Forward Viewing OCT Endomicroscopy

by

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B.S. Biomedical Engineering
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ABSTRACT

A forward viewing fiber optic-based imaging probe device was designed and constructed for use with ultrahigh speed optical coherence tomography in the human gastrointestinal tract. The light source was a MEMS-VCSEL at 1300 nm wavelength running at 300 kHz sweep rate, giving an effective A-line rate of 600 kHz. Data was acquired with a 1.8 GS/s A/D card optically clocked by a maximum fringe frequency of 1 GHz. The optical beam from the probe was scanned by a freely deflecting optical fiber that was mounted proximally on a piezoelectric tubular actuator, which was electrically driven in two perpendicular dimensions to produce a spiral scan pattern. The probe has a 3.3 mm outer diameter and is intended for endoscopic imaging. Multiple optical systems were designed to enable microscopic imaging at variable fields. The probe could also be electrically zoomed by tuning the driving voltage to the piezoelectric actuator, reducing the deflection range of the scanning fiber and thus the scanned field. The optical and mechanical design of the probe was optimized for both axial and transverse compactness.

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6. References
Background

a. High speed swept source OCT

The advent of Fourier domain OCT (FDOCT) augured a new generation of high-speed imaging that was not only faster but also promised higher signal to noise ratio and sensitivity[1, 2]. FDOCT with swept wavelength lasers, so-called 'swept source OCT' has thus far enjoyed a much more rapid scaling in speed than its 'spectral' OCT counterpart, due to limitations in line scan camera technology. In endoscopic applications, high speed is particularly favored, due to the challenges of overcoming patient motion and imaging at high resolution with sufficient transverse sampling.

One of the first early designs for a swept wavelength laser with a high sweep rate and bandwidth for clinical applications was a semiconductor laser with a polygonal mirror filter[3]. Each mirror position would reflect only a narrow band of wavelengths back into the laser cavity, such that the continuous rotation of the mirror would rapidly tune the wavelength. The polygon mirror laser was validated in an animal in vivo study demonstrating large-area coverage enabled by a sweep rate of 54 kHz[4]. A later design, known as Fourier domain mode locking (FDML), used a fiber-based Fabry-Perot tunable filter to transmit a narrow band of wavelengths, such that a sinusoidal drive to the filter would similarly produce a frequency sweep. Additionally, the sweeps were propagated into a long cavity length whose round trip time was equal to the period of the filter operation, such that light returning to the gain medium would not require repeated lasing build up[5]. This technology applied to endoscopic OCT applications was found to scale to much higher speeds; initial in vivo validation in a rabbit model attained a sweep rate of 100 kHz[5], and subsequent work with a double-buffered FDML[6] reached a sweep rate of 480 kHz[7]. More recently, a 4x buffered FDML was used to demonstrate ex vivo intravascular imaging at 1.6 MHz sweep rate[8].

Yet another technology that has enabled ultrahigh speed OCT is a vertical cavity surface emitting laser based on MEMS fabrication (MEMS-VCSEL). The extremely
small filter cavity length and highly stable actuation enabled by MEMS produced extremely high sweep rate, large tuning range, and short instantaneous linewidth, which optimized axial resolution and imaging range[9]. The extremely long coherence length was demonstrated to image objects several inches long and accurately measure the length of a meter-long optical fiber[10]. Volumetric in vivo OCT imaging of a rabbit GI tract with a 1310 nm MEMS-VCSEL running at 500 kHz sweep rate was demonstrated, giving an effective A-line rate of 1 MHz, with a micro-motor imaging probe rotating a prism at 400 Hz[11]. Swept source optical coherence microscopy with the MEMS-VCSEL was also shown, with optical clocking at 400 MHz such that the OCT fringes were sampled linear in wavenumber, and thus did not require k-space interpolation before Fourier transform processing[12].

b. Fiber optic catheter probes

i. Side viewing probes

The flexibility of OCT system design was such that the sample arm could be any form of optical path, including optical fibers that had an extremely small footprint and were suited for highly compact applications. Tearney and colleagues in 1997 were one of the first to consider a fiber optic probe device that could scan a beam inside luminal organs, using a prism to reflect the beam to the side of the probe, and a proximal motor to rotate the optical fiber and thus the beam around a full circumference[13]. The simplicity and compactness of this design has carried it to the present day, in which both commercial and research efforts continue to build and develop proximally rotated probes, where an additional proximal pullback of the probe provides a second dimension of beam scanning that enables 3-dimensional OCT[14-16]. However, there is mechanical instability associated with actuating a long probe with multiple bends at higher speeds, and the optical rotary junction has significant losses.
Multiple groups have studied the use of scanning mechanisms that could be miniaturized into the distal end of the probe. Work by Tran[17] and Herz[18] demonstrated a micro-sized rotary motor that rotated a prism inside the probe. More recently, a micromotor was used to demonstrate ultra-high speed OCT in the rabbit GI tract[11]. Tsai also showed a side viewing probe based on a piezoelectric cantilever[7]. Side viewing probes continue to see technological advances and important clinical applications, but the continued dependence on a proximal actuation for a second scan dimension limits image quality and resolution in the pullback direction. A spiral actuation based on a motorized screw thread has been proposed to provide two-dimensional scanning, but has limitations in speed and fabrication[19]. 2-dimensional side scanning has also been achieved using a 2D MEMS mirror that replaces the prism[20, 21]. Also, the side viewing nature of the probe is such that only a small section of the circumferential field can be imaged when the probe is in contact, which is the optical regime for high magnification and focal imaging. The side-viewing design has been found useful for intraluminal circumferential imaging with the help of a spacing device that centers the optics in the lumen, such as a balloon[22, 23] or capsule[24]. However this design limits the ability to image smaller, focal areas at a short working distance.

ii. Forward viewing probes

While side viewing probes have obvious advantages in imaging luminal walls, they are less optimal in the context of imaging focally or on non-luminal organ surfaces. Also, forward imaging instruments are functionally similar to that of clinical endoscopes and may be more intuitive for clinicians. Early work by Boppart demonstrated one-dimensional forward scanning with a piezoelectric cantilever[25]. Other one-dimensional forward scanning mechanisms have also been shown, such as magnetic solenoid actuation[26], use of a Risley prism to scan a toroidal geometry[27], and paired gradient index lenses with angled surfaces[28]. Similar to side viewing probe technology, groups also began to exploit 2-dimensional scanning mechanisms. These were primarily either orthogonally mounted pairs of piezoelectric bending actuators, or piezoelectric tubes capable of transverse bending in orthogonal directions, which were used to actuate an
optical fiber and thus scan the optical beam. Bender pairs could be actuated orthogonally without mechanical coupling between axes, and were thus exploited to produce nonresonant scanning such as a raster pattern[29, 30]. However, nonresonant scanning required a large voltage to generate sufficient scan range on the fiber deflection. Another implementation of the paired benders drove the scanning fiber at resonance in one axis, and nonresonantly in the other axis, thus producing a raster with a fast (resonant) and slow (nonresonant) axis[31]. However the use of benders tended to increase both transverse and axial footprint of the probe, due to the awkward asymmetric geometry.

The piezoelectric tube actuator is favored for its cylindrical symmetry, which allows an extremely compact footprint[32-35]. Seibel was the first to demonstrate use of a tube actuator to produce 2-dimensional optical scanning, by exciting the resonances in both axes with amplitude modulation to produce a spiral scan pattern[32, 36, 37]. Recent work by Seibel has achieved a footprint of 1 mm diameter and a rigid length of less than 10 mm[36]. Li has demonstrated the technology with 3-dimensional OCT and 2-photon microscopy, producing volumetric and en face images. Record speed with volumetric OCT was demonstrated by Zhang[38] using a 240 kHz FDML swept source and 338 Hz scanning resonance. However, resonant scanning in the kHz range has been limited to time-domain OCT implementations, due to speed limitations in commercially available swept source technology. This limits the potential to achieve high volumetric frame rate, which is generally a requirement for clinical applications, particularly in endoscopy where stabilizing the probe during in vivo image acquisition may be difficult.

c. Clinical endomicroscopy

i. Pit patterns in upper and lower GI
Patterns in the gastrointestinal surface (known as 'pit patterns') are a diagnostic indicator of metaplasia and advanced disease. A seminal paper by Kudo and colleagues found that neoplasia could be detected by structural markers in the mucosa i.e. pit patterns, using magnifying endoscopy and a contrast-enhancing spray of indigo carmine[39]. The indigo carmine was found to enhance the the surface patterns of mucosal lesions such that they could be classified into types, namely Type I (round pits), Type II (stellar or papillary pits), Type III (large tubular or roundish pits), Type III (small tubular or roundish pits), Type IV (branch-like or gyrus-like pits), and Type V (non-structural pits), where Types III, IV, and 5 are neoplastic.

