Last updated on 10/15/2014

All-fiber, short-cavity-length wavelength swept laser based on Fabry-Perot filter

Changsu Jun
Wellman center for Photomedicine, Massachusetts General Hospital and Harvard Medical School

Abstract: Simple, low cost and high performance wavelength swept laser can be useful in diverse optical coherence tomography (OCT) research areas. Based on the recent publication [1], we present a candidate at 1.3 μm with the key operation, detailed laser build-up and sample imaging. The laser oscillator comprises only three commercial components which are fusion-spliced each other. With the interleaver and amplifier, the performance can be customized within 50-300 kHz of laser frequency, 110-150 nm of sweep range and 40-100 mW of average output power.
A complete list of required materials is attached in a separate file.

1. Motivation

Swept source optical coherence tomography (SS OCT), or optical frequency domain imaging (OFDI) is rapidly growing as a clinical diagnostic and research tool. This has motivated concentrated efforts to develop higher performance wavelength-swept light sources over last ten years, Fig. 1(a) [2,3]. Several companies have demonstrated prospective technologies based on either short-cavity-length design or Fourier domain mode-locked laser (FDML) design. However, they are expensive and extremely difficult, if possible, to customize their performance and specifications. While lab-built wavelength swept lasers are more flexible in this regard, previous designs have been complex, requiring precise alignment, dispersion compensation, and polarization control in order to achieve performance targets. Therefore, there remains a need for an inexpensive alternative design capable of being reconfigured and optimized for different performance metrics and simple enough to be adopted broadly in order to facilitate OCT research.

In this manual, we describe a laser design that meets these objectives, Fig. 1(b). Key to our design is a short, ~0.5 m, all-fiber, ring resonator based on a semiconductor optical amplifier (SOA) and Fabry-Perot (F-P) tunable filter. The resonator design consists of only three components that are directly fusion spliced and requires no polarization controllers. Furthermore, as shown in Fig. 2 (yellow region), the performance is not behind the existing swept sources. We demonstrate 50-300 kHz operation with 110-150 nm sweep range and 40-100 mW of average output power at 1.3 µm. Up to about 300 kHz is the practical laser frequency which can be sampled with the common <400 Ms/s digitizer for 4-5 mm imaging depth. The scheme can also be applied to other wavelength band, and the micro-cavity version of the laser will further enhance the performance.

Key operation, detailed laser build-up and sample imaging results are described in the following chapters based on the recent publication [1].

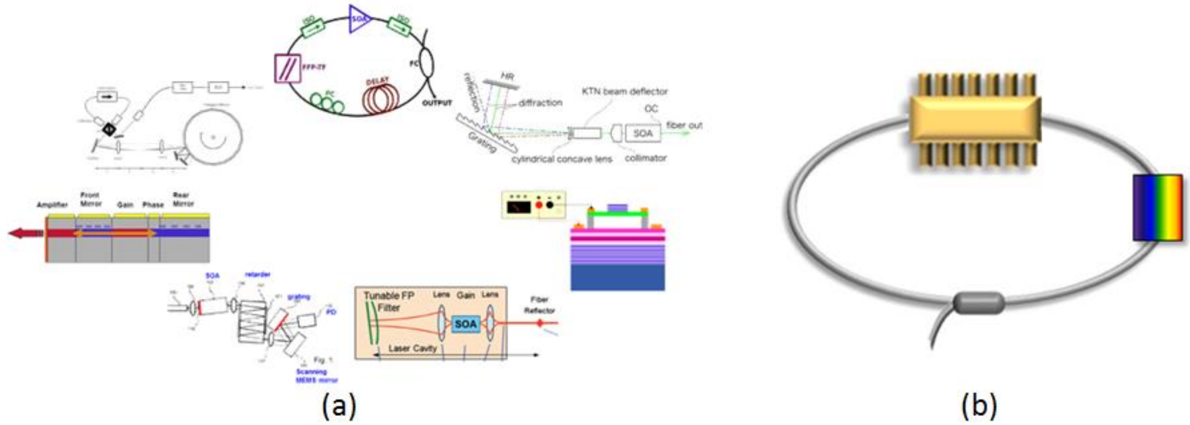

Fig. 1. (a) Various swept sources. (b) Simple configuration of proposed swept laser.

