 An illustrates an example of WSI with marked areas of villi. The size of marked areas ranged from 1548 × 2070 pixels to 10000 × 18000 pixels depending on the density of villi in the specimen.

In our study, we analyzed individual villi that were randomly picked from areas marked by the pathologist. From each of the marked area 1–5 villi were selected. In total, 70 villi were selected: 20 villi from 10 images for method development and 50 villi from 17 images for analysis. As a result, an independent data cohort has been used for method developing and testing. Fig. 1 B and C illustrates villi and other components of placental tissue.

3. Methods

The presented method consists of three major steps: preprocessing, tissue detection and background removal, and quantitative analysis. Fig. 2 illustrates the general architecture of our approach. In the first step, the image is preprocessed for the segmentation and quantitative analysis. In the second step, we differentiate between various areas such as villi, collagen, villous mesenchyme, edema area, and blood vessels. The quantitative analysis includes counting of blood vessels and measuring the degree of edema in each villus. The OpenSlide library [24] and Matlab (Mathworks, Natick, MA, USA) wrappers [25] were used to read image data from the *mrxs* files. All methods were developed in Matlab 2014b environment.

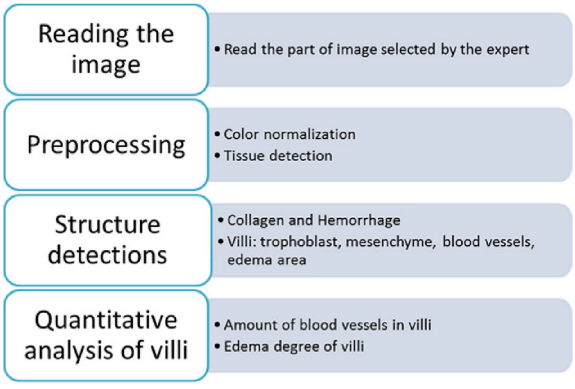

Fig. 2. Workflow of the image analysis and general architecture of the algorithm.

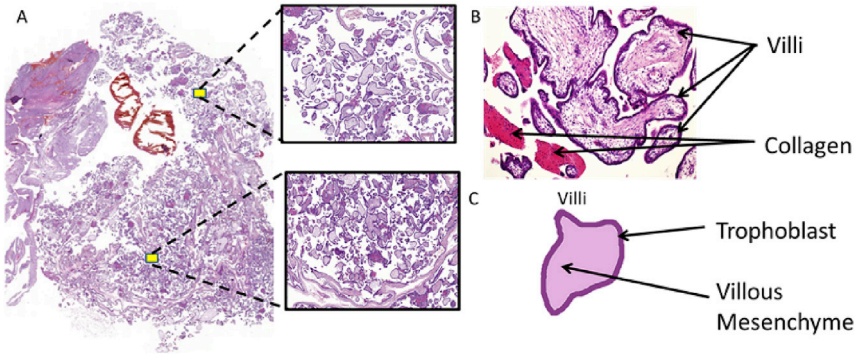

Fig. 1. Example images of placenta stained with H&E: A—WSI and regions of villi selected by pathologist, B—an example illustrating villi and collagen, C—a schema of villi components.