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SIDE VIEWING MICRO-ENDOSCOPE OPTICAL SYSTEM WITH ACROMATIZED OBJECTIVE LENS

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SIDE VIEWING MICRO-ENDOSCOPE OPTICAL SYSTEM WITH ACROMATIZED OBJECTIVE LENS

By

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Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirements for the Degree of Master of Science

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SIDE VIEWING MICRO-ENDOSCOPE OPTICAL SYSTEM WITH ACHROMATIZED OBJECTIVE LENS

By

Nanthakumar Dorai-Raj

October 2014

Chair: M.Iqbal Saripan, PhD

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High resolution microendoscopy (HRME) is a novel optical technique which utilizes optical system to view directly sub-cellular structures. Major obstacles of HRME which uses forward view optical system in achieving high quality image of sub cellular structures in GI tract wall are short depth of field and small field of view. Vibration or movement of the optical system during probing resulted in low image acquisition quality. In this thesis, design and optimization of side view micro endoscope with magnification of 3X optical system using fold mirror, doublets and aspheric lens are presented. Fold mirror incorporated into optical system with a purpose of bending light path which allows GI tract wall viewed side way while rotating for circumferential scanning. In order to minimize aberrations that degrade images created by fold mirror, aspheric lens with conic shape added before fold mirror which functions to collimate rays before reaching fold mirror. Next relationship between working distance, numerical aperture of object and image space and airy disc established to determine magnification and resolution of the optical system. Then 4 doublets lens with varying dispersion ratio used in order to achieve achromatization which functions to increase field of view, working wavelength range, minimizes aberrations and achieved acceptable image qualities. Optimization of optical system performed for optimum performance achievements. Tolerance analysis simulation performed by adding components tolerances in predicting manufacturability of the conceptual design. Simulation results across field of view for wavelength range from 0.53 μm to 0.63 μm presented. Optimum MTF value above 20% recorded for spatial frequency of 240 line/mm at axis. MTF value above 20% recorded for spatial frequency of 170 line/mm at the edge. Maximum drop of 20% of MTF achieved after adding components tolerance limit. This technology can enhance image acquisition quality of HRME while viewing sub cellular tissues such as cytoplasm and nucleus as side view allows circumferential scanning of optical

system which simplified movement mechanism. The optical system able to fit into capsule that works as pressure plate to maintain stability. In future developing prototype of the optical system can be used a basis for developing automated circumferential scanning of GI tract.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Sarjana Sains

SISTEM OPTIK ENDOSKOP MIKRO PANDANG SISI DENGAN KANTA OBJEKTIF PENGKROMATAN

Oleh

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Mikro endoskop beresolusi tinggi ialah kaedah terkini pengimejan optik menggunakan sistem optik untuk melihat struktur subsel secara terus. Halangan utama mikro endoskop berresolusi tinggi yang menggunakan sistem optik pandang depan dalam penghasilan imej struktur subsel gastrousus ialah jarak pandangan yang pendek dan bidang pandangan yang kecil. Getaran atau pergerakan sistem optik semasa memeriksa mengakibatkan kualiti pengambilan imej kurang berkualiti. Dalam tesis ini, rekabentuk dan optimisasi sistem optik mikro endoskop berresolusi tinggi pandang sisi dan pembesaran 3X yang menggunakan cermin, pasangan kanta dan kanta 'aspheric' ditunjukkan. Cermin dimasukkan dalam sistem optik ini dengan tujuan mengalih arah laluan cahaya yang membenarkan dinding gastrousus dilihat dari sisi semasa membuat putaran sekeliling. Pengurangan aberasi yang wujud disebabkan oleh cermin dilakukan melalui pengunaan kanta 'aspheric' berbentuk kon yang dimasukan sebelum cermin yang berfungsi untuk selarikan cahaya sebelum sampai ke cermin. Hubungan antara pembukaan numerik objek dan imej, jarak bekerja dan 'airy disc' dibuktikan dan seterusnya menentukan pembesaran dan resolusi sistem optik. 4 pasang kanta yang mempunyai nisbah serakan yang berlainan digunakan sebagai pengkromatan yang berfungsi untuk menambah bidang pandangan, jurang panjang gelombang dan meminimumkan aberasi. Optimisasi sistem optik dijalankan untuk mencapai prestasi yang optimum. Seterusnya simulasi analisa toleransi dilakukan dengan menambah nilai had toleransi komponen untuk menilai kebolehan pembuatan rekabentuk. Keputusan simulasi di sepanjang bidang pandangan untuk panjang gelombang antara 0.53μm - 0.63μm ditunjukkan. Di atas paksi nilai MTF merekod melebihi 20% untuk nilai kekerapan 240 garisan/mm. Manakala di hujung bahagian imej MTF merekod