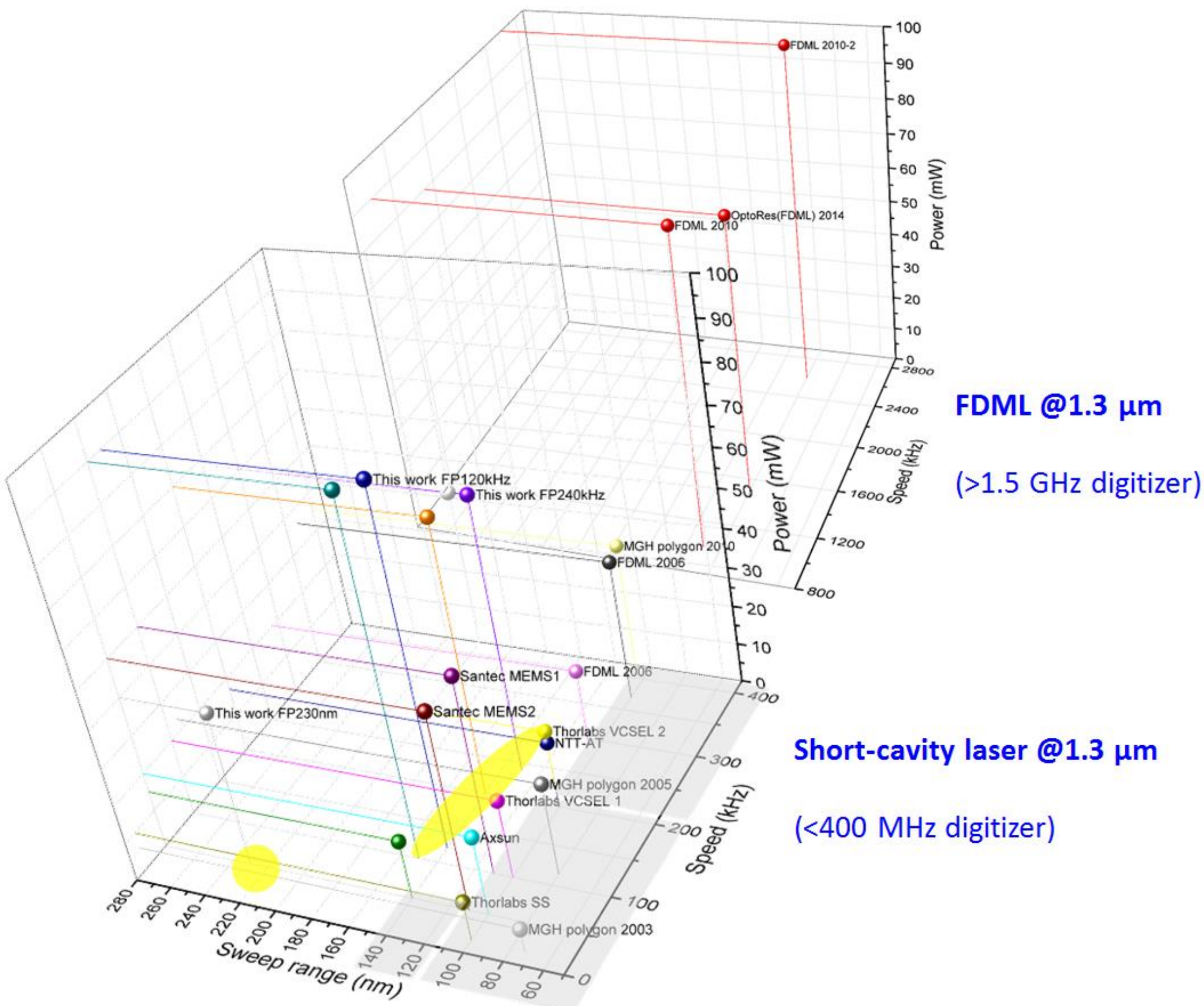

Fig. 2. Performance map of swept lasers

2. Laser operation

As shown in Fig.3, the swept laser oscillator is entirely comprised of three components that are directly fusion spliced. The interleaver and amplifier SOA are used for the laser frequency multiplication and power amplification. Section 2 focuses on the key operations that enable both a simple configuration and high performance followed by Section 3, which describes in detail how to build the laser.

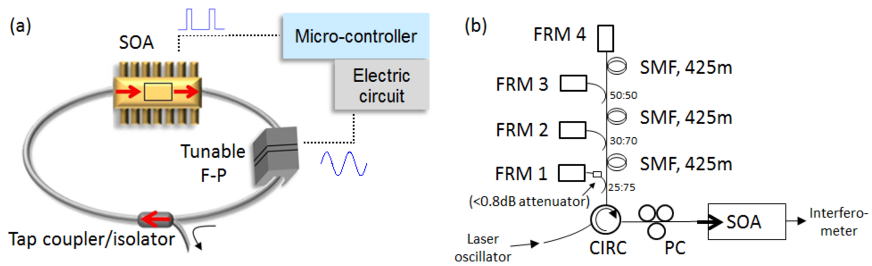

Fig. 3 Schematic setup of (a) 60 kHz laser oscillator and (b) interleaver for 4× frequency multiplication followed by an amplifier SOA. (SOA: semiconductor optical amplifier, F-P: Fabry-Perot filter, CIRC: circulator, FRM: Faraday rotating mirror, SMF: single-mode fiber, PC: polarization controller)

2.1 Fabry-Perot (F-P) tunable filter

In this design, PZT (Lead Zirconate Titanate)-driven, fiber-pigtailed Fabry-Perot (F-P) tunable filter is used as a wavelength sweeping component. It is made of two parallel mirrors which are encapsulated in a temperature-tuned package. The Transmittance function, T is expressed as a series of Lorentzian function,

$$\mathrm{T}(\lambda) = \frac{1}{1 + F sin^2(\frac{\delta}{2})} \qquad \text{with } F = \frac{4R}{(1-R)^2} \text{ and } \delta = \frac{2\pi}{\lambda} 2nl,$$

where R is the reflectance of each mirror, n is the refractive index of the material between mirrors, l is the spacing between mirrors and λ is the wavelength. T has multiple transmission peaks at the wavelengths satisfying $\delta = 2\pi N$ (N: integer) while all the other wavelengths are reflected back. Among the transmission peaks, only one peak is usually used for the wavelength swept laser while the other peaks are out of the gain bandwidth of SOA. As the mirror spacing, l increases, the transmission peak changes to longer wavelength. The sweeping speed is determined by the resonance frequency of the PZT driving the F-P mirror. Commercially available ones have 45-65 kHz resonance frequencies depending on vendors.

