Dynamic-focusing Microscope Objective for Optical Coherence Tomography

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ABSTRACT

Optical Coherence Tomography (OCT) is a novel optical imaging technique that has assumed significant importance in bio-medical imaging in the last two decades because it is non-invasive and provides accurate, high resolution images of three dimensional cross-sections of body tissue, exceeding the capabilities of the current predominant imaging technique –ultrasound. In this paper, the application of high resolution OCT, known as optical coherence microscopy (OCM) is investigated for *in vivo* detection of abnormal skin pathology for the early diagnosis of cancer. A main challenge in OCM is maintaining invariant resolution throughout the sample. The technology presented is based on a dynamic focusing microscope imaging probe conceived for skin imaging and the detection of abnormalities in the epithelium. A novel method for dynamic focusing in the biological sample is presented using variable-focus lens technology to obtain three dimensional images with invariant resolution throughout the cross-section and depth of the sample is presented and discussed. A low coherence broadband source centered at near IR wavelengths is used to illuminate the sample. The design, analysis and predicted performance of the dynamic focusing microscope objective designed for dynamic three dimensional imaging at 5μm resolution for the chosen broadband spectrum is presented.

Keywords: Optical Coherence tomography, optical coherence microscopy, dynamic focusing, bio-medical imaging, skin cancer

1. INTRODUCTION

Cancer constitutes one of the world's two most fatal diseases and is thought to originate at the cellular level, more specifically in the epithelium, the outermost layer of skin. The most efficient tool for diagnosis of cancer has remained for many centuries, the microscope. While microscope technology has allowed imaging for microstructures in exquisite detail, it still involves excision of body tissue, which can result in other complications such as cancer cell spreading, infection and hemorrhage. Research has been conducted in recent decades to investigate the possibilities of a non-invasive in vivo imaging technique as it will allow easier diagnosis, patient compliance, and earlier and more precise treatments. OCT, an optical imaging technique based on low coherence interferometry has demonstrated the ability to effectively image sub-surface structures at resolutions less than 10 μm [1]. Once the technology, its working and methods are fully established, it can radically change the way scientists study and analyze the human body and could replace conventional biopsy as the standard medical imaging tool.

1.1 Background

OCT's roots lie in early work on white light interferometry that led to the development of optical coherence-domain reflectometry (OCDR) [2], a one dimensional optical ranging technique originally developed for finding faults in fiber optic cables [3] and network components. Its potential for medical applications was soon recognized and researchers began to investigate its ability to probe biological tissue structures [4, 5]. While probing depths exceeding 2cm have been demonstrated in transparent tissues, in highly scattering media such as the skin, images are typically obtained as deep as 1-2mm [4-9].

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OCT is similar to ultrasound in that the echo time delay of backscattered light is measured as opposed to reflected acoustic radiation in ultrasound. In a typical OCT set-up, the sample arm of a Michelson interferometer is illuminated with a near-infrared broadband source. Two scans are performed, axial and depth to obtain a three dimensional section of a sample. The most commonly used configuration in recent years is *en-face* OCT, which was introduced by Izatt *et al* (1994). In this implementation a fast lateral scan is performed either by moving the probe beam or the sample, and several such lateral 2-dimensional sections are obtained by adjusting the reference mirror in the interferometer [10].

1.2 Dynamic focusing

Typically in OCT, low NA beams are used to achieve large depth of focus. While high numerical aperture optics has been used in OCT to achieve high lateral resolution leading to what is referred as optical coherence microscopy (OCM), widespread use of OCM was stalled because of the depth dependence of transversal resolution that resulted in inability to maintain invariant resolution throughout the depth of sample. One means to ensure invariant resolution across the entire scan depth is to use a dynamic focusing system.

Several implementations of a dynamic focusing system have been proposed in the last decade [11-14]. In order to ensure invariant resolution throughout the lateral and depth scans, Schmitt *et al.* (1997) introduced an OCT imaging set-up that consisted of a common transition stage for both the reference and sample arm thereby moving them in synchronicity[11]. Another approach suggested by Lexer *et al.* (1999) involves the movement of the sample for each depth scan. The arms of the interferometer remain stationary, and an oscillating beam focus magnified axially illuminates the sample. This axial magnification is computed to compensate for the path length change caused by the refractive index of the sample [12]. B. Qi *et al.* have proposed a dynamic focusing based on a deformable microelectromechanical (MEMS) mirror. The MEMS mirror deforms to shift the beam focus in the sample to correspond with the coherence gate of each lateral scan [13]. More recently, A. Divetia *et al.* investigated the possibility of dynamic focusing using a liquid-filled polymer lens whose curvature is varied by the use of hydraulic pressure in order to incorporate the variable-focus capability [14].

In this paper, we propose an OCT probe with an in-built dynamic focusing system within the microscope objective, designed and optimized to minimize aberrations and with no moving parts.