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>round pits</td>
</tr>
<tr>
<td>II</td>
<td>stellar/papillary pits</td>
</tr>
<tr>
<td>III</td>
<td>small tubular/roundish pits</td>
</tr>
<tr>
<td>IIII</td>
<td>large tubular/roundish pits</td>
</tr>
<tr>
<td>IV</td>
<td>branch-like pits</td>
</tr>
<tr>
<td>V</td>
<td>non-structural pits</td>
</tr>
</tbody>
</table>

Fig. 1. Kudo pit pattern descriptors. Adapted from [39]. Type III and above are considered neoplastic. The patterns are visible with advanced optical technologies such as magnification endoscopy and high contrast imaging methods e.g. narrow band imaging and chromoendoscopy.
This classification of pit patterns was also found by Endo to have diagnostic value in the esophagus, such that there was a statistically significant relation between the patterns and physiologic expression of mucin indicative of Barrett's[40]. The visualization of these pit patterns by advanced optical technologies accompanying conventional endoscopy has the potential to guide biopsy to regions of interest with higher diagnostic yield than conventional 4-quadrant random sampling. Multiple groups have assessed the diagnostic potential of pit patterns using a number of optical-based technologies that allow in vivo assessment (so-called ‘optical biopsy’) during an endoscopic procedure.

ii. Competing optical technologies

Several emerging optical technologies have been proposed to evaluate these patterns in vivo, such as magnification endoscopy[39], narrow band imaging (NBI)[41], and confocal laser endomicroscopy (CLE)[42]. Currently, these methods have demonstrated promising sensitivities and specificities in small clinical studies, but have not reached a consensus in large clinical studies across different centers due to variation in operator experience and proficiency, and thus have yet to achieve widespread acceptance and usage in the gastroenterology community.

Magnification endoscopy enjoyed early success in conjunction with superficial staining methods (also known as magnification chromoendoscopy), which led to seminal work in the development of pit pattern classifications in upper and lower GI[39, 43]. Kiesslich found that magnification chromoendoscopy could differentiate between neoplastic and non-neoplastic colonic lesions in patients with longstanding ulcerative colitis with a sensitivity and specificity of 93%[44]. The technique was also reported to be successful in identifying adenomas[45], and flat[46] or diminutive lesions[47] in the colon. However dye staining is known to be time consuming, messy, and not widely conducted in the US, and magnification endoscopy equipment has had a limited penetration in markets outside of Japan.
Narrow band imaging uses optical filters that select for blue light, which is known to have higher absorption by hemoglobin and only superficial penetration into tissue, which results in enhanced contrast on the mucosal surface, simulating the contrast effects of dye chromoendoscopy\[48\]. NBI has been reported to have 94% sensitivity and 76% specificity for detection of high grade dysplasia in the esophagus\[48\], and an accuracy of up to 91% when predicting colonic polyp type\[49\]. However, success with NBI has not been universal in the community, and clinicians have thus far been conservative in their evaluation\[50\]. NBI has maximal impact when used in tandem with magnification endoscopy, which has limited availability.

CLE is based on the classic confocal microscope design that uses a pinhole to focus light from a specific depth plane, enabling micron resolution and depth sectioning\[51\]. CLE is available either integrated into an endoscope (endoscopic CLE or eCLE) or as a separate probe that is compatible with an endoscopic accessory port (probe CLE or pCLE). Images are acquired with the scope or probe in direct contact with the tissue surface to minimize motion artifacts. Kiesslich found eCLE to predict Barrett’s neoplasia with sensitivity of 92.9% and specificity of 98.4%\[52\], and diagnose colorectal neoplasia with sensitivity of 97.4% and specificity of 99.4%\[53\]. pCLE has been less successful, with reported sensitivity as low as 12% in diagnosis of Barrett’s neoplasia\[54\], and accuracy of 71.9% when assessing colonic lesions\[4\]. However the field of view of CLE is limited to 475 x 475 um in eCLE and 600 um in pCLE, and has a depth penetration of 250 um in eCLE and 130 um in pCLE\[55\], such that CLE use is limited to only highly focal and superficial inspection.

Optical coherence tomography (OCT) can perform cross-sectional, three dimensional and en face visualization, with tissue depth penetration of up to 2 mm. Multiple studies have investigated OCT imaging of the gastrointestinal tract\[16, 23, 24, 56, 57\]. An early analysis of 177 biopsy-correlated images from 55 patients suggested that OCT could diagnose high grade dysplasia and intramucosal carcinoma with 83% sensitivity and 75% specificity, although the scoring was performed by a single pathologist\[58\]. The concept of mapping volumetric information over a large
circumferential area of the esophagus using a balloon or capsule has been proposed[22-24]. The capsule has been said to have potential clinical utility in the screening of Barrett's esophagus without sedation, which may extend availability of the procedure beyond endoscopy into the realm of primary care, while reducing patient discomfort and anxiety[24]. Volumetric OCT has also been shown to have an impact on guiding treatment for Barrett's esophagus, in the detection of buried glands that could be a marker of disease recurrence[56], and in the measurement of Barrett's epithelium thickness as a marker of treatment response[57]. However, there has yet to be a clinical demonstration of an OCT implementation that provides microscopic information of a focal area such as with CLE. An in vivo modality combining the variable fields of view of magnification endoscopy, and the microscopic resolution and volumetric capability of CLE could be the ultimate imaging solution for gastrointestinal precancer diagnosis.
Theory

a. Piezoelectric tube actuation

Piezoelectricity is a well-known phenomenon in which an applied force on a piezoelectric material yields an electric field, or when the converse occurs, i.e. an applied field yields a mechanical response such as stretching or bending. Here we will briefly overview piezoelectric theory and mechanical analysis of a tube, which will culminate in the expression for the actuated deflection for a piezoelectric tube. For brevity, a number of fundamental relations will be introduced ad hoc without elaborate derivation, but the reader is encouraged to seek further explanation in the references[59]. All theoretical quantities are standardized and defined in the ANSI/IEEE Standard on Piezoelectricity[60].

First we define a type of ‘total free energy’, known as electric enthalpy:

\[ H = U - ED, \]

where \( H \) is electric enthalpy, \( U \) is internal energy, \( E \) is the electric field tensor, and \( D \) is the electric displacement tensor. In linear piezoelectric theory,

\[ H = \frac{1}{2} c_{ijkl} S_{ij} S_{kl} - e_{ijkl} E_{i} S_{kl} - \frac{1}{2} \epsilon_{ij} E_{i} E_{j}, \]

where \( c \) is the elastic tensor, \( e \) is the piezoelectric tensor, \( \epsilon \) is the dielectric tensor, and \( S \) is the strain tensor on the piezoelectric material. Note that \( c, e, \) and \( \epsilon \) are intrinsic characteristics of the material, and relate electric fields to electric enthalpy. With further thermodynamic considerations, it can be shown that

\[ T_{ij} = \frac{\partial H}{\partial S_{ij}}, \]

\[ D_{i} = -\frac{\partial H}{\partial E_{i}}. \]

where \( T \) is the stress tensor. The derivatives produce the following constitutive relations of piezoelectricity:
\[ T_y = c_{ijkl} S_{kl} - e_{kj} E_k \]
\[ D_i = e_{ikl} S_{kl} + e_{ij} E_k \]

Qualitatively we may begin to appreciate the piezoelectric effect, where an applied electric field adds a term to the classic stress-strain relation, and an applied strain similarly modifies the well-known relation of electric displacement and field. For the purpose of piezoelectric actuation, i.e. the deformation of the material in response to an applied field, the first expression is more relevant. Rearranging terms in accordance with engineering convention gives

\[ S_y = s_{ijkl} T_{kl} + d_{kj} E_k \]

where the more commonly used engineering terms \( s \) is a different form of elastic tensor, and \( d \) is the piezoelectric tensor. (It can be shown that \( c \) and \( s \) are related by the Kronecker delta, and \( d \) and \( e \) by a scale factor.) The constitutive equation may be written in full matrix form (the stress/strain has 6 unique elements due to the tensorial symmetry of the shear components):

\[
\begin{bmatrix}
S_1 \\
S_2 \\
S_3 \\
S_4 \\
S_5 \\
S_6
\end{bmatrix}
= \begin{bmatrix}
s_{11} & s_{12} & s_{13} & s_{14} & s_{15} & s_{16} \\
s_{21} & s_{22} & s_{23} & s_{24} & s_{25} & s_{26} \\
s_{31} & s_{32} & s_{33} & s_{34} & s_{35} & s_{36} \\
s_{41} & s_{42} & s_{43} & s_{44} & s_{45} & s_{46} \\
s_{51} & s_{52} & s_{53} & s_{54} & s_{55} & s_{56} \\
s_{61} & s_{62} & s_{63} & s_{64} & s_{65} & s_{66}
\end{bmatrix}
\begin{bmatrix}
T_1 \\
T_2 \\
T_3 \\
T_4 \\
T_5 \\
T_6
\end{bmatrix}
- \begin{bmatrix}
d_{11} & d_{12} & d_{13} \\
d_{21} & d_{22} & d_{23} \\
d_{31} & d_{32} & d_{33} \\
d_{41} & d_{42} & d_{43} \\
d_{51} & d_{52} & d_{53} \\
d_{61} & d_{62} & d_{63}
\end{bmatrix}
\begin{bmatrix}
E_1 \\
E_2 \\
E_3
\end{bmatrix}
\]

The most commonly used piezoelectric material is known as lead zirconate titanate (PZT). PZT is a polarized ceramic and has the same crystal structure as the 6mm class[61], with the following \( d \) matrix:

\[
d = \begin{bmatrix}
0 & 0 & 0 & 0 & d_{i5} & 0 \\
0 & 0 & 0 & d_{i5} & 0 & 0 \\
d_{51} & d_{31} & d_{33} & 0 & 0 & 0
\end{bmatrix}
\]

Substituting into the above,
This shows that an applied E field in a third axis leads to equal strain in the first and second (transverse) axes, which is proportional to $d_{31}$. Spec sheets for piezoelectric materials usually quote numbers for $d_{31}$, $d_{33}$, and $d_{15}$, but $d_{31}$ is applicable for the tube due to the transverse symmetry.