2.2 Cavity isolation

In a ring laser cavity, unidirectional isolation is essential to avoid spatial hole burning and counter-propagating lasing which partitions the gain and induces spectral and intensity noise. Especially when the laser cavity includes any reflective component like the F-P filter, the level of isolation needs to be verified to avoid undesired lasing.

Figure 4 displays the difference of lasing spectra with and without sufficient isolation. Conventional isolator at 1310 nm like the left one inside the SOA of Fig. 3(a) generally provides 20-dB isolation over the full sweep range although it shows 50-dB isolation at the design wavelength. In this case of insufficient isolation, the survived backward ASE after being reflected by the F-P overwhelms the desired swept intensity as seen in Fig. 4(a). Then, the tunable and swept spectra are severely affected by the evolved ASE as shown in Fig. 4(c) and 4(e), respectively.

On the contrary, 55-dB isolation over the full sweep range by adding a hybrid coupler/isolator (as seen in Fig. 3(a)) completely removes the backward ASE like Fig. 4(b), and then the tunable and swept spectra are as clean without any spectral noise and broad as expected like Fig. 4(d) and 4(f). From the comparison of the ASE and swept intensities in Fig. 4, at least 40-dB isolation is desired and the higher isolation will guarantee the less spectral noise.

We note that the laser configuration of Fig. 3(a) requires no polarization controllers (PCs) due to the polarization dependent SOA and short cavity length. In general, two PCs in ring cavity swept laser could partly result in isolation by distorting the polarization state of residual ASE to be misaligned with the gain axis of the SOA, and compensating the polarization state of swept spectrum to be aligned with the SOA gain axis. By providing enough isolation as discussed, explicit PCs are not required. This greatly simplifies the construction of a ring resonator having a short perimeter.

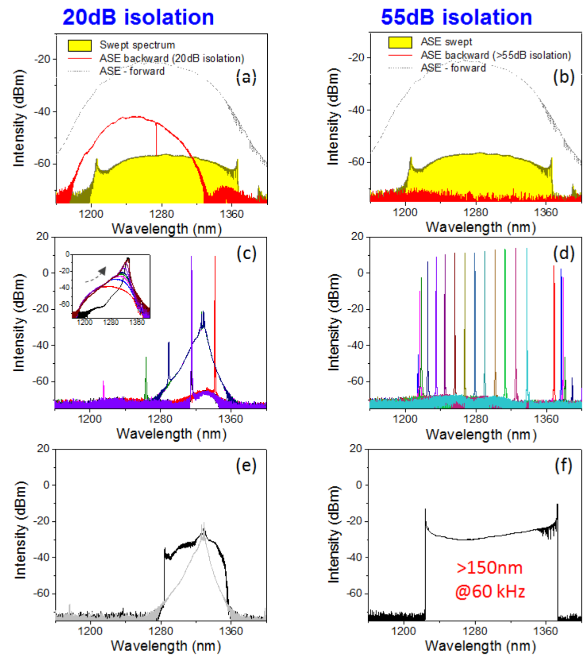

Fig. 4. Effect of laser cavity isolation. The swept ASE and backward ASE reflected by the F-P (a) for 20-dB isolation and (b) for 55-dB isolation. Tunable spectra (c) for 20-dB isolation and (d) for 55-dB isolation. Swept spectrum (e) for 20-dB isolation and (f) for 55-dB isolation.

2.3 Interleaving

Interleaving is an easy and passive way to increase the repetition rate of the swept laser by "copy and paste". The repetition rate can be increased by a factor of 2^n (n: integer) in Mach-Zehnder type [4], and by a factor of n in parallel-split delay line [5]. Figure 3(b) is a tandem structure interleaver which reduces the total fiber length 2-fold.

Figure 5 is the principle of interleaving with the example of 4x frequency multiplication. While the F-P is driven with a 60 kHz sinusoidal wave, the laser oscillator SOA is modulated with a 25% duty cycle square wave that is synchronized with the sinusoidal wave driving the F-P so that the SOA provides gain at the most linear portion of the sinusoid. Following the interleaver, the sweep repetition rate is 240 kHz and the duty cycle approaches 100%. However, the sweep range is expected to be reduced if the laser oscillator SOA is modulated with a low duty cycle. For example, SOA modulation with 25% duty cycle reduces the sweep range to 71% (~ $\sin(\frac{3\pi}{4})$) of the maximum, and 20% duty cycle to 59% (~ $\sin(\frac{4\pi}{5})$) of the maximum. By overdriving the F-P, the sweep range can be maintained close to the maximum even though the SOA is modulated with a low duty cycle.

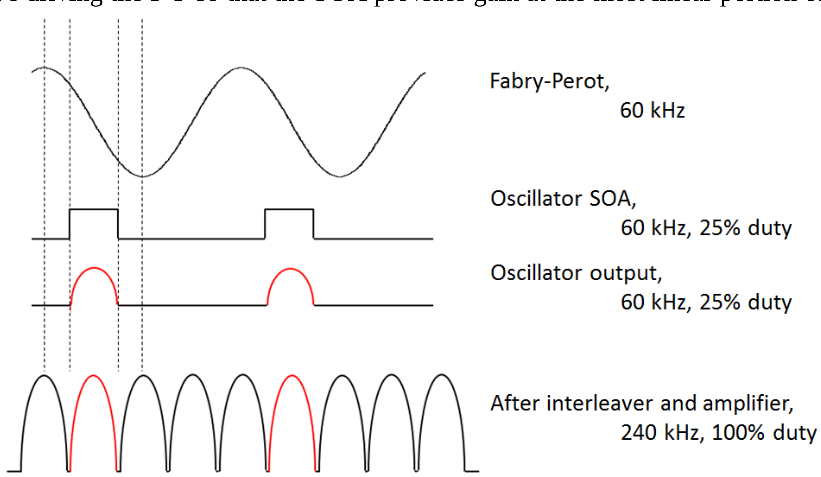

Fig. 5. Example of 4x frequency multiplication via interleaving for 60x4=240 kHz.