2. DESIGN AND DESCRIPTION

We present the design of a hand-held skin imaging probe that can dynamically focus in skin *in vivo*. The probe was designed to perform imaging of a 2mm in depth by 2mm lateral skin sample at a resolution of less than 5μm. The probe design may integrate a single-axis or dual-axes MEMS for 2D or 3D imaging, respectively. The MEMS enables the scan along the skin in either the x or y lateral dimensions. Scanning the reference arm enables the depth or z-scan, which in the case of this probe will be synchronized with the dynamic focusing in the sample arm. Ideally, the ultimate objective is to obtain video rate (30 frames/sec) high resolution imaging together with sample sizes of a few millimeters.

2.1 First-order layout

The proposed skin imaging probe comprises a microscope objective, a field lens, a microlenslet array, scan optics, and a MEMS scanning mirror. The probe set-up was constructed to image a 2mm×2mm cross-section of biological sample. Lateral scanning in the x-y plane is achieved using the single/dual axis MEMS scanning mirror. Tunability in the 'z' direction is achieved within the microscope objective using a variable-focus lens. The all-refractive 10X microscope objective was designed with an NA of 0.28. The first-order layout of the dynamic focus skin imaging probe is shown in Fig. 1.

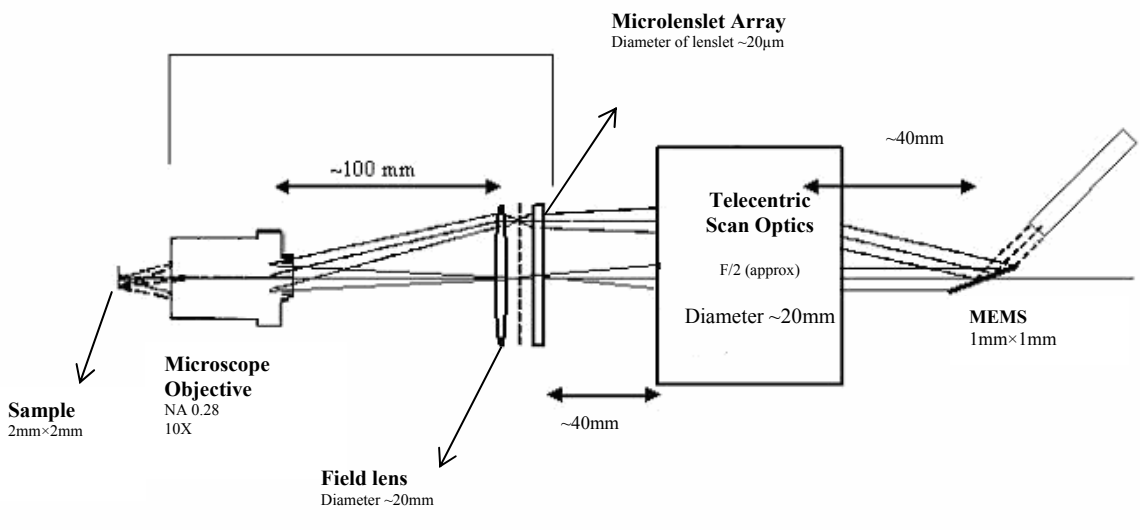

Fig.1: Design of a dynamic focusing probe

2.2 Modeling and Analysis

A liquid crystal lens was used as the variable focus element and was incorporated within the microscope objective. The liquid crystal has the property that the refractive index of the material can be varied as a function of position by adjusting the birefringence properties of the material. The birefringence is given by

$$\Delta n = n_e - n_0 = \frac{r^2}{2df} \qquad (1)$$

where r is the radius of the lens, d is the cell gap, f is the focal length and Δn is the birefringence.

When an inhomogeneous electric field is applied to a homogeneous liquid crystal layer, a refractive index gradient can be created across the surface of the layer. A centro-symmetric gradient of refractive index created in the liquid crystal will cause a focusing behavior similar to an optical lens. By varying the gradient, the properties of this liquid crystal lens can be modified to cause it function as a tunable-focus lens [15].

In order to model such variations in the refractive index in our optical design, we applied a varying index profile across the diameter of the flat lens. The electric field is therefore assumed to cause a refractive index gradient that varies as a function of the distance from the center in order to approach the optical path difference of a lens of constant refractive index. Thus, constant optical path difference can be maintained. The lens was then optimized to simulate a liquid crystal lens and the simulated images were obtained at for different cross-sections.

The overall microscope objective was designed to be refractive and its performance was evaluated in immersion in a gel of refractive index that matched that of skin. This was to ensure minimal reflection from the skin surface. The gel was chosen to have high transmissive property (100%) in the spectral region of interest. The overall design was optimized to minimize aberrations and diffraction MTF performance measures were used to analyse the system. A preliminary tolerance analysis was executed for the system in, and the tolerances were varied within user-defined limits and optimized to have similar impact on system performance.