A piezoelectric tube actuator is a tube of piezoelectric material, with plated electrodes on the outer and inner surface. These types of actuators are widely used as scanners in atomic force microscopy. The outer surface is radially quartered in the transverse plane, such that the tube is ‘quadrupole’. Opposite electrodes have opposite and equal voltages, and the inner surface is optionally grounded.

![Fig. 2. Schematic of piezoelectric tube actuator of diameter D and wall thickness h. Adapted from [62].](image-url)
We want to obtain an expression for the deflection of the tube actuator[62]. Recall from calculus that the radius of curvature $R$ can be written as

$$\frac{1}{R} = \frac{\frac{d^2 y}{dz^2}}{\left[1 + \left(\frac{dy}{dz}\right)^2\right]^{3/2}}$$

The deflection of the tube is small, i.e. assume the slope term is small:

$$\frac{1}{R} = \frac{d^2 y}{dz^2}$$

Integrating,

$$\Delta y = \frac{z^2}{2R}$$

Obtaining an expression for the curvature gives the deflection. When voltages are applied to opposing quadrants, a strain/stress is generated only in these quadrants:

$$S_{\text{piezo}} = d_{31} \frac{V}{h}$$

$$T_{\text{piezo}} = E S_{\text{piezo}}$$

where $h$ is the thickness of the tube, $V$ is the applied voltage, and $E$ here refers to the modulus of elasticity. Equilibrium requires this strain/stress to be resisted by a bending moment in the opposite direction that occurs in all 4 quadrants. We know from basic mechanics that bending strain is proportional to the distance from the neutral axis:

$$S_{\text{bend}} = \frac{y}{R} = \frac{1}{R} \left(\frac{D}{2} \sin \theta\right) \propto \sin \theta$$

where $D$ is the diameter of the tube, and polar coordinates is used. In the voltage supplied quadrants, $S = S_{\text{piezo}} - S_{\text{bend}}$ and in the grounded quadrants, $S = -S_{\text{bend}}$. We can describe the stress in a pair of adjacent quadrants:

$$\begin{cases} 
0 < \theta < \frac{\pi}{4} & T(\theta) = -T_{\text{bend}} = -\alpha \sin \theta \\
\frac{\pi}{4} < \theta < \frac{\pi}{2} & T(\theta) = T_{\text{piezo}} - T_{\text{bend}} = T_{\text{piezo}} - \alpha \sin \theta 
\end{cases}$$

where $\alpha$ is a constant of proportionality. Noting that the tube is in rotational equilibrium (bending moment $\propto$ integral of torque $= 0$), integrating over the adjacent quadrants
gives $\alpha = \frac{2\sqrt{2}}{\pi} T_{\text{piezo}}$. Combining the above results gives the following expression for the deflection of a piezoelectric tube of length L:

$$\Delta y = \frac{2\sqrt{2}d_{31}VL^2}{\pi Dh}$$

It is instructive to plug some typical numbers to get a sense for the order of magnitudes. Consider a stock piezoelectric tube from Physik Instrumente (part number PT230.94), with dimensions 30 (L) x 3.2 (OD) x 2.2 (ID) mm. The quoted $d_{31}$ is $-180 \times 10^{-12}$ m/V. Using the derived relation and the OD as diameter, the deflection is 2.3 um at 25 V. Note that this deflection is too small for an imaging field, thus nonresonant scanning is generally not feasible at relatively low voltages.

**b. Mechanics of deflecting cantilever**

In a forward viewing probe, the classic design is having an optical fiber mounted at the tip of a piezoelectric tube actuator. When the piezoelectric actuator is driven with a sinusoidal voltage input, the periodic deflection of the actuator tip drives the fiber in the direction of the deflection with the same angular displacement. The fiber can be modeled as a cylindrical cantilever with one end fixed and the other end free, which define boundary conditions of the mechanical response. If the deflection occurs at a resonance of the fiber cantilever, the cantilever deflection increases markedly.

![Diagram of a cantilever](image-url)
Fig. 3. Cantilever with a ‘fixed-free’ configuration, where the base is mounted to a fixed support such as a piezoelectric actuator, and the tip is allowed to deflect freely. Adapted from [63].

It can be shown from differential arguments that the deflection of a cylindrical beam of radius \( r \) and length \( L \) is governed by the following equation[63]:

\[
\frac{\partial^2 y}{\partial t^2} = \frac{E r^2}{4 \rho} \frac{\partial^4 y}{\partial x^4}
\]

where \( E \) is the modulus of elasticity and \( \rho \) is the density of the beam material. This equation may be solved numerically (finite difference or other methods) or in closed form; the latter we will study briefly as follows. We may assume a time-harmonic form of the complex transverse displacement \( y = \Phi(x)e^{i\omega t} \), which allows us to simplify to the following:

\[
\frac{\partial^4 \Phi}{\partial x^4} = \frac{\omega^4}{v^4} \Phi
\]

where \( v = \sqrt{\frac{\omega r}{2 \sqrt{\rho}}} \). Assuming that \( \Phi \) has an exponential form, it can be shown that \( y \) may be written as

\[
y = e^{j\omega t} \left( A e^{\alpha x/v} + B e^{-\alpha x/v} + C e^{j\omega x/v} + D e^{-j\omega x/v} \right)
\]

\[
y = \cos(\omega t + \phi) \left[ A \cosh \frac{\omega x}{v} + B \sinh \frac{\omega x}{v} + C \cos \frac{\omega x}{v} + D \sin \frac{\omega x}{v} \right]
\]

The arbitrary constants are solved by using the boundary conditions. At the mounted end \( x = 0 \), displacement \( y \) and slope \( \frac{\partial y}{\partial x} \) are zero. At the free end \( x = L \), assume that displacement and slope are small, such that their second derivatives \( \frac{\partial^2 y}{\partial x^2} \) and \( \frac{\partial^3 y}{\partial x^3} \) are zero. Applying the boundary conditions gives the following equation:

\[
\cot \frac{\omega L}{2v} = \pm \tanh \frac{\omega L}{2v}
\]
This is solved graphically (Fig. 4), to obtain the allowed frequencies of transverse resonance:

\[ f = \frac{\pi}{16} \sqrt{\frac{E}{\rho}} \left( \frac{R}{L^2} \right)^{1.194^2, 2.988^2, 5^2, \ldots, (2n-1)^2} \]

The fundamental frequency has the largest displacement at the distal tip of the cantilever, which is ideal for optical scanning. For a 125 um diameter glass (fused silica) fiber cantilever, \( E = 72 \) GPa and \( \rho = 2200 \) kg/m\(^3\), the fundamental frequency is approximately \( f = 0.1/L^2 \). For a scanning fiber length of 10 mm, the resonant frequency is 1000 Hz.

Fig. 4. Graphical solution to obtain allowed resonances. Intersections at 1.194\( \pi/4 = 0.938 \) and 2.988\( \pi/4 = 2.347 \) give the frequencies. Adapted from [63].

