Invariant resolution dynamic focus OCM based on liquid crystal lens

1-1-2007

S. Murali
University of Central Florida

K. S. Lee
University of Central Florida

J. P. Rolland
University of Central Florida

Find similar works at: https://stars.library.ucf.edu/facultybib2000

University of Central Florida Libraries http://library.ucf.edu

Recommended Citation

Murali, S.; Lee, K. S.; and Rolland, J. P., "Invariant resolution dynamic focus OCM based on liquid crystal lens" (2007). Faculty Bibliography 2000s, 7451.
https://stars.library.ucf.edu/facultybib2000/7451

This Article is brought to you for free and open access by the Faculty Bibliography at STARS. It has been accepted for inclusion in Faculty Bibliography 2000s by an authorized administrator of STARS. For more information, please contact lee.dotson@ucf.edu.
Invariant resolution dynamic focus OCM based on liquid crystal lens

S. Murali, K. S. Lee, and J. P Rolland
CREOL, College of Optics and Photonics, Univ. of Central Florida, Orlando, FL 32816
smurali@mail.ucf.edu; http://.odalab.ucf.edu

Abstract: A primary limitation of optical coherence microscopy is the lack of sufficient lateral resolution over a usable imaging volume for diagnostic applications, even with high-numerical aperture imaging optics. In this paper, we first motivate the benefit of refocusing at multiple depths in a highly scattering biological sample using optical coherence microscopy, which experimentally shows invariant 2.5 μm axial and 6.5 μm lateral resolution throughout the sample. We then present the optical system design of a hand-held probe with the advanced capability to dynamically focus with no moving parts to a depth of 2 mm in skin-equivalent tissue at 3 μm resolution throughout an 8 cubic millimeter imaging volume. The built-in dynamic focusing ability is investigated with an addressable liquid crystal lens embedded in a custom-designed optics optimized for a Ti:Sa pulsed broadband laser source of bandwidth 100nm centered at 800nm. The design was developed not only to account for refocusing into the tissue but also to minimize and compensate for the varying on-axis and off-axis optical aberrations that would be introduced throughout a 2 mm thick and 2 mm wide skin imaging volume. The MTF contrast functions and distortion plots at three different skin depths are presented.

©2007 Optical Society of America

OCIS codes: (080.3620) Lens system design; 110.4500 Optical coherence tomography; (120.3620) Lens system design; (120.3890) Medical optics instrumentation; (120.4570) Optical design of instruments; 170.3880 Medical and biological imaging; 170.4500 Optical coherence tomography

References and links
1. C. A. Puliafito, M. E. Hee, J. Schuman and J. G. Fujimoto, Optical Coherence Tomography of Ocular Disease (Thornofare: Slack Inc, 1995).
2. J. A. Izatt, “Optical coherence microscopy in scattering media,” Opt. Lett. 19, 590–591 1994.
3. J. Welzel, “Optical Coherence Tomography in dermatology: a review,” Skin Res. Tech. 7, 1-9 (2001).
4. N. D. Gladkova, et al., “In vivo optical coherence tomography imaging of human skin: norm and pathology,” Skin Res. Tech. 6, 6-16 (2000).
5. M. Moncrieff, “A simple classification of the resolution and depth of imaging systems for pigmented skin lesions,” Melanoma Res. 12, 155-159 (2002).
6. J. M. Schmitt and G. Kumar, “Turbulent nature of refractive-index variations in biological tissue,” Opt. Lett. 21, 1310-1312 (1996).
7. C. A. Akcay, P. Parrein, and J. P. Rolland, "Estimation of longitudinal resolution in optical coherence imaging," Appl. Opt. 41, 1-7 (2002).
8. V. Mahajan, Aberration Theory Made Simple, (SPIE Press, Bellingham, WA, 1991) pp. 30-34.
9. C. A. Akcay, E. Clarkson, and J. P. Rolland, “Effect of source spectral shape on task-based assessment of detection and resolution in optical coherence tomography,” Appl. Opt. 44, 7573-7580 (2005).
10. J. M. Schmitt, S. L. Lee, and K. M. Yung, “An optical coherence microscope with enhanced resolving power in thick tissue,” Opt. Commun. 142, 203-207 (1997).
11. J. Izatt, Personal communication (2006).
12. B. M. Hoebling A. Fernandez, R. Haskell, E. Huang, W. Myers, D. Petersen, S. Ungersma, R. Wang, M. Williams, and S. Fraser, “An Optical coherence microscope for three dimensional imaging for developmental biology,” Opt. Express 6, 136-146 (2000).
13. F. Lexer C. K. Hitzenger, W. Drexler, S. Molebny, H. Sattamann, M. Sticker and A. F. Fercher, “Dynamic coherent focus OCT with depth independent transversal resolution,” J. Mod. Opt. 46, 541-553 (1999).
1. Introduction

