

Medical Imaging Applications

Subjects: **Others**

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The advancement of micro-electro-mechanical systems and small-sized optical components enable the fabrication of imaging devices with promising performance as compared to the traditional medical devices. Such devices enable the detection of lesions/tumors at an earlier stage and act as a guide during surgical procedures, increasing diagnostic capabilities. A variety of different imaging techniques used in medical applications are reviewed in here.

optical scanners

medical imaging

MEMS actuators

OCT

confocal

non-linear

photoacoustic

endoscopy

1. Introduction

The growth and development of optical components and, in particular, the miniaturization of micro-electro-mechanical systems (MEMSs), has motivated and enabled researchers to design smaller and smaller endoscopes. The overarching goal of this work has been to image smaller previously inaccessible luminal organs in real time, at high resolution, in a minimally invasive manner that does not compromise the comfort of the subject, nor introduce additional risk. Thus, an initial diagnosis can be made, or a small precancerous lesion may be detected, in a small-diameter luminal organ that would not have otherwise been possible. Continuous advancement in the field has enabled a wide range of optical scanners.

2. Imaging Technologies

Imaging devices used in medical applications are characterized by their resolution. Non-invasive technologies, such as MRI, CT, and ultrasound, provide *in vivo* imaging of tissue structures with a large penetration depth, but the resolution is limited. Endoscopic imaging permits imaging body structures with finer details, however, they are invasive in some cases. Fiber optics allow the fabrication of imaging devices that are flexible and can image the target area via hollow cavities. The recent advances in the optical and mechanical fields allow *in vivo* imaging of tissue surfaces to be performed by using devices having a very fine resolution at the micrometer level.

In an endoscopic optical imaging device, the laser light is illuminated on the target surface using an optical fiber or by deviating the light by micro mirrors. The image can be either reconstructed by direct reflectance, or via detection of the fluorescence light using optical fibers, lenses, or CCD/CMOS cameras. In the case of direct reflectance imaging, the morphological information of the tissue structure is obtained, while fluorescence provides information about the inner cell or tissue structures by labelling them using fluorophores. Fluorophore materials are usually

added from outside to stain the target sample and emit light at a wavelength higher than that of illumination, increasing the contrast in the images.

In biomedical imaging devices, OCT is one of the most used techniques. OCT is a direct reflectance imaging technique where the imaging contrast is provided by the change in the refractive index of the tissue media causing a variation of intensity of the reflected light^[1]. Most of the current OCT systems are FD-OCT based, where the information about the depth scan is calculated by using the inverse Fourier transform of the backscattered light spectrum. The fast-axial scanning is obtained by sweeping the light source, which gives high-resolution images due to fast signal acquisition and provides images with a large signal to noise ratio. Given the current state of the art, ophthalmology is the predominating application for OCT due to the low laser output compatible with the ophthalmological structures permitting the imaging without damaging the tissue structures^{[2][3][4]}. The transparency and low light scattering of the aqueous humor media allows imaging of the ocular surfaces at a greater depth with resolution independent of the surface depth. In addition to ophthalmology, deep tissue penetration and high resolution morphological and functional imaging make OCT a promising technology to assess the artery lumens in cardiology^[5], tissue structures of the biliary tract, and the gastrointestinal (GI) tract, especially for Barrett's esophagus^[6]. Furthermore, the skin is a highly light-scattering tissue that contains a large number of inhomogeneities. OCT makes it possible to detect and diagnose various skin diseases and lesions^[7]. OCT is also a useful method to monitor lesions in the enamel and dental structures of the teeth^[8].

Another promising technology is confocal microscopy, which provides high-resolution imaging of thick specimens by virtually slicing them using optical sectioning^[5]. It is possible to image the tissue structures in either confocal or fluorescence mode. In the latter case, the target tissue structure is stained using fluorescent dyes to enhance the contrast in the image. Combining confocal microscopy with the optical fibers in a fibered confocal fluorescence microscopy (FCFM), Cell-viZio-developed mini optical probes can be used for microcirculation imaging of the stomach, ear, mesentery, kidney, and conjunctive tissues^[9]. Other applications of confocal endomicroscopy include functional imaging of the GI tract^[10], liver, pancreas, and reproductive tracts after the application of a fluorescent agent that provides contrast to the image^[11].