Classical resonator theory may be applied to the fiber cantilever. The quality or Q factor is a measure of the damping of a resonator. A high Q factor implies very low damping, such that oscillation amplitude takes a long time to decay to zero after an excitation. A high Q also implies that the resonance peak on the frequency axis is very
narrow, such that the resonator may be excited only at a very narrow range of frequencies. The Q factor may be approximated by the following expression:

$$ Q = \frac{f_{\text{res}}}{f_{\text{FWHM}}} $$

such that Q is the ratio of the resonant frequency to the bandwidth of the resonance, specified by the full width at half maximum of the resonance peak. A high Q resonator will have a strong oscillatory response (deflection range for the fiber cantilever) at resonance, but will be sensitive to resonance shifting and environmental perturbations due to the narrow bandwidth. A low Q resonator will have a weaker response but be more robust to perturbations. It has been reported that adding a weight to the fiber cantilever tip[35, 64] increases the Q of the resonator, resulting in a larger deflection range, but leads to much higher sensitivity to environmental changes.

c. Scan pattern generation and scan parameters

Driving the piezoelectric tube with a modulating voltage waveform deflects the tube and the mounted fiber. Depending on the frequency of the modulation, the fiber deflection may be resonant or non-resonant. These characteristics may be exploited to produce different 2-dimensional scan patterns. A scan pattern should allow an optical beam spot to fully sample a 2-dimensional area, ideally with roughly balanced sampling density over the entire area. Each scan pattern has different sampling characteristics that may be preferable depending on the application. In this section we will review a number of scan patterns that are feasible for a scanning fiber.

i. Raster

A raster scan involves one ('fast') axis of the beam moving rapidly across the scanned area, and the orthogonal ('slow') axis moving much slower, such that the beam scans consecutive lines on a rectangular area. Using galvanometric scanners, the beam may be driven with a sawtooth waveform, such that the beam scans across the fast axis then rapidly returns to start the next line scan. This scan pattern has advantages that
the scans are easily reconstructed to produce en face views, and also yield true cross-sectional images in OCT without further remapping. This pattern is preferred for galvanometric scanning but is much more difficult with deflecting fiber scanners, because it is generally difficult to produce large movements in a fiber with controllable speed changes that are cleanly decoupled in orthogonal axes. These fiber movements also need to be non-resonant in order to be steered. Fiber-based raster scanners that use decoupled piezo bender pairs in orthogonal axes have been demonstrated, but these typically require high voltages to produce appreciable fiber deflections and are limited to small fields of view, and are usually bulky due to the awkward size and geometry of the benders[29, 30, 65].

![Fig. 5. Raster scan with resonant fast axis and non-resonant slow axis. (left) Sparsely scanned area. (right) Densely scanned area. Density increases with slowness of slow axis.](image)

Xu and colleagues[31] developed a scanner with piezoelectric benders that scanned the fast axis at resonance, and the slow axis non-resonantly. This has the advantage of exploiting the rapidity and large magnitude of resonant movement for the fast axis, while requiring only simple sinusoidal and linear drive waveforms, such as

\[
x = \sin(2\pi ft) \quad \text{fast}
\]

\[
y = at \quad \text{slow}
\]
The Xu scanner required 200 $V_{pp}$ to produce 650 $\mu m$ of non-resonant deflection (slow axis), and 50 $V_{pp}$ to produce over 1 mm of resonant deflection (fast axis). The nonresonant actuation also allowed an arbitrary positioning of the fiber tip in that axis by means of a DC offset to the waveform, effectively translating the scan pattern.

ii. Spiral

The spiral scan uses resonant sinusoidal motion in both orthogonal axes, and modulates amplitude to produce circles of increasing diameter to cover a 2-dimensional circular area. The amplitude may be modulated by a triangle (ramp) or sinusoidal waveform. This has a significant advantage of requiring much lower drive voltage, due to the large resonant deflection. However, the scanned lines are circular, and require post-processing to re-map the scan to a Cartesian area or volume. Additionally, each circle takes the exact same amount of time to complete, due to the periodicity of the resonant motion, and thus results in unbalanced sampling density of the center of the scan versus the outer regions where the circumference of each scanned circle is relatively larger. The orthogonal axes also require a constant phase difference to produce a repeatable circular pattern, and a small deviation in phase can produce a distorted pattern that results in an incorrectly sampled tissue area. The phase relationship may depend on mechanical characteristics of the fiber mount and environmental changes.
Fig. 6. Spiral scan with resonant motion in orthogonal axes. (left) Sparsely scanned area. (center) Densely scanned area. (right) 60 (not 90) degree phase shift.

Groups such as Profs. Seibel[36] and Li[66] that have used the piezoelectric tube actuator have reported success with the spiral scan pattern, that is generated with simple sinusoidal waveforms:

\[ x = A(t) \sin(2\pi ft) \]
\[ y = A(t) \sin(2\pi ft + \pi / 2) \]
\[ A(t) = at \text{ or } \sin(at) \]

Drive voltages as low as 40 Vpp have been reported[36], which are more feasible for in vivo clinical applications. The movement of the fiber may be recorded by a position-sensitive detector to generate a lookup table to facilitate remapping, or may simply be mapped to the drive waveforms, but the former may better account for nonlinearities in the actual scanned pattern.

iii. Lissajous

The Lissajous scan is a resonant scan that requires a small mismatch in drive frequency between the orthogonal axes. The Lissajous is able to sample an area with more balanced uniformity. Another advantage is that the phase difference between the input waveforms is zero, which may improve stability:

\[ x = \sin(2\pi ft) \]
\[ y = \sin(2\pi (f + \delta f)t) \]

One group has reported improved stability with the Lissajous scan, with orthogonal driving frequencies of 62.76 Hz and 62.60 Hz (resonance at about 63.3 Hz) at 70 Vrms. They also note that the center of the scanned area may be an approximation for a raster scan[35]. However it has been suggested that the strong mechanical coupling between
axes on the piezoelectric tube actuator leads to significant distortion of the scan pattern that requires precise tracking and correction[67].

Fig. 7. Lissajous scan pattern. (left) Sparsely scanned area (large mismatch of frequency). (right) Densely scanned area (small mismatch of frequency).

ev. Scan parameter determination

Swept source OCT is depth-priority, such that the repetition rate of the swept laser determines the number of sampling points that are scanned. Therefore the selected scan frequency of the imaging beam needs to be calculated based on the imaging system parameters. This is additionally important if the scanning fiber is to be driven at resonance, which requires a particular resonant frequency to be specified in probe construction, and a resonant deflection range (also known as 'scan diameter') that is enabled by a particular design. The modulation of the drive waveform is also determined by sampling considerations. In this section we will consider the spiral scan pattern, but similar considerations are relevant for other scan patterns.

In the spiral scan pattern, the sampling density in each scanned circle varies with diameter, because the period of each circle is equal. Hence adequate sampling should be checked for the largest circle, i.e. the outer circle of the spiral. For illustrative
purposes, assume that a scanning fiber with \( m = 10 \text{ um} \) mode field diameter has a deflection range of \( d = 1 \text{ mm} \) at maximum drive voltage. The largest circle will then have \( \frac{\pi d}{m} = \frac{\pi (1 \text{ mm})}{10 \text{ um}} \approx 300 \) mode field diameters; in other words, one period of the fiber resonance traces over a length equal to 300 mode field diameters. In SS-OCT, one sweep period should interrogate a single transverse spot in the image field, which is equivalent to the time that the fiber traces over 1 mode field diameter. (Sampling could also be equivalently calculated using the image field diameter and 1/e\(^2\) spot size, because the magnification of the imaging system linearly scales the deflection range and mode field diameter.)

Therefore, to achieve Nyquist sampling, one period of the fiber resonance should contain at least \( \frac{2\pi d}{m} \approx 600 \) laser sweeps. For a high speed swept laser of \( F = 100 \text{ kHz} \) repetition rate, this requires a fiber resonance of at most \( f = \frac{F m}{2\pi d} \approx 170 \text{ Hz} \), which is achieved with a 24 mm long fiber cantilever. Groups have shown that the resonance of a shorter fiber may be brought lower by adding weight to the distal tip, which also increases the Q factor of the resonator[35, 64]. This increases deflection range, but worsens the perturbatory effects of environmental factors that may shift the resonance slightly[35].

<table>
<thead>
<tr>
<th>MFD / um</th>
<th>Deflection diameter / um</th>
<th>Spots per scan period at Nyquist</th>
<th>Laser rep rate / Hz</th>
<th>Fiber resonance / Hz</th>
<th>Circles per volume at Nyquist</th>
<th>Volumetric frame rate / fps</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>1000</td>
<td>600</td>
<td>100,000</td>
<td>170</td>
<td>100</td>
<td>1.7</td>
</tr>
<tr>
<td>10</td>
<td>1000</td>
<td>600</td>
<td>600,000</td>
<td>1000</td>
<td>100</td>
<td>10</td>
</tr>
</tbody>
</table>

\[
m \quad d \quad 2\pi d \quad m \quad F \quad \frac{F m}{2\pi d} \quad \frac{d}{m} \quad \frac{F m}{2\pi d^2}
\]

