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Fast and accurate identification of fat droplets in histological images

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ABSTRACT

Background and objective: The accurate identification of fat droplets is a prerequisite for the automatic quantification of steatosis in histological images. A major challenge in this regard is the distinction between clustered fat droplets and vessels or tissue cracks.
Methods: We present a new method for the identification of fat droplets that utilizes adjacency statistics as shape features. Adjacency statistics are simple statistics on neighbor pixels.
Results: The method accurately identified fat droplets with sensitivity and specificity values above 90%. Compared with commonly-used shape features, adjacency statistics greatly improved the sensitivity toward clustered fat droplets by 29% and the specificity by 17%. On a standard personal computer, megapixel images were processed in less than 0.05 s.
Conclusions: The presented method is simple to implement and can provide the basis for the fast and accurate quantification of steatosis.

1. Introduction

Steatosis, the abnormal retention of fat in cells, is a common disease of the liver. Liver steatosis can have a variety of causes, such as obesity, diabetes, and alcohol abuse. Due to the growing problem of obesity among the Western population, steatosis is expected to become ever more widespread [13]. Severe steatosis increases the risk of liver dysfunction after surgery. It is, therefore, frequently assessed in order to decide whether to perform an extended liver resection or whether to accept a liver graft.

The gold standard for the assessment of steatosis is the histological evaluation of tissue samples. Here, steatosis is most often assessed in routine stains, such as hematoxylin and eosin (H&E). Under the microscope, steatosis becomes visible as separate or clustered fat droplets in the cytoplasm of cells. Because fat is dissolved in the course of the normal histological processing, these fat droplets are actually empty spaces within the tissue. Nevertheless, they can usually be distinguished from other empty spaces, such as vessels or tissue cracks, by their distinctive roundish shape (Fig. 1).

Steatosis is typically assessed in terms of a semiquantitative scoring system that captures the percentage of cells with

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0169-2607/

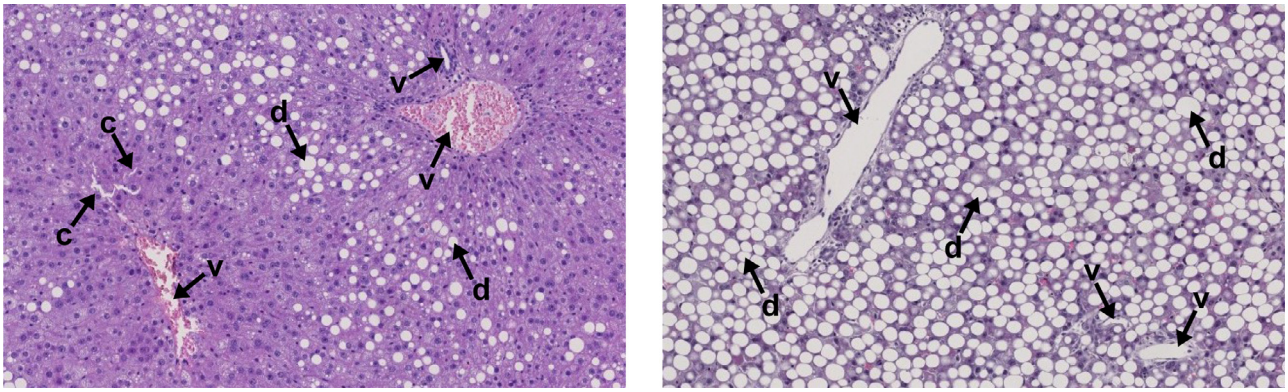

Fig. 1 – Histological images of mild steatosis (left) and severe steatosis (right). The arrows mark examples of fat droplets (d), vessels (v) and tissue cracks (c).

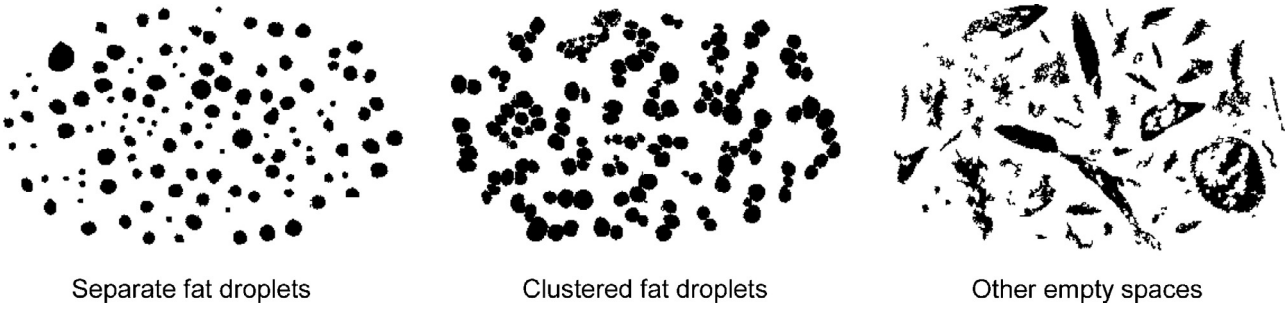

Fig. 2 – Typical blob shapes of separate fat droplets, clustered fat droplets and other empty spaces.

fat droplets [2]. Recent studies have shown that the results are often only poorly reproducible. In [5], no significant correlation could be demonstrated between 4 pathologists from 3 countries. In [6], nearly a quarter of 75 specimens were scored differently in a second assessment.

Errors in the assessment of steatosis can lead to inappropriate treatment decisions. For this reason, several image analysis methods have been proposed in order to automate and improve steatosis measurements.

The main operation of these image analysis methods is the identification of fat droplets. Afterwards, the amount of steatosis is simply quantified as the area fraction occupied by the fat droplets. Although the resulting values differ from the semiquantitative scoring system, they often provide a good correlation with biochemical measurements of the fat content of the tissue [10,4].

Most methods for the identification of fat droplets start with some kind of thresholding operation in order to segment all empty spaces within the tissue. The resulting segments, called "blobs", are then classified into either fat droplets or other empty spaces by their shape. Here, the existing methods generally assume that fat droplets have a distinctive circular shape. In [5], the size or arc length of a blob is required to be similar to a circle which covers its area in order to be classified as a fat droplet. In [11,10,9,4], fat droplets are identified by applying static thresholds to the size and roundness or eccentricity of a blob.

The assumption of a circular shape generally holds true for images of mild steatosis where fat droplets are clearly separated and every droplet is represented by an individual blob. In images of severe steatosis, however, multiple fat droplets in close proximity often coalesce into single blobs, thereby exhibiting all kinds of complex or elongated shapes (Fig. 2). In these cases, the reliance on the roundness as a classification criterion produces severe classification errors.

The method proposed in [9] appears to be the only one to tackle this problem. Here, clustered droplets are separated prior to the classification with a combination of distance and watershed transformations. When applied to whole-slides images, these operations are computationally very expensive. In [9], this problem is solved by utilizing a large-scale grid-computing environment which is generally not available in clinical practice.

In this paper, we present a new method for the identification of fat droplets in histological images. This method directly identifies both separate and clustered fat droplets with high accuracy. At the same time, this method is very fast and can be quickly executed on standard personal computers.

2. Methods

2.1. *Overview*

Like most existing image analysis methods for the identification of fat droplets, the presented method has two main processing steps (Fig. 3). In the first step, individual pixels are classified into either background or tissue. In the second step, blobs of connected background pixels are classified into either fat droplets or other empty spaces by their shape.