Optical Coherence Tomography (OCT) is an imaging technique based on low-coherence interferometry that has the ability to image biological structures at sub 10 μm resolution approaching depths of up to 2 cm in transparent tissue [1]. An emerging area in high-resolution OCT, also referred to as Optical Coherence Microscopy (OCM),[2], is the field of dermatology for the diagnosis of skin disease[3]. As an example, skin cancer is a major public health problem in the United States and other developed countries. According to the American cancer society, one in every five Americans will get skin cancer during their lifetime. By 2010, the deadliest form of skin cancer, namely melanoma, is projected to one in fifty Americans. Excisional biopsy is the proven standard method for cancer detection. However, biopsies are typically done on a hit or miss basis because only small pieces of tissue are excised and dissected to check for cancerous cells. False negative rates are high in the early stage of the disease. Moreover, excisional biopsy imposes problems like the risk of cancer cell spreading, infection, and hemorrhage. An optical imaging procedure would aid the ability to follow suspicious lesions over time, non-invasively, maximizing the likelihood of detection at the earliest stage of the disease. Furthermore, since optical imaging is non-invasive, patient compliance is expected to increase significantly for periodic screening. Various optical techniques and their combinations are still under development to reach resolutions currently obtained in histopathology. OCM has been found to provide high resolution and to penetrate up to a depth of 2 mm in skin, a highly scattering media, which covers the epidermis and dermis layers, within which skin cancer cells may form [4,5]. Such lateral resolution and probing depths achieved so far have allowed distinguishing tertiary structures of skin lesions such as aggregates of melanocytes or naevocellular cells. Further improvement in this technique can make it possible to resolve and image secondary structures in skin at level 1 or the epidermis [5]. Thus OCM may in the future play a key role in the development of optical sensing for skin cancer diagnosis. OCM is also being developed towards greatly enhancing conventional biopsy by more precisely identifying the areas to be excised in vivo based on images of the epithelial layers. Finally, when OCM is developed to provide in the order of the micron lateral and axial resolution throughout the imaging volume, it will find applications not only in the clinic but also in various areas of material sciences including biology.

One of the established primary limitations of OCM today is the lack of sufficient lateral resolution over a usable imaging volume for diagnostic applications, even with high-numerical aperture imaging optics. While some sources of degradations are associated with the light scattering throughout the medium, dominant sources of image degradations that can surely be corrected using lens design techniques are (a) the out of focus image acquisition throughout most of the depth of the biological sample in the case of a fixed focus, typically aimed at half the depth within the biological sample to minimize the spread in the point spread function caused by defocus, and (b) the on-axis and off-axis optical aberrations introduced...
throughout a thick (i.e. up to 2 mm) and wide (i.e. ≥ 1 mm) imaging volume of mean index of refraction \( n \) significantly greater than 1 (e.g. \( n \) equals 1.4 for skin). In this paper, we present an investigation of how the technique of optical system design can be used to engineer an OCM imaging probe that overcomes these limitations, thus enabling, to a first order, invariant lateral resolution throughout the imaging volume. Scattering within the sample is also anticipated to contribute some additional broadening to the point spread function in spite of the tissue-induced phase distortions occurring close to the focus point[6] such effects are higher order and will be addressed in future reports of the research.