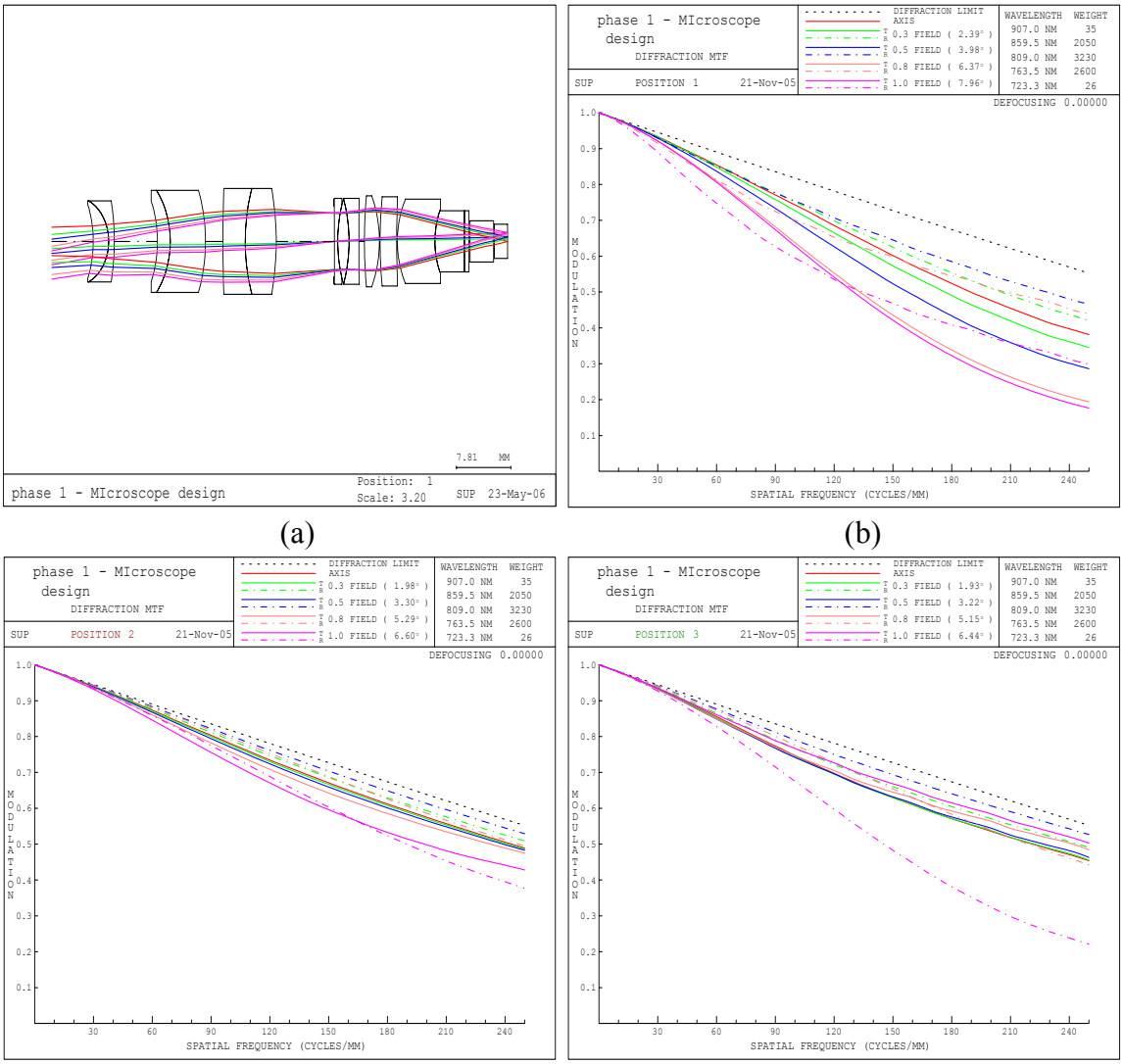

Fig.2: Design and MTF – (a) Lens layout; (b) MTF at skin surface; (c) MTF at 1mm depth; (d) MTF at mm depth

3. RESULTS

A theoretical model for an OCT imaging probe with axial dynamic focusing ability is presented. A mode-locked Ti: Sa laser was used as the broadband source. The overall system and performance are shown in Fig.2. The analysis of the microscope objective system was done at three depth positions, 0mm that constitutes the surface of the skin, 1mm within the skin and 2mm within the skin. The system was designed to refocus at each of these three positions and its performance was evaluated across these different depths.

The optical layout of the microscope objective is shown in Fig 2(a). MTF analysis shows an MTF of 20% on the surface of the sample (Shown in Fig. 2(a), 50% at a depth of 1 mm into the sample (Shown in Fig. 2(c)) and 50% at a depth of 2 mm into the sample (Shown in Fig. 2(d)) at a spatial frequency of 250 cycles/mm. Such frequency corresponds to a resolution of 4μm and therefore the system has achieved better than a 5μm resolution. Overall system tolerance analysis showed approximately 15% drop in diffraction MTF.

4. CONCLUSION

This paper demonstrates the feasibility of a dynamic focusing OCT imaging system at 5μm resolution with no moving parts. Future work will involve adapting the system to liquid lens based electro-wetting technology in order to satisfy imaging speed constraints given that currently available liquid crystal lens technology has proven to be slower than required.

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