melebihi 20% untuk nilai kekerapan 170 garisan/mm. Penurunan nilai MTF sebanyak 20% apabila nilai had toleransi komponen ditambah. Rekabentuk sistem ini mampu meningkatkan kualiti pengambilan imej oleh micro endoskop beresolusi tinggi semasa melihat struktur subsel seperti nuklues dan sitoplasma kerana pandang sisi membolehkan sistem optik memutar sekeliling yang memudahkan mekanisme pergerakan. Teknologi ini juga mampu dimasukkan dalam kapsul yang berfungsi sebab plat tekanan yang mampu mengawal kestabilan. Di masa hadapan penghasilan prototaip sistem optik ini mampu menjadi asas penggunaan teknologi putar sekekeliling gastrousus secara automatik.

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I certify that a Thesis Examination Committee has met on 15th October 2014 to conduct the final examination of Nanthakumar Dorai-Raj on his thesis entitled " Side viewing micro-endoscope with achromatized objective lens in accordance with the Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U.(A) 106] 15 March 1998. The Committee recommends that the student be awarded the Master of Science

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This is to confirm that:

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Signature:	
Name of Member of Supervisory Committee:	Ahmad Shukri bin Mohammad Noor, PhD

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LIST OF ABBREVIATIONS

MRI	Magnetic Resonance Imaging
CT	Computer Tomography
HRME	High Resolution Micro-Endoscope
PSF	Point Spread Function
MTF	Modulation Transfer Function
OPD	Optical Path Difference
OCT	Optical Coherence Tomography
OCM	Optical Coherence Microscopy
CCD	Charged Coupled Device
SIM	Structured Illumination Microscopy
BE	Barrett's Esophagus
GI	Gastrointestinal
LED	Light Emitting Diode
FOV	Field of View
NA	Numerical Aperture
DOF	Depth of field
IR	Infrared
UV	Ultraviolet
SLM	Spatial Light Modulator
GRIN	Gradient Index Lens

CHAPTER 1

INTRODUCTION

1.1 Overview

Since its inception, microscope played a vital role in enhancing human's understanding of microscopic details of nature [Singer 1914]. Meanwhile in medical field microscope utilized by researchers and doctor's to observe, understand and characterize diseases (Murali and Rolland 2006). A disease such as cancer identified when cells begins to grow exponentially without control and halt body's ability to function properly. Cancer cells created when normal cell's DNA (deoxyribonucleic acid), a molecule that holds genetic instructions of cell development and functions damaged (Anon. 2013). Most of cancers estimated about 85% originated from epithelial cell, a thin layer that covers body organ. Meanwhile cancers of gastrointestinal (GI) tract are the most common, surpassing lungs or cervix cancers. Most of GI tract cancers detected in colon followed by esophagus gastric and pancreatic. Unfortunately, GI tract cancer does not show any symptoms during early stages. Symptoms such as abdominal pain and vomiting only occurred at the last stage of cancer when prognosis is poor (Plevris 2005). Estimated one in twenty people diagnosed for colorectal cancer in their lifetime (Anon. 2013).