Table 1: Summary of scan parameters for illustrative purposes.
The volumetric frame rate, i.e. the time required for a full amplitude modulation to achieve one complete spiral also needs to be calculated based on Nyquist requirements. The volumetric frame rate is controlled by the number of circles in the spiral, which is determined by Nyquist sampling in the radial direction of the spiral. A deflection radius of $\frac{d}{2} \approx 500$ um contains 50 mode field diameters. Therefore the spiral requires $\frac{d}{m} = 100$ circles for Nyquist sampling. Using a fiber resonance of 170 Hz, the time required to complete a single spiral is $\frac{d}{fm} = \frac{100 \text{ circles}}{170 \text{ Hz}} \approx 0.60$ seconds. This is a volumetric frame rate of $\frac{fm}{d} \approx 1.7$ fps. A low scanning frequency and consequently low volumetric frame rate is susceptible to motion artifacts (appearing as a 'ringing' effect[64]) when either the imaging target or the probe is not perfectly stationary. Both resonant frequency and volumetric frame rate are linearly related to laser sweep rate, such that the availability of sufficiently high repetition rate swept source lasers directly enables forward viewing OCT technology.
Methods

a. OCT system design

The OCT system was a classic dual circulator design at 1310 nm wavelength as previously reported[1]. The data acquisition card (Alazar Technologies) had a 12-bit 1.8 GS/s sampling rate, and was optically clocked by a Mach-Zehnder interferometer (MZI) with a fixed path length mismatch of about 6 mm producing a maximum fringe frequency up to 1.1 GHz, such that sampling was performed at each period of the Mach-Zehnder fringes. Sampling at this ‘optical clock’ was linear in wavenumber because the argument of the cosine term representing the interference is linearly proportional to $k$ (by a factor of the path length mismatch). A prototype balanced detector at 1.8 GHz produced a digital clock signal from each rising edge in the interference pattern, which was used to externally clock the data acquisition card. The MEMS-VCSEL[9] (Praevium Research and Thorlabs) was driven sinusoidally by an arbitrary waveform generator and high-voltage amplifier at a frequency of 300 kHz. Both forward and backward wavelength sweeps were used, to achieve an effective axial scan rate of 600 kHz. The acquisition card was triggered by the waveform generator such that one spectral line (to be Fourier transformed) would be acquired for each trigger.

Data acquisition commenced at the click of a button in the custom control software, which initiated at the same time the drive waveforms to the piezoelectric tube in the probe. Therefore data was acquired at the same moment that the fiber began to move from a stationary position. The software acquired 1696 samples per period of the bidirectional laser sweep, such that each frequency sweep (forward and backward) had 848 samples. The number of samples per sweep could be approximately determined by the ratio of the A/D sampling rate (just over half the peak frequency of the sampling clock at 1 GHz) to the laser sweep rate. Data acquisition for a particular volume was terminated once the total number of stipulated samples (specified by number of A-lines per scanned ‘circle’ of the fiber, and number of circles in the spiral) was acquired. Numerical dispersion compensation was applied to the raw spectral data, which was
then fast Fourier transformed to obtain the A-lines containing image intensities. The data was acquired with optical clocking, so no resampling step based on MZI fringe phase re-calibration (as previously reported[11]) was required. An intensity level indicative of background noise was subtracted from the entire volume, and the logarithm was taken. (Linear or square root scaling are also possible.) Each A-line was then mapped to a Cartesian grid based on a lookup table generated from either an assumed or measured spiral trajectory.

![Diagram of OCT system and control layout](image)

**Fig. 8.** OCT system and control layout. The system integrates high speed electronics, optical systems, and patient interface design.

In lab experiments, the sweep bandwidth of the VCSEL source was 100 nm, and the measured axial resolution was 15 μm, which can be further optimized by increasing the VCSEL bandwidth up to 120 nm. In clinical testing, the sweep bandwidth was 120 nm, and the imaging range was 3.3 mm in air. A custom C++ software was used to
control the data acquisition sampled with external clocking. The A-lines were then remapped to the polar geometry in the en face plane in a real-time display of about 1 fps, based on a preloaded calibration file that specified the remapping transformation. The software allowed arbitrary selection of z-planes in the remapped volume for real-time preview.

Characterization of the VCSEL system was performed and are described in this section. The figure below illustrates the long coherence length of the VCSEL. A single reflector was translated over the imaging range and any reduction of the intensity peak was measured. An optical attenuation of 15 dB was used in the sample arm. There is close to no sensitivity loss over a 2 mm imaging range. The long coherence length is a result of the extremely narrow instantaneous line width (inversely related) of MEMS-based VCSELs. The cavity length of the MEMS-VCSEL is extremely small and allows the laser to operate in a single longitudinal mode (so-called 'mode hop free operation').

Fig. 9. Sensitivity rolloff showing long coherence length of the VCSEL. There is no appreciable rolloff over 2 mm of imaging range.
Previous swept source OCT systems had limited imaging range due to shorter coherence lengths, such that dispersion effects would quickly limit the visibility of interference at longer depths. The long coherence length of the VCSEL enables much longer imaging range that is now limited only by the A/D sampling rate. The system described here used a sampling clock at up to 1 GHz with a 1.8 GS/s acquisition card that is already considered state of the art. Extremely long imaging ranges exploiting the VCSEL coherence length have been demonstrated by slowing the sweep rate of the laser, so that each sweep period can be more densely sampled[10].

![VCSEL integrated optical spectrum with 115 nm tuning range](image)

Fig. 10. Time-integrated optical spectrum showing 115 nm tuning range.

The optical spectrum as measured on an optical spectrum analyzer (OSA) was presented in Fig. 10. The OSA does not sweep fast enough to capture the instantaneous spectrum, but instead delivers a time-integrated spectrum, which is useful to understand the bandwidth and tuning range of the laser output but does not show the actual intensity modulation.
Fig. 11. Laser intensity versus time over two sweep periods. Each period contains two sweeps representing the forward and backward sweeps.

The laser intensity was first measured over time, by disconnecting one arm of the OCT balanced detector and disconnecting the sample arm, and sampling the RF output from the detector, such that the detector functioned simply as a photodiode measuring the modulation of the laser intensity. Fig. 11 shows the modulation of the laser intensity over time. Each period has two nearly symmetric sweeps from the forward and backward sweep of the MEMS filter. The laser is sweeping in frequency over time, so the intensity shape is closely related to the spectral profile. However, the sampling was linear in time, so the shape does not accurately represent the true spectrum, which is sampled in wavelength.
Fig. 12. Laser intensity over two sweep periods sampled linearly in k, using optically clocked sampling. This is the actual swept wavelength spectral shape.

The laser intensity was then sampled with optical clocking, i.e. linear in wavenumber. This is analogous to sampling with a high-speed spectrum analyzer, because the samples are evenly spaced in wavelength. The waveform therefore shows the true power versus wavelength. The waveform is highly nonlinear. The forward and backward sweeps are nearly but not exactly symmetric. Each sweep may be used to obtain a separate A-line.

The waveform for an interference signal can be obtained with a single reflector in the sample arm. The signal is a cosine with argument k times the path length mismatch between the reference arm and the sample arm. The envelope is similarly indicative of the laser sweep profile.
Fig. 13. Interference of one sweep period from a single reflector. The envelope similarly shows the nonlinearity of the sweep.

The control software used a National Instruments card to generate the drive waveforms for the probe. The probe was driven by sinusoidal waveforms with a triangular amplitude envelope to generate the spiral scan pattern. The phase difference and maximum amplitudes of the waveforms for the two axes could be adjusted in the software to account for mechanical asymmetry, such that a circular scan could be obtained. The waveforms were fed to a custom high voltage amplifier circuit of gain 40x. The output current was limited to 100 uA for electrical safety. The probe was driven at voltages no higher than 60 Vpp, which is under the limit set by the International Electrotechnical Commission standards[68].

b. Probe design

i. Optical design
Optical systems were designed for two imaging regimes; high magnification imaging in close proximity to tissue surface simulating microscopy, and intermediate magnification imaging at a larger working distance from tissue similar to a magnification endoscope[39]. A single GRIN lens was used for simplicity of assembly and minimal aberrations. Future designs could use aspheric lenses for better compactness and scanning performance.
Fig. 14. System characteristics of high magnification design. (top) Optical layout. (center) Huygens PSF cross section in image plane. (bottom) Through-focus spot diagram. Spot diagram shows significant curvature.

The high magnification design used an 'extended' 0.40 pitch 1.8 mm diameter GRIN lens to achieve a 500 um working distance in water with 60 um focus into tissue, simulating gentle endoscopic contact on a tissue surface. The 1/e² spot diameter was 8 um and the image field was 0.9X. There was significant field curvature in the imaging plane as evident from the spot diagram. The extended pitch GRIN lens was custom manufactured in-house by grinding two separate standard 0.25 pitch lenses at an 8 degree angle then gluing them together with optical epoxy.
Fig. 15. System characteristics of intermediate magnification design. (top) Optical layout. (center) Huygens PSF cross section in image plane. (bottom) Through-focus spot diagram.

The intermediate magnification design used a stock 0.23 pitch 1.8 mm GRIN lens to achieve a 8 mm working distance in air, simulating the use of a magnification endoscope surveying a relatively larger area. The $1/e^2$ spot diameter was 40 um and the image field was 4X. Similarly, field curvature was not well corrected off axis.
The image fields could be scaled smaller, i.e. 'zoomed' by reducing the voltage amplitude to the piezoelectric tube, thus scaling down the fiber deflection, as has been described by Seibel[37]. This so-called 'electrical zoom' process does not improve the imaging resolution as determined by the optical system, but reduces the field of view and increases sampling density, which improves image quality.