2.4 Overdriving the F-P

Exceeding the free spectral range (FSR) by overdriving the F-P can result in lasing through multiple transmission orders of the filter. However, by controlling the time window of the SOA gain, lasing can be constrained to a single order, thereby resulting in a larger, more linearized sweep as shown in Fig. 6(a). This is done by increasing the peak-to-peak voltage, V_{pp} applied to the F-P, and phase-adjusting between the sinusoidal wave for the F-P and the square wave for the SOA.

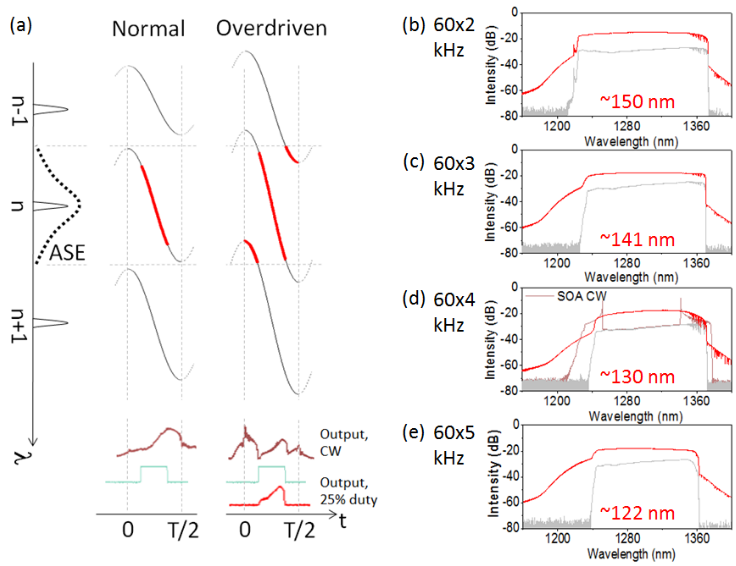

Fig. 6. (a) Overdriving the F-P. The swept spectra when the cavity SOA is modulated with (b) 46% duty cycle for 60×2 kHz frequency, (c) 31% duty cycle for 60×3 kHz, (d) 25% duty cycle for 60×4 kHz and (e) 20% duty cycle for 60×5 kHz. The gray and red ones are the spectra before and after the amplifier SOA.

At every duty cycle, the sweep range can be close to the maximum, for example 150 nm which is about the FSR of the F-P, unless the displacement of an overdriven F-P mirror exceeds the F-P spacing and the sinusoidal PZT response to high V_{pp} becomes unstable. However, high speed wavelength sweep results in output power loss due to the reduced number of roundtrip of each instantaneous linewidth. That is, there is a tradeoff between the output power (or sweep range) and laser speed to maintain maximum sweep range (or high output power). Nonetheless, sweep range of >110 nm with the output power of >40 mW can be achieved within 300 kHz laser speed as shown in Fig. 6(b)-6(e).

Figure 7 is the approximate relation between the sweep range and laser frequency to maintain high output power. The number of roundtrip is calculated from the cavity roundtrip time and slot opening time of instantaneous linewidth,

$$\mathrm{N} = \frac{(slot\ opening\ time)}{(roundtrip\ time)} = \frac{T'}{T} = \frac{\dfrac{(duty\ cycle)/f}{\Delta\lambda/\delta\lambda}}{\dfrac{nL}{c}},$$

where N is the number of roundtrip, f is the laser oscillator frequency, $\Delta\lambda$ is the sweep range, $\delta\lambda$ is the instantaneous linewidth, n is the effective refractive index of optical fiber, L is the physical cavity length and c is the light speed. In the regime of a few numbers of roundtrip which is not significantly affected by the linewidth narrowing, this calculation is in good agreement with the experiment. For example, between 2 and 3 roundtrips, about 40-80 mW output power could be acquired depending on the sweep range at each laser frequency, and more than 3 roundtrips were required for about 80-100 mW, which is around the SOA saturation output power.

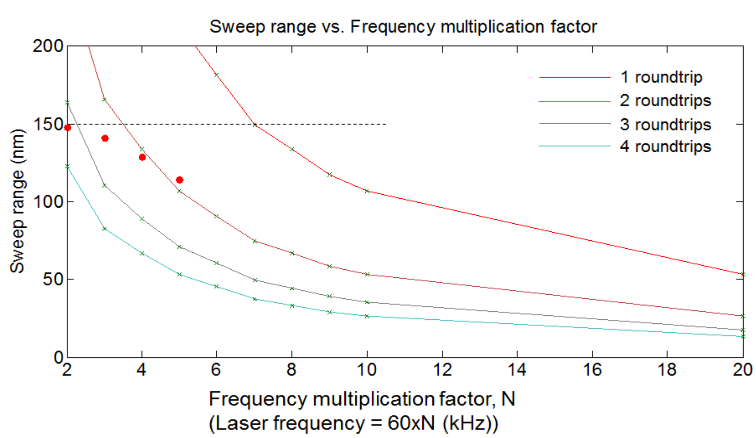

Fig. 7. Approximate relation between the sweep range and laser frequency for high output power. Each color represents 1, 2, 3 and 4 roundtrip(s) of each instantaneous linewidth in the cavity. Dotted data are the experimental values.