GI tract is a very long tract divided into two regions called upper gastrointestinal that consists of esophagus, stomach and duodenum meanwhile lower gastrointestinal consists of small and large intestines. GI tract function includes transporting food through peristalsis movement, digesting foods for nutrient absorption and wastes removal. Abnormalities on gastrointestinal (GI) tract such as abnormal growth or cancer will cause GI tract cease its function (Anon. 2013). There are 3 types of epithelial cell based on shape differences viewed under microscope namely squamous cell, glandular cell and transitional cell that covers organ such as gastrointestinal (GI) tract. Cancer names correspond to the type of cell it originated. Adenocarcinoma is a type of cancer cell that developed from glandular cell which can be found along gastrointestinal tract GI tract wall and is on the rise since last decade. Glandular cells have hair like protruded shape called microvillus which involves in food absorptions (Anon. 2013).

Currently cancer screening for general population particularly high risk group helps in detecting pre-malignant condition such as Barrett's esophagus, gastric atrophy and or adenomatous colonic polyps. Detection of these pre-malignant conditions allows periodic surveillance for early cancer detection. Early detection of abnormal structures in sub-cellular level before it grows and halts normal functions of organs would increase chances of defeating the cancer. Early stage cancer cells have irregular, large or multiple nucleuses (Bowles and Benjamin 2013). By viewing microscopic details of sub-cellular structures such as nucleus, abnormal changes in cells can be detected. Conventionally endoscopes used for screening suspected area and biopsies, a term coined for tissue removal from body performed. Then histopathology analysis, a process of scrutinizing cell or tissues under microscope by pathologist to view sub-cellular structures such as nuclear size, cell shapes and ratio between nucleus and cytoplasm performed on biopsy tissues. The results obtained by pathologist then will be evaluated by doctors for next course of action in cancer managements.

Alternatively another method called 'optical biopsy', a technique of viewing and judging tissue conditions in vivo without lesion removal for histopathology analysis introduced in medical imaging field. 'Optical biopsy' was a natural progression in medical imaging technology in reducing screening and diagnosis process time, assisting clinicians in reducing workload and minimizing misdiagnosis. Also with ever increasing total health cost, optical biopsy technologies may help in reducing cost of cancer management in future. Most of optical biopsies technologies are still in development stages and operating cost are still higher compared to normal cancer screening procedures.

Various diagnostic tools which utilizes imaging techniques includes high resolution micro-endoscope (HRME), fluorescence endoscopy, optical coherence microscopy (OCT) and confocal microendoscopy introduced in reaching 'optical biopsy goal'. Even though in vivo microscopic imaging technologies have evolved tremendously in medical field, biopsy still performed. Conventional histopathology analysis still considered as a gold standard in screening and diagnosing cancer patients. Therefore success of imaging techniques relies on additional improvements in current technologies such as improvement in optical systems, sensors, image processing algorithm and etc. which ultimately improve sensitivity and specificity of cancer detections (Wang and Van Dam 2004; Egger *et al* 2003). One of the newest in-vivo microscopic imaging diagnostics tool called High Resolution Microendoscopy (HRME), a novel imaging tool which has demonstrated the ability to view image of microscopic structures with < 10 μm resolution in real time gained popularity recently. Compared with other imaging technologies the main advantages of HRME lie on its cost and simplicity. HRME has simple set-up and works with normal visual light. By incorporating fluorescence imaging technique and further image enhancing algorithm the technology has potential to provide an alternative technique for clinicians, researchers and scientists to observe and analyze microscopic structures of human organs. It may have high possibilities in replacing histology analysis of excised tissues which currently classified as gold standard in the future when said technology matures (Shukla 2011). HRME is a new microscopy technology and not commercially available. HRME was mainly utilized in observing and analyzing gastrointestinal tract (GI) tissues. With ever increasing medical cost particularly in cancer screening procedures, searching for better screening procedure while maintaining lower operating cost becomes vital. Thus, more researches concentrated on HRME which is cheaper compared to other in vivo imaging technique. Feasibility of HRME technology has been explored by observing normal squamous mucosa, metaplasia and high grade dysplasia. Comparison with gold standard showed HRME able to characterize all 3 types of cell structures (Regunathan 2011; Muldoon 2008). The study of the thesis includes improving sensitivity and specificity of HRME early cancer cells detection by designing an optical system that minimizes handling difficulties by clinicians in GI tract.