In addition to OCT and confocal microscopy, nonlinear microscopy also finds many applications in tissue structure imaging. Nonlinear microscopy comprises multiphoton imaging, higher order harmonic generation, and coherent Raman scattering microscopy. These techniques allow the structural and chemical changes of cells, tissues, or organs to be inspected with deep tissue penetration and minimal photobleaching and phototoxicity. The use of a pinhole and the signal generation from only a localized specific area provide high-contrast images. The cellular level resolution allows these techniques to be used for imaging and diagnosing tumors at early stages in the skin and ovary. In particular, TPEF is used to image endothelial cells, while SHG is used to image collagen fibers, and CARS is used for the detection of chemical changes at the cellular levels^[12].

Another technique is photoacoustic imaging. In this case, laser pulses are emitted towards the target tissue surface, which absorbs the light and generates an ultrasonic emission detected by an ultrasonic transducer. Thus, the imaging contrast is based on the absorption spectra of the media. These devices find applications in measuring

the oxygen level in the blood and guiding surgical tools during surgical procedures. Furthermore, photoacoustic imaging is particularly suitable to image the breast, brain, and GI tract for cancer diagnosis due to the high optical absorption contrast^{[13][14]}.

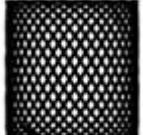
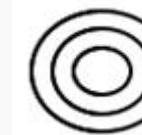
Apart from imaging techniques, optical devices can monitor the target sample either from a side of the distal end perpendicular to its axis, or from the front end of the device providing a peripheric or en face image, respectively. In side-viewing devices, the probe is rotated to visualize the circumferential structural area. A forward-viewing imaging probe provides an image of the front surface and can be used as a guide for surgical procedures. It should be noted that forward-viewing imaging requires a transverse scan of the light beam, which poses challenges in the miniaturization of the imaging device.

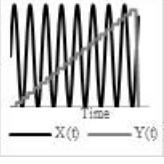
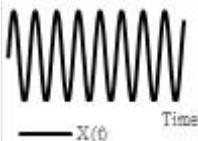
In advanced imaging systems, the resolution of images is improved by scanning the laser beam across the surface. Often the systems are vibrated at resonance to get maximum light displacement at the distal end of the scanner. Since it is difficult to get resonant scanners for applications requiring low-frequency scanning, imaging devices based on the use of non-resonant or semi-resonant frequencies have been developed for this specific requirement.

Optical fibers are mainly actuated using electrostatic, electrothermal, piezoelectric, electromagnetic, or shape memory alloys. The electrostatic actuators are easy to fabricate and rapidly responsive but have a limited scanning range and moderate actuation force. On the other hand, electrothermal actuators can be made in very small dimensions and can provide large forces. In this case, they can actuate at very high frequencies, but the heat dissipation can compromise the material performance. Piezoelectric actuators are widely used in optical fiber endoscopes because of their fast response. However, the manufacturing of very small-sized endoscopes based on these actuators pose some challenges. The electromagnetic and shape memory alloy actuators are better suited for larger dimensional scales.

Based on the type of the actuator and power/voltage profile provided as the input, it is possible to generate 2-D scanning patterns in a raster, spiral, Lissajous, circular, or propeller shape. Raster and Lissajous patterns provide uniform light intensity within the light scanning area. The spiral pattern is easy to obtain but has more light intensity in the center compared to the edges. Each pattern has its own advantages and disadvantages. [Table 1](#) summarizes the pros and cons of the different scanning patterns in detail.

Table 1. Comparison table for different scanning patterns

	Raster	Spiral	Lissajous	Circular	Propeller
Scanning pattern					

Actuation pattern				 Y(t) constant rotation
Advantages	Uniform light intensity	Easy to get, area is swept by changing the driving voltage	Uniform light intensity, most used	Possible to get circular pattern with 1D actuation, area is swept by changing the driving voltage
Disadvantages	Points are scanned at different times can lead to motion artifacts	Light intensity is higher in center	Fill factor highly depends on the frequency ratio, quasi-random pattern	Non uniform light intensity, the rotation of miniaturized structure requires complex and expensive devices

A descriptive summary of some recently developed optical imaging devices for medical purposes using a variety of different imaging techniques, configurations, actuating methods, and scanning patterns is shown in [Table 2](#). The scanning catheter developed by Aguirre et al. is a side-viewing OCT endoscope, where the light is transported to the distal end using an SMF, and the forward mirror used to deflect the light is vibrated at resonance using angular vertical electrostatic comb drives and generates a raster scanning pattern^[15]. Park et al. developed a forward-viewing spectral domain OCT endomicroscope. In this case, an SMF is excited at resonance using piezoelectric tube actuators and describes a Lissajous scanning pattern^[16]. Myaing et al. reported a forward-viewing two-photon fluorescence microscope. A double clad fiber (DCF) is used to deliver light to the target sample and collect the fluorescence signal. The spiral pattern is generated by the fiber tip using a piezoelectric actuator exciting the tip at resonance^[17]. Recently, Li et al. developed a 2.4-mm confocal endomicroscope using electrostatic actuators for laser light scanning. Such a probe with a 1.5-μm lateral and 12-μm axial resolution is compatible with the finer operating channel of current endoscopes^[10].