3. Laser setup

The following laser setup utilizes a 1.3 μm swept laser as an example and consists of the laser design, component descriptions, laser build-up and basic characterizations.

3.1 Laser design

From Fig. 7, the sweep range and output power can be estimated depending on the target laser frequency. Similarly, the tolerance of cavity length can also be estimated from Fig. 8. The performance of ref. [1], 240 kHz laser frequency, 0.51 m ring cavity length and 130 nm sweep range, corresponds to about 2 roundtrips, resulting in >70 mW output power. Longer cavity lengths of 0.51-1 m lie between 1 and 2 roundtrip(s), which will result in lower output power of <50 mW. In the example of 120 kHz, 0.51 m ring cavity length and 150 nm sweep range corresponds to higher than 3 roundtrips (crossed point in the right graph of Fig. 8), resulting in >90 mW output power which is close to the SOA saturation output power. 0.6-0.92 m cavity lengths at 120 kHz lies between 2 and 3 roundtrips which are expected to generate 50-80 mW output power.

Based on the calculations of Fig. 7 and 8, the cavity length tolerance and output performance can be estimated depending on the final laser frequency.

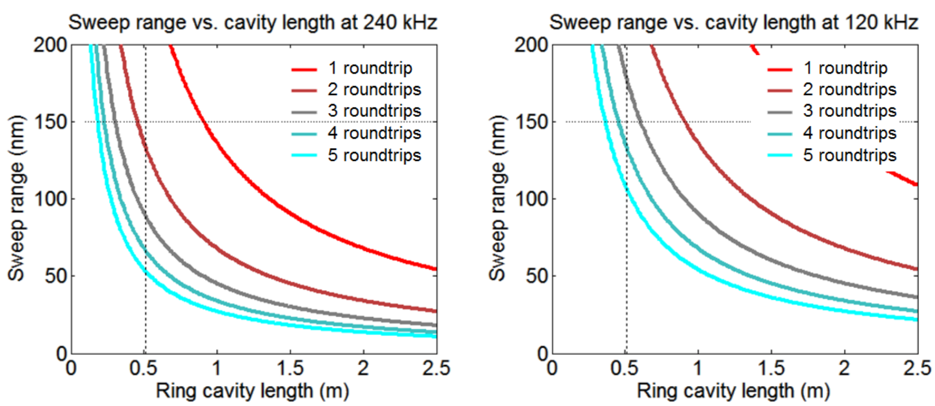

Fig. 8. Approximate relation between the sweep range and cavity length for high output power. Examples of 240 kHz and 120 kHz are displayed. 150 nm sweep range and 0.51 m cavity length are cited from ref. [1].

3.2 Components

As shown in Fig. 3(a), the laser is made up of three components, a SOA, a F-P tunable filter and a hybrid output coupler/isolator. Prior to splicing, each component should be tested to confirm it performs according to specifications.

The SOA has built-in isolators on both ends to suppress the reflection from the F-P. However, as described in Section 2.2, the built-in isolator provides only ~20-dB isolation over the full sweep range as shown in Fig. 9(a). The isolation will be compensated with the hybrid output coupler/isolator. Not to use any polarization controllers in the laser cavity, polarization-dependent SOA is preferred in this work. The already polarized ASE from this SOA will then be maintained along the 0.51 m-long single-mode fiber (SMF) ring cavity, resulting in well-polarized laser output over the full spectrum. And for the easiness of jacket-stripping during the fusion splicing, loose jacket along the optical fiber is more useful than tight one. Small signal gain, saturated output power and 3-dB bandwidth is preferred to be as large as possible. BOA 1130U3 (Thorlabs Inc.) can be a candidate.

The F-P tunable filter limits the maximum sweep range and imaging depth by the FSR and filter linewidth, respectively, as shown in Fig. 9(b). The offset voltage applied to the F-P determines the center wavelength of the swept spectrum, and the peak-to-peak voltage does the sweep range. Two companies, LambdaQuest LLC and Micron Optics Inc, will be considered in this work because they can provide high resonance frequency F-Ps. The LambdaQuest LLC does not provide many customized specification, but the model having Finesse 1000 with 160 nm FSR (around 60 kHz resonance frequency) is one of the good candidates for a swept laser. The Micron Optics Inc can serve extensive customization of FSR and linewidth (around 50 kHz resonance frequency), but the maximum input optical power is inversely proportional to the Finesse value. Finesse value higher than 1000 are prone to damage of F-P internal coating, so that the one having Finesse 1000 (damage threshold: ~35 mW) seems to be good for a swept laser. In many cases, the optical damage is caused by the high power of the single wavelength lasing right after the SOA is turned on while the F-P is not operated. Therefore, by operating the F-P first before turning on the SOA, optical damage can be bypassed more or less. Maintaining the laser oscillator power low while compensating the power with the amplifier SOA can be an alternative. The Micron Optics F-P is rather expensive. By the same reason with the SOA, loose protection jacket is preferred.

The hybrid output coupler/isolator plays an important role in satisfying isolation and short cavity length simultaneously. It's a hybrid between a tap coupler and isolator, which are integrated in a single package as shown in Fig. 9(c). Dual-stage one provides >35-dB isolation over the full sweep range (+/-50 nm) at a low price. 50 % tap ratio is used in this work, but 10 % tap ratio will further widen the sweep range by reducing the cavity loss (Ex. DPM Photonics, TAPI-31-D-10-1-222-BBB-1, +/-50nm).