1.2 Problem Statement

HRME emerged as one of the important 'optical biopsies' imaging technique. HRME advantages lie in cost effectiveness, simplicity and portability compared with other imaging techniques. Even though HRME has advantages but its simple set-up prevents high quality image acquisitions. The reasons of low image quality acquisition identified as below:
.

1. HRME optical system as with other microscopy imaging has very small depth of field (DOF) which in order of microns. DOF defined as a range of depth where object remain sharp at image plane. Given the DOF in microns, minor changes or vibration of probe position during tissue viewing by clinician creates blurry images as tissue position not within focusing zone (Hughes and Yang 2012; Ussui, Michael and Wang 2011).

2. HRME optical system as with other microscopy imaging also has very small field of view (FOV) and usually in the range of 200 μm to 700 μm. FOV defined as viewable area at image plane. With the current technology it's an impossible task to view microscopic image continuously along GI tract as the length of small intestines is around 25 m while the length of colon approximately 5 m. Therefore clinician only views suspected area and not the whole GI tract and as a result certain percentage of cancerous cell missed out (Paull PE 2011).

Thus, to enhance quality of cellular structures visualization and characterization, addressing both problems are vital for higher GI tract image quality acquisitions of HRME.

1.3 Aim and Objectives

The aim of this thesis is to further improve HRME image acquisition by reducing probe handling difficulties. A number of objectives identified in order to achieve our main aim and listed as follows:

1. To design encapsulated side view optical system with magnification and field of view (FOV) that allows circumferential scanning and minimizes vibration during image acquisitions.
2. Run performance simulation and tolerance analysis on designed optical system.

1.4 Scope of Thesis and Limitations

This thesis focuses on optical system in in-vivo microscopy technology and concentrated on optical system of HRME. The scope of thesis is to design optical system for image acquisition enhancement by minimizing handling difficulties of HRME. Side viewing optical system with FOV and magnification proposed to allow circumferential scanning and minimizes handling mechanism during image acquisitions. Performance simulations of optical system performed in order to examine quality of optical system. Tolerance analysis simulation performed by adding manufacturing errors into all components of optical system and performance evaluated for manufacturability of designed optical system. The optical system modeled and simulated using OSLO optical system software.

1.5 Improvement Contributions

The optical system intended able to capture magnified images of GI tract with minimum probe mechanism. Design contribution to in-vivo imaging field listed below:

1. Side way viewing which made possible by incorporating 45° tilted mirror which allows optical system to be rotated 360° along GI tract wall and images captured continuously. Thus simplifies movement mechanism of optical system in GI tract.
2. Encapsulated optical system designed to have contact with GI tract wall which allow constant pressure applied without introducing external mechanism or relies on skilled clinicians in performing hand free probe handlings. Applying constant pressure is important to maintain shape of GI tract wall as deformed wall will cause blurry images. It is due to the fact that microscopy imaging has very small depth of field.

3. A painless screening method achievable as the optical system designed for miniature CCD or CMOS and not transmitting through big fiber bundle. A thin caterer attached on the capsule for maneuvering and rotating of capsule in GI tract wall.

