Automated Quality Assurance in Whole Slide Pathology Images: Blurred Region Detection

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INTRODUCTION

Virtual microscopy (VM) is a growing field where glass tissue slides are scanned to a digital image. Digital pathology, enabled by VM, is an image-based process that provides the ability to acquire, manage and interpret pathology cases from digitized glass slides. Challenges exist, however, and a wide range of issues can contribute to an overall lower quality of image. One such issue, blurriness, causes a loss of important image data and thus results in a significant amount of staff time and effort to manually assess these whole slide images. The Biomedical Imaging Team (BIT) at Nationwide Children's Hospital aims to automate the detection of blurred regions in these images and reduce the manual labor involved in quality assurance.

BACKGROUND

Blurring in whole slide pathology images (WSI) occurs because of software and hardware errors, vibrations during scanning, incorrect focus point placement, tissue folds and other factors. Blurriness in an image obscures image data, causing problems for pathologists who have to formulate a diagnosis based on these images. Image analysis algorithms also often have difficulty overcoming blurry image quality.

In order to detect poor quality images before they reach the pathologists and analysis algorithms, imaging technicians assess the quality after scanning, assuring the image does not have any prohibitively blurred regions. If the image is of insufficient quality, rescanning of the entire image is repeated until the proper quality has been attained. While automated rescanning isn't available, image analysis can automate the quality assessment step. The Blurred Region Detection algorithm developed by the Biomedical Imaging Team (BIT) scores the severity of blurring within a WSI and annotates the image for rapid assessment of whether the image needs to be rescanned.

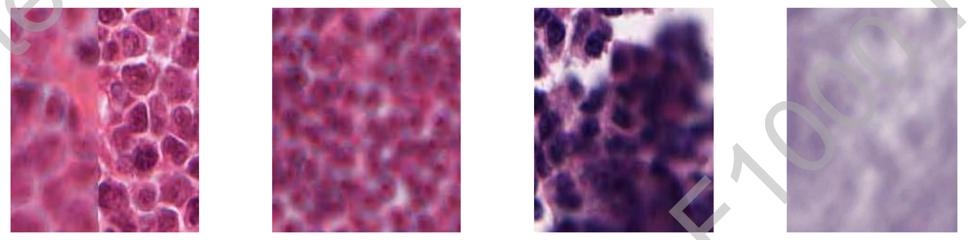

Figure 1. Examples of blurred sections from whole slide pathology images

METHODS

Reading the Image

- The WSI is broken into smaller, independent blocks for parallel processing.
- Image pixel data from the Aperio™ proprietary format is accessed with the aid of Bio-formats, an open-source Java library, within MATLAB™.

Screening of blocks

- Because biological tissue isn't present over the entire WSI, blocks are prescreened for whether they contain a significant amount of non-background colored pixels.
- A block that is completely or nearly completely white is disregarded by the algorithm to help reduce the computational time as they do not require further processing.
- The remaining blocks then undergo a series of image processing steps and a metric is calculated, measuring the amount of blurriness in a region.

The algorithm makes use of the idea that blurred and non-blurred regions can be distinguished on the basis of homogeneity and contrast. In this algorithm, the differences are quantified using numerical gradients. More gradients are found in clear, in-focus regions as compared to blur regions.

Calculation of metric

- A block of tissue is first blurred using an averaging filter to attain a distinct pair of images.
- The number of gradients in the original image and its blurred version are calculated.
- Gradient counts are normalized by the number of colored pixels in the block.

A metric for each block is produced by the following formula:

$$\frac{Gradient\ changes\ in\ original\ image - Gradient\ changes\ in\ final\ blurred\ version}{Total\ number\ of\ colored\ pixels}$$

Blocks are then classified by their metric as good (green), passable (yellow), or not passable (red). These are used to annotate the WSI for visual inspection by the imaging technicians (as seen in Figure 3). A global metric is also calculated using the following formula:

$$Global\ Image\ Metric = \frac{\sum_{i=1}^{n} Difference\ in\ gradient\ changes\ for\ block_i}{\sum_{i=1}^{n} Colored\ pixels\ in\ block_i}$$