Table 2. Comparison of some advanced optical scanning devices.

	Working Principle	Frequency	FOV	Drive Voltage	Scanner Dimensions	Scanning Pattern	References
OCT using rotational MEMS probe	Micromotor	1 kHz	-	>1 V	2.4 mm (in diameter)	Radial	[18]
MEMS fiber scanner for confocal microscopy	Electrothermal actuation	239 Hz (x-axis) 207 Hz (y-axis)	378 μ m \times 439 μ m	16 Vpp (duty cycle 13%)	Diameter (1.65 mm) Rigid length (28 mm)	Lissajous scanning	[19]
Fiber scanner for forward viewing endoscope	Piezoelectric tube	86 Hz (x-axis) 97 Hz (y-axis)	732 μ m \times 591.7 μ m	40 Vac	Diameter (3.2 mm) Rigid length (50 mm)	Lissajous scanning	[16]
OCT based on 2D MEMS mirror	Electrothermal actuation	1.25 Hz (fast scan actuator pair) 0.0125 Hz (longitudinal)	2.3 mm \times 2.3 mm	0–4 V ramp (fast scan) 0.5–3.5 V ramp (slow axis)	Diameter (5.8 mm) Rigid length (12 mm)	Lissajous scanning	[20]
Scanning fiber endoscope	Piezoelectric tube	5 kHz	200 μ m (in diameter)	<20 Vac	Diameter (1.2 mm -1.7 mm) Rigid length (9 mm)	Spiral scan pattern	[21][22]
Multi-Photon Endoscope	Piezoelectric tube	35 Hz	900 μ m (in diameter)	40 Vac	Diameter (5 mm) Rigid length (4 cm)	Circular pattern	[23]
OmniVision camera	Chip on tip camera	-	364 μ m \times 364 μ m	3.3 Vac	650 μ m \times 650 μ m \times 1158 μ m	-	[24]
FCFM using Cellvizio	Scanning mirrors at proximal end	4 kHz	160 μ m \times 120 μ m \div 400 μ m \times 280 μ m	-	350 μ m \div 1.8 mm diameter 20 mm	-	[9]

Working Principle	Frequency	FOV	Drive Voltage	Scanner Dimensions	Scanning Pattern	References	
Scanning confocal microscope	Electrostatic torsional mirrors	4.3 kHz (fast scan) 1.07 kHz (slow scan)	100 μ m (in diameter)	20 V	1.2 mm \times 2.5 mm \times 6.5 mm	Lissajous scanning	[25] [26]
Two-photon microscope	Electrostatically actuated mirrors	1.08 kHz (fast scan) 0.65 kHz (slow scan)	295 μ m \times 100 μ m	60 V	2.0 cm \times 1.9 cm \times 1.1 cm	Raster scanning	[27]
Side view endomicroscope	Electrostatically driven mirror	12 kHz (fast scan) 3 kHz (slow scan)	350 μ m \times 350 μ m	60 V _{pp}	2.4 mm (in diameter)	Lissajous scanning	[10]
Non-resonant MEMS scanner for OCT	Thin film piezoelectric	50 Hz	1 mm \times 0.7 mm	40 V _{pp}	2.2 mm \times 2.7 mm	Lissajous scanning	[28]

devices are better at imaging the tissue surface by illuminating the light from the side of the probe, while others are designed for direct en face imaging. In addition, the selection of an imaging device for a medical purpose is also based on the size, the usage simplicity, and the ergonomics of the device. Another relevant consideration for endoscopic devices is their suitability for reprocessing; that is their suitability multiple uses. Reprocessing, which generally requires washing optical devices using chemicals to reduce risks of infection, can be a very expensive process. Endoscopes should also be mechanically robust; the handling of the endoscopes during reprocessing may damage the endoscopes. For example, a small crack could be initiated, leading to light leakage and the consequent considerable degradation of the performance of the device.

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