In the rest of this paper, we review resolution metrics in OCM and previous work in dynamic focusing. Next, we experimentally show the impact of high lateral resolution in an onion sample, a highly scattering biological sample, with an off-the-shelf 20X and 0.1 numerical aperture microscope objective integrated in an OCM setup. Finally, we provide the optical system design and layout of a custom-designed novel dynamic focus optical imaging probe operating at 800 nm across a 100 nm spectrum width, followed by the detailed design of its major component, a 10X and 0.28 numerical aperture liquid-crystal based dynamic focus microscope objective. Further, the imaging performance of this dynamic focus microscope objective is detailed.

2. Axial and lateral resolution in OCM

The depth resolution in OCM is imposed by the coherence length of the source, which in the case of a Gaussian power spectrum is given by

\[
\ell_c = \frac{2 \ln 2}{\pi} \frac{2 \lambda^2}{\Delta \lambda} = \frac{l_{\text{FWHM}}}{2}
\]

where \( \lambda \) is the mean wavelength in air, \( \Delta \lambda \) is the spectral width, and \( l_{\text{FWHM}} \) is the full width at half-maximum of the Gaussian source spectrum. The generalization to a non-Gaussian spectrum has been investigated by Ackay et al [7].

The lateral resolution in the sample, as in any optical system, is determined by the numerical aperture of the microscope objective \((NA_{\text{objective}})\) given by

\[
\hat{\delta} = \frac{1.22 \lambda}{NA_{\text{objective}}}
\]

Given that the depth of focus (DOF) is proportional to the transverse resolution of the system, invariant high lateral resolution, for example for an NA of 0.28 (of relevance to the design proposed in this research), can be obtained only across a small depth of the sample of the order of ±7 μm.

There exists a critical need in OCM to create optics with invariant lateral resolution throughout the depth of the sample being imaged and furthermore to match the lateral resolution set by the numerical aperture of the optics to the axial resolution set independently by the light source spectrum. Consequently, invariant resolution throughout the volume of the sample being imaged can be achieved. While conventionally, imaging optics such as for microscopy has been designed for a given fixed working distance, the goal of the research presented in this paper is to demonstrate that the design of imaging optics can be advanced to invariently image throughout a small volumetric sample in the order of a few millimeters in three dimensions, accounting for both refocusing as well as the optical aberrations introduced by the thickness of the sample, equivalent to the well established optical aberrations of a plane parallel plate placed in the path of a focused beam.[8]. Ultimately, task-based image quality assessment metrics can be defined for various optical and detection architectures of the OCM system to quantify and optimize the benefit of dynamic focusing optics in various applications, including clinical diagnostic [9].
3. Review of previous works in dynamic focusing and related techniques

The critical need for dynamic focusing in OCM has been recognized in order to empower OCM to effectively improve on imaging resolution [10]. Dynamic focusing has been previously investigated and implemented using several schemes for OCM. Schmitt et al first described a system that dynamically focused inside the sample by the use of a common translation stage for both the imaging objective and a retro-reflector used in the reference depth scan, thereby mechanically moving both the reference and sample arm in synchronicity [11]. In order to enhance depth resolution, multiple sources were simultaneously used to synthesize a very short temporal coherence length. Such a system or its equivalent is now in widespread use in laboratory experimental work [12].