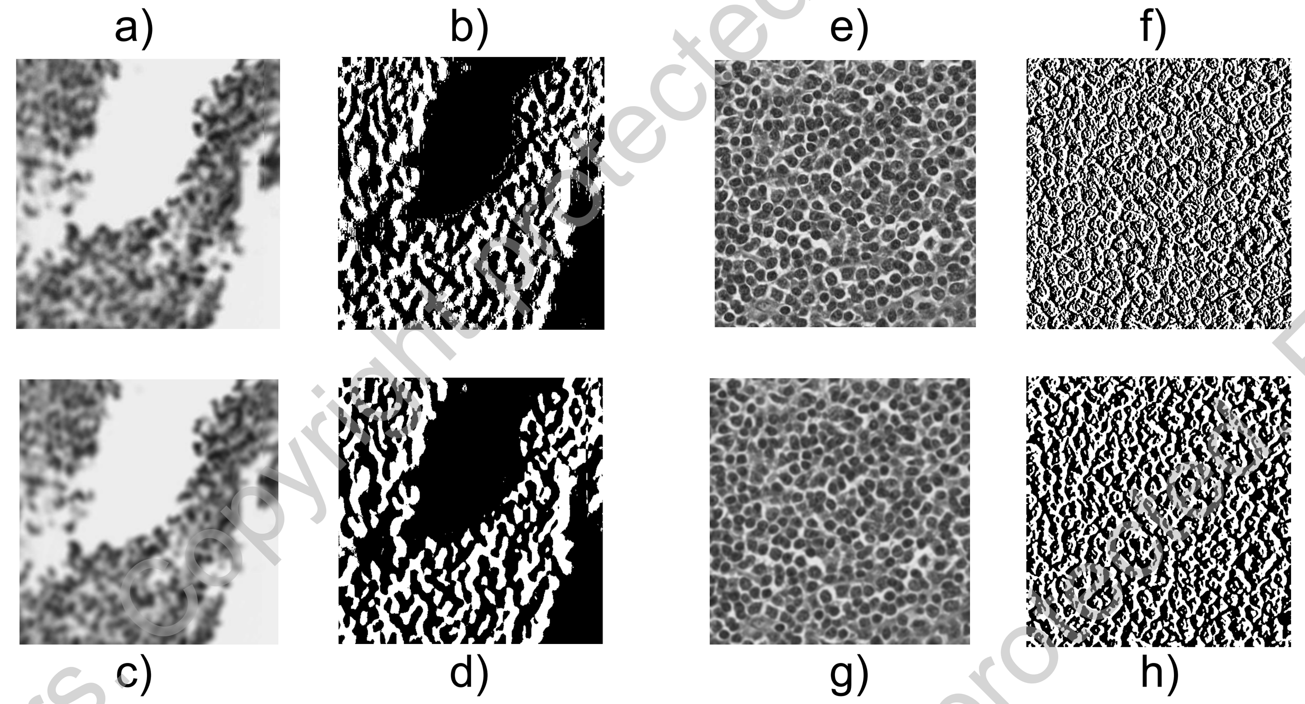

Figure 2: a) Blurry image. b) Gradient image of 2a. c) Image 2a blurred four times. d) Gradient image of 2c. e) Clear image. f) Gradient image of 2e. g) Image 2e blurred four times. h) Gradient image of 2e.

RESULTS

Expert imaging technicians were asked to manually assess 52 WSI consisting of quality and poor images. Technicians were asked to grade each WSI as good, passable, and non-passable. They were asked to only focus on the blurring issues. The algorithm's global metric and the distribution of good and poor blocks within the image were each used to formulate a good, passable, or poor algorithmic grade for each image.

Percent of WSI in agreement	Agreement between:
78.8%	Technicians and both algorithmic metrics
88.4%	Technicians and distribution metric
11.5%	Neither technicians nor metrics

Table 1: Amount of agreement between two algorithmic metrics and expert imaging technicians.

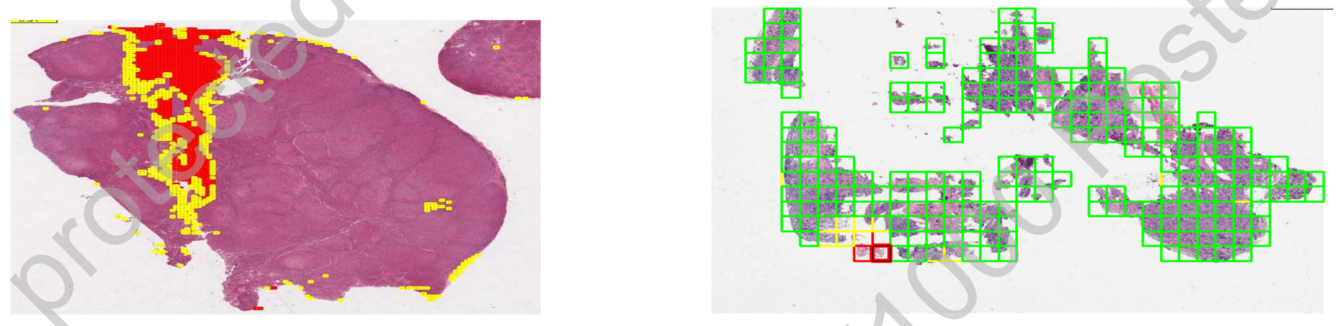

Figure 3: a) Annotated image with blocks outlined in red showing significantly blurred regions and outlined in yellow showing mildly blurred regions b) Blocks outlined in green showing clear, in-focus regions

DISCUSSION

The algorithm came to an agreement with the expert technicians on 88.4% of the WSIs. The global metric, however, was not as effective in its assessment of the entire image quality. A subset of blocks may have a metric which contributes an inordinate amount in one direction or the other, thus moving the global average with it. With the distribution metric, each block contributes equally.

There are several specific situations where the algorithm and the technicians were not in agreement:

- Over-staining: The image has dark blobs without sufficient definition, though the technician may deem the tissue as sufficiently clear to pass.
- Under-staining: The algorithm may not be able to distinguish very lightly colored tissue from the background of the slide.
- Thick tissue: While a technician may be able to look through the haziness that a mix of out-of-focus and in-focus tissue can cause, the algorithm may not. This haze reduces edge definition and the number of gradients that will be found.

Future work

- The use of an image thumbnail to separate out completely white blocks and applying the algorithm to only the block containing tissue could significantly decrease computation time. Only a few pixels of the thumbnail would need to be processed as opposed to an entire block's worth of pixels.
- High performance computing and "bursting" to the cloud is in the testing phase, and will assist the analysis of WSIs on a real time basis diminishing the delay between scanning and quality assessment of the image.
- The precise annotation of the blurred areas in the form of region outlines and contours instead of placing square blocks over a blur region would create a more accurate visual representation.

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