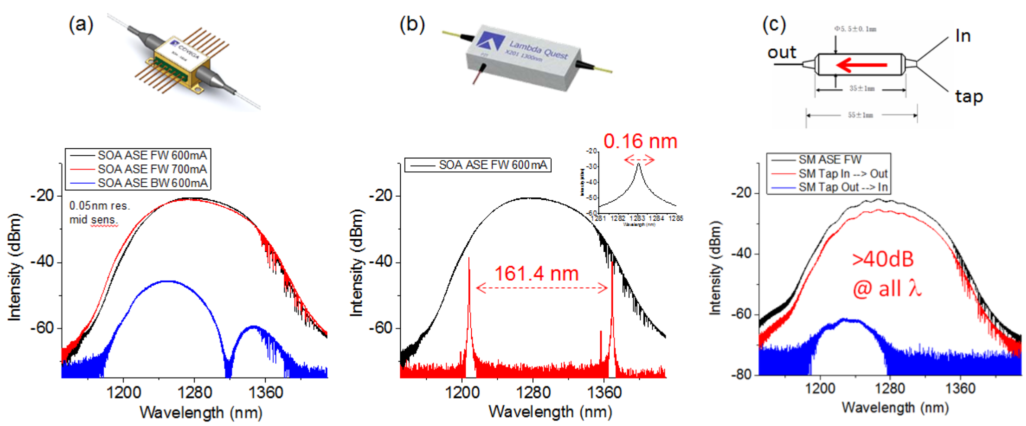

Fig. 9. (a) SOA, ASE and isolation (b) F-P, FSR and filter linewidth (c) Hybrid tap coupler/isolator, isolation

The resonance frequency of the F-P is determined by the PZT used inside. The high electrical impedance around the resonance and anti-resonance frequency of PZT shows high voltage response when we applies the same voltage over the frequency bandwidth, from which the resonance frequency of maximum displacement can be measured as shown in Fig. 10. Typically electrical and mechanical resonance of PZT is pretty much the same. The LambdaQuest F-P has a resonance frequency bandwidth at around 55-65 kHz (Fig. 10(a)) while the Micron Optics F-P has at around 45-55 kHz (Fig. 10(b)). Usually, the Micron optics F-P has another resonance at around 120-140 kHz which may be a shear vibration mode or 3rd harmonics. The LambdaQuest F-P (Finesse 1000) at 60 kHz is mainly used in this work.

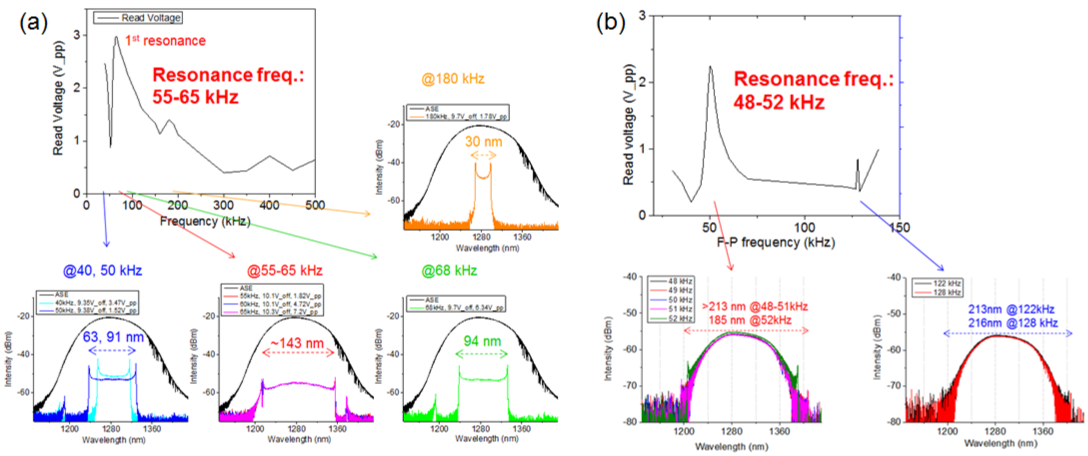

Fig. 10. F-P resonance frequency and ASE sweep. (a) LambdaQuest LLC. (b) Micron Optics Inc.

3.3 Splicing components

Fusion splicing between each component is straightforward.

- Fiber length to be spliced: Considering the clamping length of fiber cleaver and splicer, please be careful not to make the fiber length on both ends of each component too short. Practice-splicing with longer fiber length on each component is recommended before actual splicing. Fusion splicers which require short clamping length is preferred (Ex. Siecor M90 or Cover-removed splicers).
- Polymer jacket to be removed: For later protection with a short sleeve unit and for short diameter bending, the 250 µm polymer jackets need to be remained close from the cleaved fiber tip, by less than half the length of a protection sleeve unit.
- Protection sleeve: The crocodile splice unit (Diamond Inc, 1059600) can be used as a protection sleeve after fusing splicing, as shown in Fig. 11(a). After cutting off the joint part, wrap the unjacketed region of the spliced point with the built-in sticky tape of the protection sleeve. For permanent sealing, epoxy glue can be additionally used. Or ~20-mm-length protection sleeve can be used too.
- Handling the spliced components: After each splicing, the components need to be fixed on a small plate for the stability during the next splicing. Once spliced, the optical fiber is not easily broken unless it is intentionally bent with small diameter or pulled out by force. Figure 11(b) and 11(c) is the completed ring laser setup which comprises three components and three protection sleeves. To confirm the splicing loss, one can measure the transmitted spectral intensity before and after each splicing.