Lexer, et al., suggested the use of an optical setup where the sample is moved for each depth scan while the arms of the interferometer remain constant. In this method, an oscillating beam focus formed through reflection from an oscillating mirror was axially magnified M times by lenses before illuminating the sample. At each discrete point of the oscillation, the optical path difference resulting from the oscillating beam focus first formed caused a corresponding dynamic shift in the beam focusing in the sample [13]. More recently, B. Qi, et al., proposed a high-speed dynamic focus control system based on a micro-electromechanical (MEMS) mirror that is deformable. The MEMS mirror shifts the focus position of the sample beam to match with the coherence gate position for each lateral scan [14]. With this design, dynamic focusing is achieved at high speeds since it does not involve bulk optics. An alternate method was proposed by A. Divetia et al. where dynamic focusing was demonstrated experimentally using a liquid-filled polymer lens whose curvature is controlled by variation of the hydraulic pressure in the lens. The latter system required no moving parts. Authors demonstrated a resolution of 10 μm across a 1.4 mm wide resolution target in air at the shortest focal length of the lens of 3 mm. While it was shown that the lens can vary its focal length up to a value of 16 mm, no quantification of resolution across depth was provided [15].

Drexler, et al., investigated a related technique to dynamic focusing he called zone focusing [16]. In this technique, individual layers in depth were imaged, each depth with a new focusing of the beam in that layer. An image fusion technique was then used in which tomograms from different layers were fused to form a 3D data set. This technique, similar to C-mode scanning used in ultrasound imaging, can be considered an alternate form of dynamic focusing, particularly applicable in Fourier Domain OCT (FDOCT). Three dimensional C-mode OCT imaging was proposed by Huber et al. using a high speed, frequency swept 1300nm source [17]. Multiple three dimensional data sets were obtained at various focal depths and fused to overcome the limitations of depth of field imposed by small focus spot sizes needed for high lateral resolution.

In a previous publication [18], we presented the early feasibility of the design of a dynamic focusing microscope, a precursor of that detailed in this paper. The new contribution of this paper is the final design and performance of the tunable-focus immersion microscope objective with an embedded addressable liquid crystal lens. Compared to the feasibility design, the overall form employs a lesser number of elements and glasses. Finally the lens was optimized to minimize distortion and to further improve the MTF across various zoom positions that define various focus depths. In both cases, the probe was designed to operate with a Ti: Sa pulsed laser centered at approximately 800 nm and a bandwidth of 100 nm.

4. Imaging at invariant high lateral resolution in a thick highly scattering biological sample

High lateral resolution requires a high NA beam focusing in the sample. In order to compensate for the loss in depth of focus, two dynamic focusing schemes can be implemented. In a time-domain OCM setup, enface scans can be performed [2], where the focal plane is moved continuously and synchronously with the position of the coherence gate in the sample. Such focus tracking in real-time allows maintaining invariant lateral resolution.
In a Fourier Domain (FD) OCM setup, multiple images acquired at different focal depths using C-mode zone focusing can be fused to get an invariant resolution 3D data set. The skin imaging probe presented in this paper has the ability to re-focus both continuously and in steps and can be used to obtain invariant high resolution in either OCM imaging scheme. In the imaging experiment presented here, we combined dynamic focusing in discrete steps together with a Fourier domain (FD) OCM system based on a fiber optic interferometer shown in Fig. 1. The FD-OCM experimental setup shown in Fig. 1 consists of a low-coherence broadband light source that illuminates the sample through a Michelson interferometer. Two scans were performed - a lateral B-scan that addresses the laterally adjacent sample positions, and a depth C-scan that synthesizes images from different depth positions in the sample by performing a series of laterally adjacent time-domain Low Coherence Interferometry (LCI) depth-scans.

In this experiment, we demonstrate the degradation of the images caused by a lack of depth of focus and the benefit of dynamically focusing with imaging in depth. The light source illuminating the system is a Titanium:sapphire laser (Femtosource Integral OCT; Femtolasers Inc.) with a spectral bandwidth of 120 nm centered at 820 nm corresponding to \( \approx 2.5 \mu \text{m} \) axial resolution in air or \( 1.7 \mu \text{m} \) in skin-equivalent tissue. The detector is a spectrometer with a 3648 CCD pixel line array (HR 4000; Ocean optics Inc.). In this imaging layout, 80% of the beam intensity from the coupler is collimated with a 1.3 mm diameter beam size (full width at 1/e\(^2\)) and then incident on a 20X magnification, 0.1 NA microscope objective integrated into the sample arm of the OCM system. The light was then focused on a piece of onion sample. The focusing achieved a 6.5 \( \mu \text{m} \) transverse resolution and a depth of focus range of approximately 100 \( \mu \text{m} \) in air. The remaining 20% of beam intensity was reflected by a mirror through a Fourier domain optical delay line located in the reference arm, whose main function is to control the overall dispersion in the system. Polarization was also adjusted by a polarizer placed in the reference arm to yield maximal signal modulation depth.