4. A basis for future development of in vivo imaging technique with automated scanning.

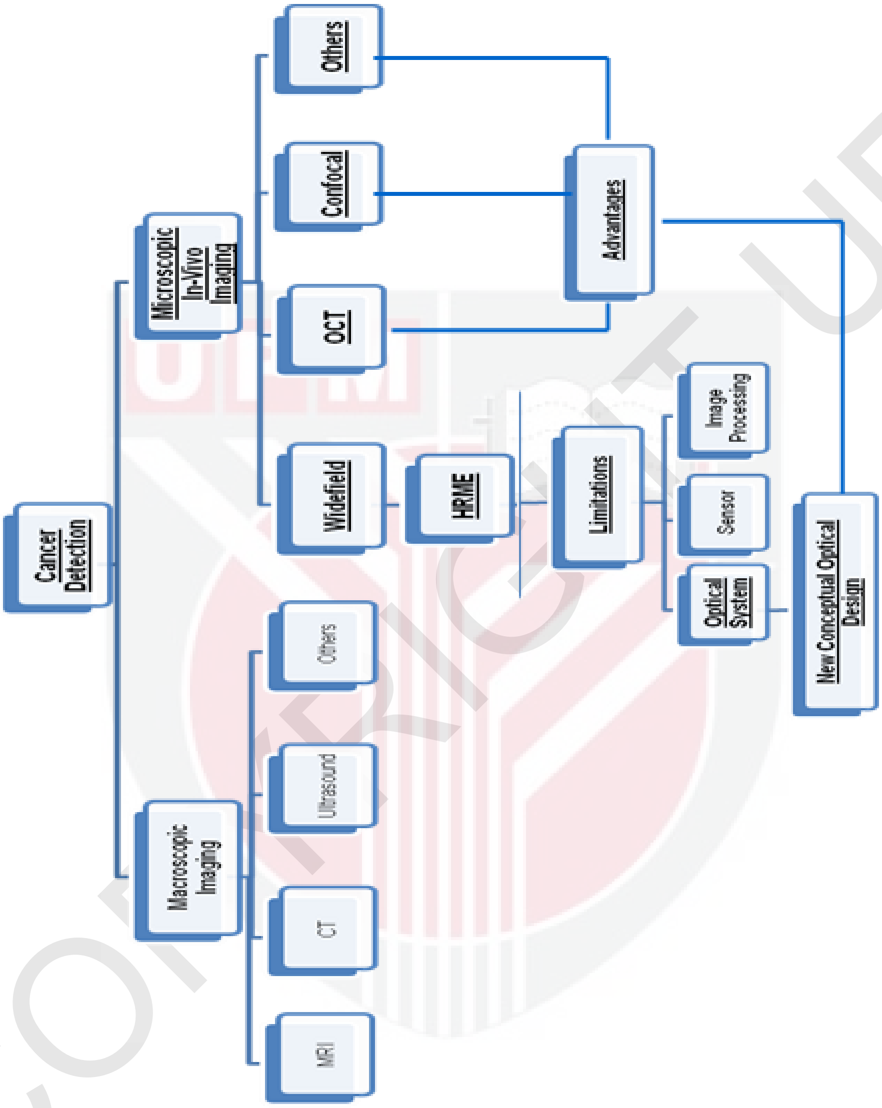

Figure 1.1: Study outline

1.6 Outline

This thesis describes the conceptual design and analysis of encapsulated side viewing optical system for micro-endoscope that enhance image quality acquisitions. Chapter 2, common microscopic imaging techniques available presented and compared. HRME explained in detail and latest development reviewed and analyzed. Recent contributions in other imaging tools discussed and finally way of minimizing handling difficulties in order to enhance image quality proposed. Validation of OSLO optical software with reference performance data from published paper, followed by the listing of preliminary design specification and overall HRME optical system design lay out discussed in chapter 3. Then optimization of optical design in lens design program explained and finally tolerancing technique in establishing reliability of design discussed. In chapter 4, OSLO optical software validated result presented. Detailed performance result of designed optical system presented and explained, followed by listing of final optical system's design specification. Marginal and paraxial rays traced with trigonometrical ray tracing program to compare simulation results. Tolerance analysis results of the optical system that predicts performance after fabrication presented. The conclusion and future works discussed in chapter 5.

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