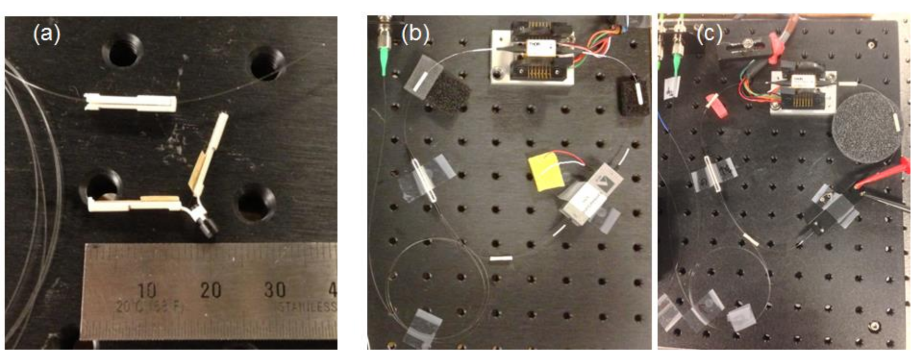

Fig. 11. (a) Optical fiber protection sleeve. (b)(c) Completed ring laser setup after all the fusion splicing.

3.4 Micro-controller circuit for functions generation

To operate the F-P and modulate the cavity SOA, duty-controllable function generator and voltage amplifier are required in general. Micro-controller and subsidiary circuit can replace them at a low price. Figure 12 is an example using the Arduino UNO micro-controller. The frequency can be manipulated using the internal Timer and Prescaler. Several functions can be synchronized and phase-adjusted by proper programming. In Fig. 12, the sinusoidal wave for the F-P is filtered from the square wave, and then amplified and combined with DC voltage via the clamper circuit. The peak-to-peak voltage and offset voltage of sinusoidal wave, and the peak-to-peak voltage of square wave can be adjusted by the potentiometers. Due to the high capacitive load of the F-P, high output current, buffer circuit and capacitance bypass for stabilization are important. Circuit for different frequencies can be optimized via the free website or simulation tools (Ex. http://sim.okawa-denshi.jp/en/RLCtool.php, Texas Instrument Tina).

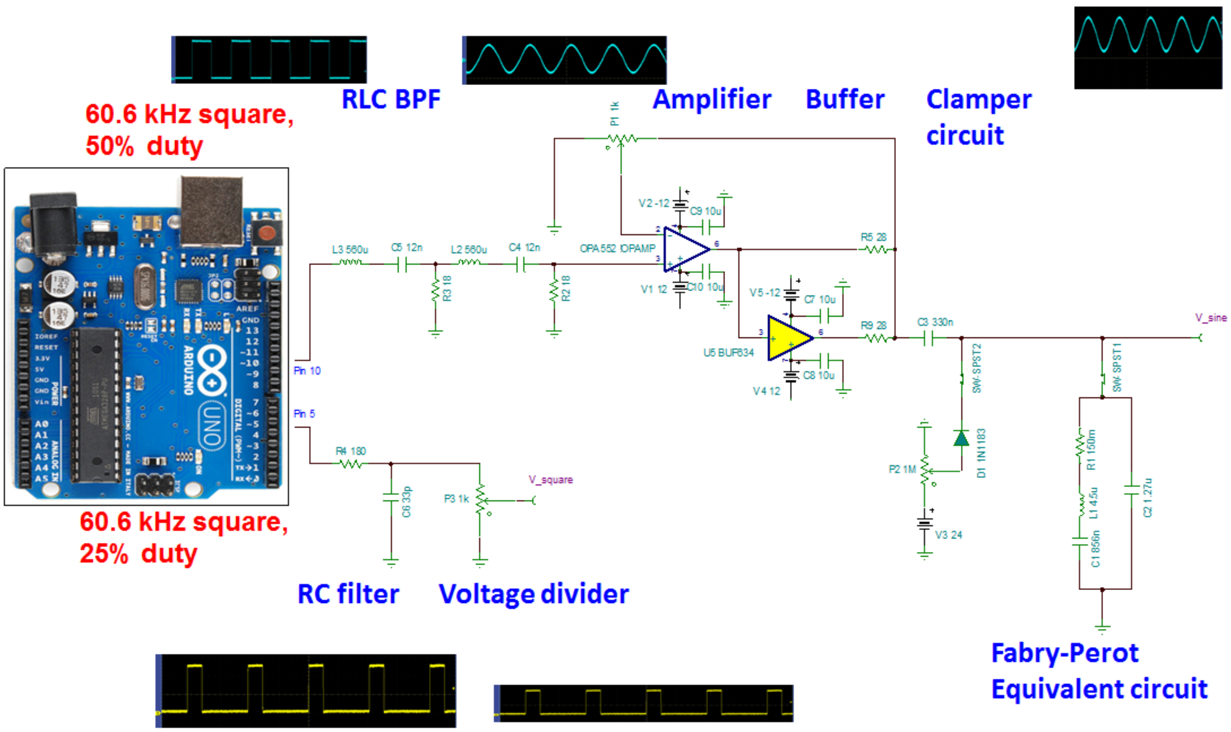

Fig. 12. Circuit example to generate ~60 kHz sinusoidal wave for the F-P and ~60 kHz, 25 % duty cycle square wave for the SOA.