A piece of onion sample was scanned 1 mm laterally using a translation stage. Given the mechanically driven scanning in this experiment, each frame was acquired in 53 s with real time signal processing including zero padding, \( \lambda \)-k domain conversion and FFT. The sample of onion was analyzed at different depths by re-focusing the microscope objective, and images of different layers inside the sample were obtained. The small depth of focus caused by the high numerical aperture results in image degradation outside of the focused zone, which is shown in Figs. 2(a)-2(c) where the loss of lateral resolution and contrast is distinctly visible as we...
move out of the depth-of-focus region of the objective. The three images (a-c) were then fused to create a single image shown in Fig. 2(d) with an extended depth. The individual onion cells are easily resolved in these high resolution images because their cell size is much larger than the lateral resolution of the objective throughout the imaging volume. From visual inspection of the images, dynamic focusing is shown to help maximizing lateral resolution across a large depth of the sample.

5. Design of a dynamic focus microscope objective

5.1 Overall system design

Figure 3 shows the overall first-order probe layout comprising from left to right a microscope objective, a field lens, a microlenslet array, scan optics and a single or dual axis MEMS mirror for lateral scans. This probe was conceived to scan a 2 mm×2 mm sample cross-section and to image through a 10X microscope objective onto a 20 mm diameter field lens and microlenslet array. The choice of a 10X magnification is to create a handheld probe of about 25 mm in diameter. The purpose of the field lens is to render the beam parallel to the optical axis in order to match the telecentric operating condition of the scan optics. Telecentric scan optics minimizes sensitivity of the positioning of the microlenslet array in this design. The microlenslet array in this design enables matching of the NA of the field lens to the working NA of the scan optics in object space. The sampling interval in tissue is 2 μm and each corresponding microlenslet is 20 μm in diameter which accounts for the 10X magnification.
The illuminating beam is scanned and collected by the MEMS mirror via the scan optics and detected by a CCD camera.

5.2 Design and analysis of the dynamic focusing microscope objective

Among all components of the probe shown in Fig. 3, the novelty of the design lies in the integration of the dynamically focusing optical element inside the microscope objective. A liquid crystal lens constitutes an enabling technology to varying focus depths without physical motion of the optics; it however requires integration into an optical design. Fig. 4(a) shows the optical layout of the dynamic focus microscope objective, where the liquid crystal lens was built into the microscope objective. In any ideal imaging system, the optical path traveled by the chief and marginal rays from the object to image is equal. Such constant optical path difference can be maintained either by varying the curvature or the refractive index of the optics. A liquid crystal element with flat surfaces functions as a lens when a refractive index gradient is created along the radius of the element in order to simulate the optical path difference of a normal, spherical bi-convex lens of constant refractive index. Such refractive index variations can be achieved by the application of an electric field gradient, altering the birefringence [19]. The GRIN profile in a lens element can be specified by a double power series which depends on the spatial coordinates in the element:

\[ \Delta n = n_2 - n_1 = \frac{r^2}{2df} \]  

where \( r \) is the radius of the lens, \( d \) is the cell gap, \( f \) is the focal length, and \( \Delta n \) is the birefringence. The GRIN profile in a lens element can be specified by a double power series which depends on the spatial coordinates in the element:

![Image](image_url)
\[ n(r, z) = n_{00} + n_{01} z + n_{02} z^2 + n_{03} z^3 + n_{04} z^4 + n_{10} r^2 + n_{20} r^4 + n_{30} r^6 + n_{40} r^8 \]  

(4)

where \( n \) is the index at some point in the lens, \( n_{00} \) is the base index of the lens, \( n_{0i} \) and \( n_{0j} \) are coefficients of the index gradient and \( r \) is the radial position where the index is evaluated \((r^2 = x^2 + y^2)\). When the index of refraction depends only on the distance from the optical axis \( r \), the gradient is said to be radial and its representation simplifies to

\[ n(r) = n_{00} + n_{10} r^2 + n_{20} r^4 + \ldots , \]  

(5)

also known as a Wood lens [20].