<table>
<thead>
<tr>
<th>Design</th>
<th>Lens</th>
<th>Working distance</th>
<th>Field magnification</th>
<th>Spot diameter (1/e²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High magnification</td>
<td>0.40p 1.8mm GRiN</td>
<td>500 um water</td>
<td>0.9X</td>
<td>8 um</td>
</tr>
<tr>
<td>Intermediate</td>
<td>0.23p 1.8mm GRiN</td>
<td>8 mm air</td>
<td>4X</td>
<td>40 um</td>
</tr>
</tbody>
</table>

Table 2: Summary of imaging system design and parameters.

ii. Mechanical design

A prototype fiber scanning probe was partially assembled by collaborators in Prof. Xingde Li's group at Johns Hopkins University for testing purposes and was employed in ex vivo feasibility studies. The design has been described previously[64, 69]. The piezoelectric tube is mounted on a steel base, which accepts a detachable cap that contains an optical system such as a GRiN lens. An optical fiber is mounted in the center of the tube, with the free length determining the fiber resonance. The distance between the fiber tip and the lens surface is carefully controlled to determine the magnification of the optical system. The fiber was angled cleaved at 8 degrees. The GRiN surfaces were not angle polished, to avoid high reflections occurring when the fiber was scanning off axis. The entire probe had an outer diameter of 2.1 mm (without protective sheath) and a rigid length of about 35 mm with the extended pitch lens mounted.
Subsequent designs were optimized for clinical use. It was verified that a device of rigid length longer than 20 mm would not be able to pass the Y-band section of the endoscopic accessory port. Previous work tested creative designs to reduce the rigid length of the probe by actuating the fiber on the proximal end of the tube actuator (so called ‘reverse mount’)[38]. A major disadvantage of such a design was that the maximum resonant frequency of the scanning fiber was capped at the fiber length permitted by the piezoelectric tube length, due to the fiber having to protrude out of the distal tube end. A cap on scan fiber frequency would not be able to scale with developments on available high speed swept source systems.

Fig. 16. Illustrative schematic of a typical piezoelectric tube actuated fiber scanning probe.

Fig. 17. Compact probe design. The rigid length of the probe consists entirely of the lens, the scanning fiber, and the piezoelectric actuator, minimizing unnecessary rigidity in the axial direction to optimize clinical feasibility.
New designs were considered that reduced the axial rigid length while maintaining the forward-mounted fiber for optimal design flexibility and simplicity in construction. Reductions in length of the piezoelectric tube were generally difficult to accommodate, because the deflection scales inversely with the square of length, such that even a small length reduction would require a relatively large increase in drive voltage to compensate. The tube actuator mount was replaced by a sleeve-like 'collar' part that was custom manufactured on a miniature lathe machine. The collar was machined with two inner diameters, serving to provide electrical separation between the soldered wire connections on the piezoelectric tube and the external hypotube, while also centering the piezoelectric tube in the housing. The collar functioned as a mount without adding rigid length to the probe. The entire probe was then encased in an FEP sheath for added protection and insulation, to give an overall OD of about 3.3 mm.

The optical fiber was jacketed proximal to the hypotube for best robustness. Choice of wire size was in the range of 100 um diameter, due to limitations on probe diameter and available clearance for the wiring and solder under the collar. The distal hypotube was electrically insulated by a plastic sleeve, that was glued with epoxy to the FEP sheath, such that the hypotube was completely separated from external surfaces or fluids. Previously published designs incorporated a detachable optical assembly, but this was deliberately omitted for simplicity and compactness. Detachable sections are also difficult to manage in devices for clinical deployment that need to be fully and robustly sealed with epoxy for disinfection and \textit{in vivo} use.
Fig. 18. Illustrative photo of assembled probe. The probe is entirely encased in non-conductive material and is sealed from fluid penetration for electrical safety.

iii. Electrical safety

Electrical medical device safety requirements and recommendations are stipulated in published standards. The FDA 'Guidance for Industry' documentation suggests two main references that provide recommendations for medical device safety, namely the International Electrotechnical Commission 60601 (IEC 60601) standard[68] and the Underwriters Laboratories 60601 (UL 60601 formerly 2601) standard[70]. ANSI also publishes a set of safe current limits for medical electrical equipment (ANSI/AAMI ES1)[71].

Safety provisions are necessary for patient-connected parts (known in the literature as "applied parts") and all other externally accessible parts (known as "accessible parts"). These provisions (known as "means of protection") include some or all of the following: insulation impedance, insulation surface distance (known as "creepage distance"), air clearance, and protective earth connection. The IEC standard (section 8.5.1) specifically stipulates two or more means of protection for both applied parts and accessible parts, such that protection is afforded both in normal use (known as "normal condition") and in the case of a fault (known as "single fault condition"). The standards propose limits on electrical current that flows through a patient connection to ground (known as "patient leakage current") in both normal condition and single fault condition. The standards also propose voltage limits for powered components within the device.

<table>
<thead>
<tr>
<th></th>
<th>Normal condition</th>
<th>Single fault condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Applied and accessible</td>
<td>42.4 V peak a.c. or 60 V d.c.</td>
<td></td>
</tr>
<tr>
<td>voltages</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient leakage current</td>
<td>100 uA</td>
<td>500 uA</td>
</tr>
</tbody>
</table>
Table 3. Rule of thumb limits for voltage and current in electromedical apparatus design. Adapted from [68].

The IEC 60601-1 stipulates that the voltage from accessible parts to earth should not exceed 42.4 V peak a.c. or 60 V d.c. in both normal condition and single fault condition. The piezoelectric tube electrodes are driven at about 50-60 Vpp, which is below the stipulated limit. By strict definition, the electrodes are not considered accessible because they are impossible to access without destroying the insulating sheath and hypotube, and will contact the patient only in the case of double fault as a result of grievous mechanical failure, i.e. the hypotube is shorted to the electrodes and the distal epoxy seal is breached allowing a potentially conductive path between the hypotube and outer surfaces. The probe is designed to pose no significant risk in either normal use or in the case of a single failure of precautionary design.

Patient leakage current is stipulated at 100 uA in normal condition and 500 uA in single fault condition for non-cardiac devices. Output current from the amplifier circuit is limited to 100 uA, such that the circuit output is shut off when more than 100 uA is drawn. This serves to limit any leakage current from the amplifier circuit to that level. For additional safety, the applied part of the probe (the distal end) is designed to be electrically non-conducting, i.e. zero leakage current in normal condition. At 30 V peak and 2 kHz drive frequency, current may be estimated at $\frac{V}{Z} = \frac{V}{\omega C} \approx \frac{2\pi fCV}{\omega C} \approx 0.04 V$. At 100 uA limit, the permitted capacitance of a single quadrant of the piezoelectric actuator is 250 pF. Higher frequencies scale the current linearly. If necessary in future design iterations, the current limit could be increased within the ceiling of 500 uA.

c. Overtube scope
Probes or other devices with a rigid length of longer than 20 mm will not pass the endoscopic accessory port due to the Y-junction near the entrance, even if their outer diameter is smaller than the port channel width. One possible method to deploy such devices is via a separate tube catheter that runs alongside the endoscope. The tube diameter may be selected such that the required device passes without obstruction, while not excessively increasing the overall diameter of the assembly to the point where it is not tolerated by the orifice being scoped. The tube is attached to the endoscope by 2 or more silicone rubber bands, to ensure that the tube follows approximately the contours of the endoscope body during use. Use of the overtube as a probe channel also frees up the endoscope channel for biopsy tools, snares, or other interventional devices that may be used in tandem with imaging, allowing true spatial correlation of imaging with biopsy sampling at sites of interest. The overtube and silicone rubber bands may be disinfected for repeat use, but their relatively low cost may permit single use.

i. Design

The overtube material should be reasonably sturdy with thin yet non-collapsible walls (unlike Tygon or other soft tubing) while sufficiently flexible to accompany the contours of the endoscope. The inner surface of the material should also be lubricious so that inserted catheters do not lock up during introduction or withdrawal. The material should also be highly resistant to kink formation; kinks in the tubing would result in constriction or obstruction of the channel when the tubing is made to flex with the endoscope. Extruded materials such as PTFE or FEP are highly lubricious and strong with thin walls, but have poor kink resistance. One feasible design is the use of steel-braided tubing, which is strong, thin-walled, flexible, and kink resistant. Catheter tubing may be produced with multiple layers, such that an inner layer surface could be lubricious Teflon, an intermediate layer steel braiding, and an outer layer Teflon or other biocompatible material.
The silicone rubber bands that are more proximal may be simple rings that gently hold the overtube adjacent to the endoscope (overly tight bands will be time-consuming to apply during the clinical procedure), but the band that holds the overtube at the distal tip requires more design optimization. The band should hold the tip of the overtube alongside the tip of the endoscope at the same position, without allowing the overtube to slip and slide. Additionally, the band should also hold the distal overtube parallel with the endoscope tip, such that the angle of the overtube does not change during use (a simple band would not constrain angle). Such an attachment band would be similar to an EMR cap or the attachment band of a BarRx Halo90 catheter, but with the capability to not only slip over the distal endoscope but also hold a second catheter tube.

