論文 / 著書情報
Article / Book Information

題目(和文)	
Title(English)	A study towards device-independent histological quantification and automatic classification system
著者(和文)	Abdul Aziz Maulana
Author(English)	Maulana Abdul Aziz
出典(和文)	学位:博士(工学), 学位授与機関:東京工業大学, 報告番号:甲第10992号, 授与年月日:2018年9月20日, 学位の種別:課程博士, 審査員:山口 雅浩,小林 隆夫,熊澤 逸夫,金子 寛彦,渡辺 義浩
Citation(English)	Degree:Doctor (Engineering), Conferring organization: Tokyo Institute of Technology, Report number:甲第10992号, Conferred date:2018/9/20, Degree Type:Course doctor, Examiner:,,,,
学位種別(和文)	博士論文
Category(English)	Doctoral Thesis
種別(和文)	論文要旨
Type(English)	Summary

（博士課程）
Doctoral Program

論 文 要 旨

THESIS SUMMARY

専攻： Department of	物理情報システム　専攻	申請学位（専攻分野）： Academic Degree Requested	博士 Doctor of　(Engineering)
学生氏名： Student's Name	Maulana Abdul Aziz	指導教員（主）： Academic Supervisor(main)	山口雅浩
		指導教員（副）： Academic Supervisor(sub)	

要旨（英文 800 語程度）
Thesis Summary（approx.800 English Words ）

Studies by International Agency for Research on Cancer (IARC) show that the number of cancer incidences and mortalities has been increasing and the trend is projected to continue. The studies also show that the number of cancer incidence in a region is not correlated with the number of cancer mortality as cancer survival rates highly depend on early-stage cancer detection, diagnosis, and treatment. Histopathological analysis plays an essential role in cancer detection, where pathologist observes and analyzes the tissue specimens resected from the patients, which conventionally performed by microscope. On the other hand, the development of whole-slide scanner (WSS) has allowed the digitization of pathological samples, called whole-slide image (WSI). By using WSI, it becomes possible to examine tissue specimens with computer screen and implement advanced image processing and analysis techniques on the histopathological images so that fully-objective quantification of tissue morphology can be obtained. Various works have been carried out on digital pathology with the hope to aid the pathologists and advance the diagnosis process, which includes tissue feature extractions and quantifications, detections of tumor areas, and the development of computer-assisted diagnosis (CAD) system.

NEC Corporation has been developing an anatomical pathology diagnosis system called *e-pathologist*® since 2001 in order to assist pathologists in analyzing and detecting malignant tumors on WSIs of hematoxylin and eosin stained biopsy samples. The system has been used to detect several types of cancer, including gastric, colorectal, breast, and prostate cancer, having nuclei of epithelial cells as the main object used for the cancer detections. Later on, a prototype system to measure features of liver tissue were developed in order to diagnose liver cancer called hepatocellular carcinoma (HCC) at early stages. As part of the project, several studies on liver tissue structure quantifications and a color correction method to overcome color varieties in WSI due to the staining process were introduced. Nevertheless, the effectiveness of the new features on cancer detections have not evaluated. Meanwhile, the imaging system implemented WSSs may cause quality differences on WSIs, including the color. The prototype system itself was developed based on histological images acquired by one type of WSS. Yet, it is essential for the system to be able to receive images from the other type of WSSs.

The primary goal of this research is to carry out an investigation towards a histological quantification and automatic classification system that is independent to the device used to acquire the histopathological images, with the mentioned prototype system as the case study. The work is elaborated into three parts. The first part focuses on the enhancement of the automatic classification of histopathological images. Two factors affecting the results of the classification system were studied, which are the features and the number of training data. Features related to tissue structures and removal of non-liver nuclei through masking process during nuclear quantification are evaluated. The results show that a combination of tissue structural and nuclear features can improve the classification rates, especially in lower grades HCC. This is an important point since lower grades HCC are more difficult to be differentiated from the normal cases. The masking process improves the reliability of nuclear features as falsely detected nuclei are removed from the quantification. The evaluation on the sample types used for the training data shows that it is possible to increase the number of training data by using biopsy and surgical resected samples. In fact, the inclusion of surgical resected samples will make the results more stable and robust.

In the second part, a series of evaluations were carried out to evaluate the effectiveness of three color correction methods on quantitative pathology, consisting stain-based color correction, device-based, and a combination of device- and stain-based color correction. Each color correction method was developed to reduce color variety on WSIs. Based on the evaluations, the stain-based color correction gives better

impact compared to the device-based color correction. The stain-based method can even compensate the color difference due to the device varieties. Color correction is essential in the process of feature quantifications of histopathological images, especially in order to gain reliable nuclei morphological features. The study also shows that the texture related features of nuclear are more sensitive to image contrast, compared to the morphological features. Nevertheless, some differences on the quantified features are still existed, which possibly caused by the difference on image quality due to the image sharpness.

The last part focuses on the sharpness correction on histopathological images and its effects on quantitative pathology. Differences on image sharpness can be caused by the focus method implemented on the WSS. The sharpness correction is implemented based on images instead of devices. Here, a sharpness correction approach by utilizing Gaussian point spread function is proposed. The evaluations were carried out by observing the intensity profiles and the quantified nuclear features. The results show that the method has the potential to improve the reliability of the features.