The liquid crystal dynamically focusing element was modeled as a special case of the Wood lens, where the base index \( n_{00} \) was allowed to vary independently across the different focus positions. On the other hand, the radial coefficients \( n_{0i} \) were coupled to vary simultaneously across all focus positions. This would imply that a single equation describing the relationship between required refractive index at the center of the liquid crystal element and the focal ‘z’ depth in the sample would be sufficient to address the dynamic lens effectively. The refractive indices at all other spatial positions on the lens can be computed from the base index based on the radial coefficients, and represent a similar gradient in all focus positions. This enables a smoother and more accurate transition from each focus point, and significantly reduces the amount of numerical data computation and simulation time.

The immersion microscope objective was designed for a NA of 0.28 to achieve a resolution of 4 \( \mu \)m. The liquid crystal lens serves to dynamically refocus into skin tissue up to 2 mm in depth. An immersion gel of refractive index 1.45, closely matching that of skin was used since it enables finer resolution and brightness by index matching between the last element of the probe and the skin. In the absence of gel, losses caused by reflection at the air-skin interface would be significant [21]. Such a gel was chosen to yield 100% transmission over the operating spectrum. The liquid crystal lens was designed to be the first element of the objective, where the aperture diameter is the smallest, since the effective speed of focus achieved is inversely proportional to the diameter of the lens. The design was optimized for invariant resolution at three depths of the skin sample, namely, 0 mm (skin surface), 1 mm inside the skin, and 2 mm inside the skin. The MTF performances of the system at these focus positions are shown in Fig. 3. Given that the maximum frequency of each plot is 240 cycles/mm, results show that the microscope objective achieves a resolution of 4 \( \mu \)m, where resolution is defined to correspond to the spatial frequency at 30% MTF. Such MTF performance further yields, an as-built MTF of 20%, given that tolerancing of the system indicates a maximum 10% drop in MTF across zoom positions for precision grade tolerances. Results (see Fig. 4) also reveal a less than 2.5 \( \mu \)m distortion in all three zoom positions.
6. Conclusion

We investigated the scope of a dynamic focusing optical coherence microscope design for imaging deep in biological tissue, not only at high axial but also high lateral resolution throughout the imaging volume. A lateral resolution of 4 μm across a focus depth of up to 2 mm in tissue was achieved. In the current implementation of the dynamic focusing, LC technology was considered, which, for a 3 mm diameter lens as needed in this design, has the primary disadvantage of being unable to scan at sufficient speed in order to facilitate video rate imaging. Specifically, a liquid crystal lens approximately 3 mm in size needs several hundred milliseconds to complete one z-scan. Thus, given the cost of custom optics, hardware implementation of this novel design would be premature given that it would not yet achieve video-rate scanning of tissue in vivo. This paper however clearly demonstrates via experimental imaging and a detailed custom optical design that invariant high lateral resolution can be achieved in OCM for biological tissues. Future breakthroughs in the response speed of liquid crystal lenses or equivalent technologies, liquid lenses being a potential candidate, will enable the emerging technology of dynamic focusing with no moving parts and high image quality performance.

Acknowledgments

We thank the Florida Photonics Center of Excellence, the I2-Lab Foundation at the University of Central Florida and US Army Medical Research and Material Command for supporting this research. We also thank Shin-Tson Wu for technical discussions about the capability of state of the art liquid crystal lenses, and Optical Research Associates for the educational license of CodeV™ to conduct this research.