Fig. 19. CAD model of proposed overtube attachment accessory. (left) isometric view. (right) top view. The larger hole passes the endoscope and the smaller hole the overtube.

An overtube attachment accessory was designed to mount to the distal tip of the endoscope, and accept an overtube catheter while maintaining the catheter position and angle relative to the endoscope. The hole sizes are specified to provide a snug fit to prevent slippage while retaining ease of mounting. The accessory was cast out of silicone rubber that could be disinfected for single use or multi-use.
ii. Fabrication

The accessory material selected was food grade silicone rubber (Smooth-On SORTA-Clear series), which would tolerate clinical disinfection and be safe for use in the gastrointestinal tract. The hardness of available material options were quoted by the manufacturer on a Shore A scale; Shore 40A was deemed most suitable for the intended purpose, such that the material was stiff to provide holding strength yet sufficiently elastic to slip over the endoscope. A mold was designed for casting the accessory. The shape and structure of the accessory was such that the mold required careful design for ease of casting and demolding. The mold was designed in CAD software and produced by 3D printing. The mold was designed to open into two halves, with removable rod cores for producing the hole shapes. The mold was first filled with the cores not fully inserted, such that the mold could fill completely with the viscous liquid rubber without significant air gaps (the mold will not fill uniformly if the cores are fully inserted, due to high viscosity of the liquid rubber). The cores were then inserted fully after. The removable base and halves were screwed together tightly with threaded bolts.
Fig. 20. Exploded view of mold for casting overtube attachment accessory. The two halves and removable base and cores allow convenient demolding of the silicone rubber.

Thereafter, a degassing step was necessary to remove large and small air bubbles that occur naturally after mixing. (The liquid rubber should be pre-degassed before pouring into the mold.) Degassing can be performed at either high vacuum or high pressure, depending on availability of equipment. The liquid rubber was degassed at over 29 mmHg vacuum in multiple iterations up to 45 minutes to fully remove all air pockets. The bubbles if left in the material produced voids in the cast rubber that greatly weakened the structural integrity and toughness of the product.

d. Image reconstruction

i. Lookup table based on drive waveforms

The data is acquired with depth priority on the trajectory of the scanning fiber tip. Due to the spiral (or other non-raster) scan pattern, the acquisition sequence does not automatically sort the data into a Cartesian geometry that is easiest to interpret, nor does each period of the fiber resonance give a conventional 'B-scan' cross-section as do conventional raster scanning galvanometric scanners. Thus each A-line of data requires a remapping from the spiral geometry to a Cartesian stack. Before remapping, a lookup table providing one-to-one correspondence (nearest neighbor) between each point on a 2-dimensional Cartesian grid to a sample on a spiral trajectory is generated. The A-lines are assumed to be acquired in a sequence dictated by the spiral trajectory, and are thus assigned to the Cartesian grid based on the lookup table. The lookup table may be generated in a number of different ways.
In the Theory section the drive waveforms producing the spiral scan pattern were defined as follows:

\[ x = A(t) \sin(2\pi ft) \]
\[ y = A(t) \sin(2\pi ft + \pi / 2) \]
\[ A(t) = at \text{ or } \sin(at) \]

The waveforms are linearly related to the deflection of the piezoelectric tube tip, as described earlier. It may be assumed that the deflection of the fiber tip is linearly related to the deflection of the piezoelectric tube tip and differs primarily by a phase lag. The input waveforms can then be used to generate a spiral trajectory, which can be mapped to a Cartesian grid. This method requires no calibration with the probe and works with a theoretical assumption on the fiber displacement. However, the early motion of the fiber as it starts from a stationary position and evolves into resonance is not yet sinusoidal, and will not follow the assumed trajectory. This may produce a remapping artifact at the center of the scan. Also, mechanical coupling between axes can produce a phase shift that is dependent on amplitude, giving a large swirl artifact if remapped to the theoretical spiral. It has been suggested that these artifacts may be corrected in post-processing[66].
Fig. 21. *En face* images at a single depth (3-pixel average) of fixed *ex vivo* normal human colon obtained at various fields, i.e. approximately 5.0 mm, 2.5 mm, 1.5 mm, 750 μm. Images were remapped with a lookup table generated using the drive waveforms. A spiral-like artifact in the center of the image is clearly visible.

Images of *ex vivo* human colon tissue were acquired and remapped using the drive waveform trajectory. Samples were obtained under an IRB protocol approved by the Beth Israel Deaconess Medical Center and the Massachusetts Institute of Technology; these were discarded tissue and not required for clinical diagnosis. The images appeared largely undistorted, except for a spiral-like artifact that occurred in the center of the image. This was attributed to the fiber starting to reach resonance but had not yet reached pure sinusoidal displacement in the early number of circles. Without tracking the actual position of the fiber tip and instead relying on an assumed trajectory, such distortions cannot be reliably corrected. Adjustments in the assumed frequency or phase relationship (such as non-90 degrees or amplitude-dependent) may correct distortions to some extent that may or may not be acceptable for a clinical context.

ii. Lookup table based on position sensitive detection

Using a position sensitive detector (PSD) the 2-dimensional position of the scanned beam may be tracked in real-time. By obtaining beam position information over
the full scanned spiral pattern, a lookup table can be generated that maps the Cartesian grid to the exact positions that are being sampled, which greatly improves the accuracy of the reconstruction. There are no assumptions on beam trajectory and any mechanical nonlinearities or coupling in the fiber actuation can be tracked and accounted for. The lookup table is generated as a calibration process before the probe is used for imaging, and is used to remap all subsequent data that is acquired. This method has been previously reported by Seibel[72]. PSD measurements can also be used to monitor variation of scan pattern over time or due to other environmental parameters.

The PSD outputs RF data for the two orthogonal axes of which the voltage level is indicative of displacement from the center of the sensor. The frequency bandwidth of the detector should be higher than the frequency of the moving signal, i.e. the resonance of the fiber scanner. Simply plotting the RF data will generate a scaled version of the actual beam trajectory. This can be used to produce the lookup table as previously described. The PSD should be operated in near-darkness to minimize low-frequency noise from ambient light sources. The beam spot incident on the PSD may have a stipulated power/size as specified by the manufacturer, so the output beam from the probe may need to be re-imaged by a second lens onto the sensor. Additionally, most PSDs available on the market are silicon and intended for wavelengths up to 1100 nm, and would not work at 1300 nm. A shorter wavelength laser could be used for calibration only, but may produce multimoding and/or stray reflections. Germanium or InGaAs detectors are available for longer wavelengths. The RF data may be acquired with either an oscilloscope or a data acquisition card. It is critical that the correct start and endpoint of the fiber motion as recorded on the PSD is used to generate the lookup table. Small errors may result in significant distortion of the remapped image.
Results and discussion

a. Deflection response

The fiber deflection performance for the constructed probes were characterized. The deflection of the fiber was observed and quantitatively measured with a modified web camera with its lens replaced by a magnifying objective lens that imaged the fiber onto the CCD. Plots of deflection range versus drive frequency were obtained for the two orthogonal axes. Fig. 22 shows illustrative deflection response curves for a particular probe that was designed to resonate at around 2 kHz. Deflections were measured at 1 Hz intervals over a 20 Hz range around the resonance, such that the full width at half maximum could be captured.

![Fiber deflection vs frequency](image)

Fig. 22. Illustrative deflection response curves for orthogonal axes of the piezoelectrically resonated fiber cantilever of resonance near 2 kHz.
The two axes had slightly mismatched resonance frequencies. This was probably due to the very slightly mismatched cantilever lengths in each axis, which occurred from the fiber cleaving and possibly asymmetrical mounting of the fiber base at the piezoelectric tube tip. It was discussed earlier that the resonance frequency of a fiber cantilever was governed by the following relationship:

\[ f = \frac{\pi \sqrt{\frac{E}{\rho L^2} (1.194^2, 2.988^2, 5^2, \ldots, (2n-1)^2)}}{16} \]

A 2 kHz resonance of a 125 um fiber was achieved by a 7 mm fiber length. An approximately 10 Hz mismatch in resonance between axes would be produced by a length mismatch of about 20 um. This suggested that an extremely precise fabrication process was necessary to achieve an idealized matched resonance in orthogonal axes, particularly at higher frequencies. The full width at half maximum (FWHM) of axis 1 of about 12 Hz was larger than the FWHM of axis 2 of about 8 Hz. Using \( Q = \frac{f_{\text{res}}}{f_{\text{FWHM}}} \), the Q factors are about 180 and 270 for the two respective axes. The non-Lorentzian profile of the peaks may be due to mode coupling between the axes.

The optimization of Q factor depends heavily on the mounting of the fiber at the base. It has been shown that Q factor may be increased by simply increasing the mass of the fiber, by adding a section of hypodermic tubing to the tip[35, 64]. However this method will be extremely sensitive to perturbations, as was reported by Moon[35], such that the motion of the fiber tip is highly nonlinear especially when mechanically agitated during resonant operation. This mode of operation would not be ideal for endoscopic applications, in which significant bulk motion due to patient voluntary/involuntary motion and endoscope articulation is unavoidable and will inevitably perturb the probe. This method also slows the fiber by lowering the resonance significantly (reported resonances were around 60 Hz). At such a low scan rate, motion artifacts from unstable imaging targets particularly in endoscopy will be difficult to eliminate. For clinical feasibility, the fiber scanner must resonate at high frequencies (in the kHz range). In OCT applications, a high speed system is crucial. Although high Q factor is favored for strong deflection range (thereby increasing the number of mode field diameters in the
It was also noted that there was non-trivial mechanical coupling between the two axes, such that the electrical excitation of one axis only could induce a small resonant deflection in the second axis. It has been suggested that some level of mechanical coupling is inevitable, due to the 4 quadrants sharing a single tubular surface[67]. Coupling may be minimized by ensuring an extremely high precision in the quartering of the outer conductive surface, such that opposing electrodes are aligned exactly. Coupling produces nonlinear behavior in the fiber tip that would not be predicted by a simple model governed by the drive waveforms. Therefore remapping methods based on beam trajectory calibration may be more robust, because any nonlinearities will be captured by the position sensitive detection.

**b. PSD trajectory analysis**

The input and actual trajectories as measured on a position sensitive detector (On-Trak Photonics PSM2-4) were plotted. As previously described, the fiber was excited by sinusoids with ramping amplitude to produce a spiral trajectory. The spiral was driven with 90% duty cycle, such that the last 10% of the waveform was reversed with the intention of driving the fiber rapidly to the zero position. The measured waveforms show significant decay time, which may be used to estimate Q factor with the following relation:

$$Q = \pi f_{re} \tau$$

where \( \tau \) is the decay time to the 1/e level. Assuming the decay is purely exponential, the Q factors are estimated to be 273 and 477 respectively for the two axes. This is a similar order of magnitude to the estimates from the deflection response plots. A high Q is desirable but the long decay limits the usable frame rate. Seibel has reported using a high amplitude, out of phase braking sequence at the top of the amplitude ramp to actively drive the fiber more rapidly to the home position[36]. Alternatively, noting that...
the decay sequence is almost symmetric with the ramping sequence, a PSD-based calibration could be generated for the decay trajectory and used to generate imaging, which could theoretically double the frame rate.

Fig. 23. Input and measured trajectories. The output trajectories show gradual falloff of amplitude representative of a decaying resonator. The peak to peak amplitudes in each axis is different, indicating a less than perfectly circular scan.

The ratio of normalized deflection range to voltage versus voltage was plotted for both axes. The behavior is highly nonlinear. If deflection range scaled linearly with voltage amplitude (as was assumed if remapping were to follow the drive waveforms),
then the ratio of deflection to voltage should be simply a constant scale factor. However, the measured ratio appears to increase at higher voltages. This further points to the necessity to track the actual spot trajectory for accurate image reconstruction uncompromised by fabrication imperfections and environmental uncertainties.

Fig. 24. Ratio of normalized deflection range to drive voltage versus voltage for (top) x- and (bottom) y-axes. The actual displacement of the fiber tip does not linearly scale with the voltage.

One of the axes also appears asymmetric, i.e. one side of the voltage appeared to drive the fiber to a larger deflection. This would produce a non-circular scan pattern, which would not sample the image plane as originally intended, or displayed in a way that is intuitive for a clinician. This asymmetry can be effectively corrected by adjusting the phase difference and relative driving amplitudes. At zero phase difference, the two axes produce a single diagonal scanned line, while at idealized 90 degrees difference, they produce a circle. Thus varying phase will also alter the relative amplitudes. Asymmetries and other imperfections during fabrication, as well as mechanical coupling will introduce a phase shift between axes. This phase shift may also be amplitude dependent, which is difficult to correct for all amplitudes.
Fig. 25. Phase relationship of input and output trajectories. Unstable behavior occurred only at low voltage, which indicates the early onset of the scan where the fiber just begins to vibrate. Thereafter the phase difference between the two axes is highly consistent.

In the non-ideal case, it may be sufficient to simply optimize the circularity of the outermost circle in the spiral, which circularizes the scanned area. The circularity of the inner scanned circles is irrelevant, as long as sampling remains reasonably distributed and even, discounting the unavoidable fact that the spiral is intrinsically oversampled in the center. Before the calibration step, the driving amplitudes and phase difference between the waveforms should be first be optimized for scan circularity. Thereafter, the
measured trajectory should be reasonably consistent under similar environmental conditions[36]. A high-Q resonator would be more susceptible to variations than a low-Q resonator.

The unwrapped phase of the driving and measured trajectories were also plotted in Fig. 25. Phase mismatch appears to occur only at low voltage, which may be associated with unstable behavior as the fiber comes to resonance from a stationary position. After initially random phase behavior, the phase difference becomes remarkably consistent for the rest of the scan. This suggests that in this particular iteration of the probe design and construction, the phase of the fiber tip trajectory is reasonably consistent and should give repeatable performance.
Conclusion and future work

The feasibility of forward viewing endomicroscopy with OCT has been studied and developed in a number of separate but closely related efforts: use and characterization of a state of the art swept source OCT system based on a MEMS-VCSEL light source, development of an optical and mechanical design for a forward viewing probe based on resonant fiber scanning, and optimization of feasibility in deployment for clinical endoscopy.

The OCT system was optically clocked at up to 1 GHz, enabling high-speed, linear in k sampling. The laser was run at a sweep rate of 300 kHz, with bidirectional sweeping providing an A-line rate of 600 kHz. The high A-line rate supports a new generation of high speed beam scanning technology with applications in endoscopic imaging, where high resolution, volumetric information promises strong clinical impact.

The resonant fiber scanner was investigated as a potential technology that could harness the capabilities of the high speed system. The mechanical performance of the piezoelectric tube and resonant fiber was studied and optimized for high quality factor. Multiple optical designs were evaluated for imaging in different magnification regimes similar to microscopy, namely high magnification for evaluating tissue microstructure, and intermediate magnification for larger field surveillance similar to magnification endoscopy. The mechanical design was optimized for compactness and robustness. Clinical needs and safety requirements were carefully considered and incorporated into relevant design details, such as the reduction in the probe axial length for compatibility with the endoscopy accessory channel, resilience of the design to repeated clinical disinfection, and electrical safety of the piezoelectric circuitry as defined by professional medical device standards. Different image reconstruction methods were discussed and analyzed for accuracy of remapping. The position sensitive detection method appeared to be important for accurate reconstruction, when considering the significant nonlinearity of the fiber motion.
Future work includes both technological and clinical challenges. Increasing the imaging range will be important particularly for probes with a long working distance, so that finding the correct focal plane (non-aliased image) during endoscopic imaging, in which accurately judging distance on the fisheye camera view is difficult, may be expedited. Slowing the sweep rate will increase the imaging range, but decrease the A-line rate, which will negatively affect sampling and image quality. Imaging range may be improved by working at higher (internally clocked) sampling rates, or driving the MEMS filter with a modified waveform.

The probe design also requires further optimization and testing to ensure that it will fit in the endoscope accessory channel (rigid length < 20 mm, outer diameter < 3.7 mm). While the overtube may be a usable technological stopgap in the short term, it is a significant deviation from standard endoscopic protocol. Future iterations of the probe must fit easily in the accessory channel with a relatively uncomplicated design, which will garner wider clinical acceptance. Reduction in the length of the fiber cantilever will increase the resonant frequency with a squared dependence, which needs to be carefully balanced with A-line rate and scanning range (which may also decrease) to maintain sufficient sampling. Reduction in the length of the piezoelectric tube will reduce actuating deflection also with a squared dependence, which may be difficult to manage without significantly increasing the drive voltage (linear dependence) over the safety limit. Further work on the assembly and design to improve Q factor is required.

The ability to acquire and reconstruct undistorted image volumes regardless of motion artifact and environmental perturbations requires rigorous benchtop and clinical validation. Distorted images may lead to misdiagnosis and are unacceptable in a clinical context. While the details of PSD based remapping should be well understood at this point, the effects of momentary perturbations on nonlinearities in the fiber trajectory need to be studied and reduced as much as possible, to ensure accuracy of the pre-calibration. Calibration may or may not be required before every use, depending on the repeatability of the scan pattern.
Clinical feasibility experiments will involve the imaging of pit patterns in a wide range of GI pathologies, in both the upper and low GI tract. Images will be validated with conventional endoscopic views and histological sampling where available. With accumulation of more data, an OCT classification system based on the Kudo criteria can be determined.
References