3.5 Interleaver and amplifier SOA

As shown in Fig. 3(b), the interleaver comprises all passive components. Just fusion splicing between each component is all and exact fiber length calculation is not important because, although the swept pulses are not equi-distant after passing through the interleaver, digitizer sampling will be triggered by a certain wavelength within the swept spectrum. Hand-coiled optical fiber and stacking, even in case of ~km long optical fiber, can reduce the device volume as shown in Fig. 13. The polarization controller between the interleaver and amplifier SOA is set to maximize the laser power by aligning the incident light to the gain axis of the amplifier SOA.

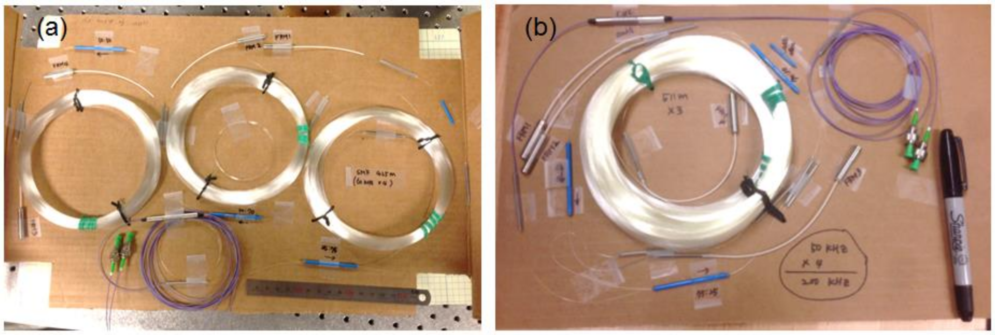

Fig. 13. Interleavers for 4x frequency multiplication. (a) Separate fiber spools. (b) Stacked spools.

3.6 Laser performance

Figure 14(a) is an example of completed F-P based swept laser built on 12”×18” optical table. The setup consists of the following:

- the ring laser oscillator
- micro-controller circuit for function generation
- interleaver beneath the optical table
- amplifier SOA
- two SOA drivers and
- power supply

The single power supply can provide voltages for two SOA drivers, two operational amplifiers (Op-amp) in the circuit and the clamper circuit to provide offset voltage to the F-P. The laser performance is not sensitive to the environment unless the cavity optical fiber is intentionally twisted or bent. Daily operation of the micro-controller showed consistent performance.

Figure 14(b) is the DC voltage-tuned laser spectra. It can be well tuned within the FSR of the F-P, and shows high signal-to-noise ratio of ~80 dB. Single channel has ~40 mW output power which can be increased up to 150 mW by an amplifier SOA. Figure 14(c) and 14(d) are the outputs with the LambdaQuest F-P, which show 130 nm sweep range and 71 mW output power at 240 kHz, and 148 nm and 80 mW at 120 kHz, respectively. Figure 14(e) and 14(f) are the outputs with the Micron Optics F-P, which show 150 nm sweep range and 65 mW output power at 200 kHz, and 150 nm and 91 mW at 100 kHz, respectively. Measured coherence length is 2-2.5 mm, which corresponds to the imaging depth of 4-5 mm by removing the depth degeneracy in OFDI setup [6].

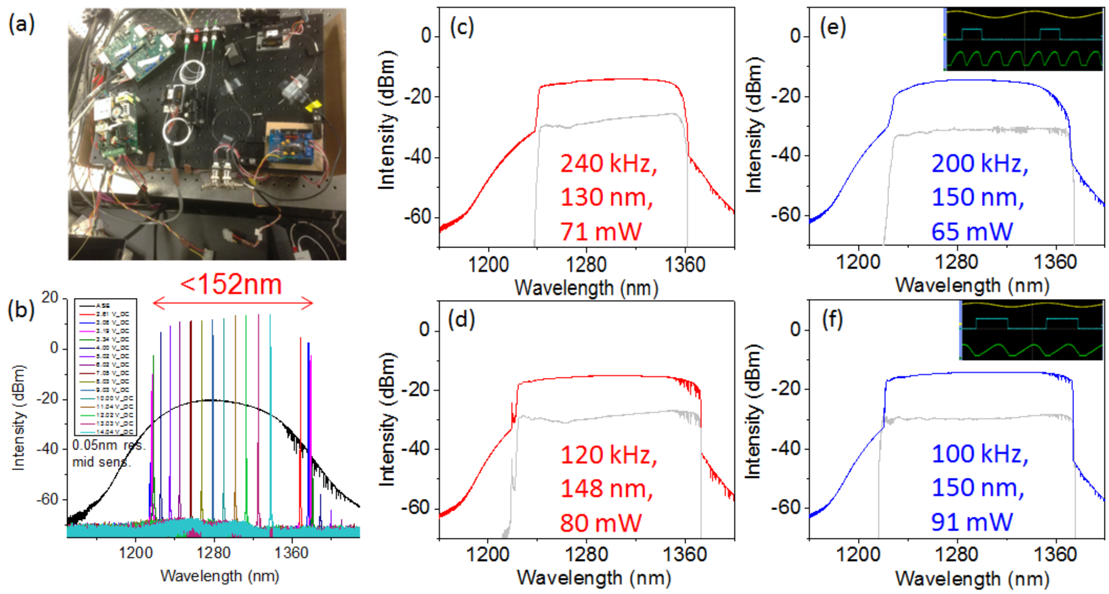

Fig. 14. (a) F-P based, short cavity swept laser built on 12"×18" optical table. (b) Tunable laser spectra. Laser performance with the LambdaQuest F-P at (c) 240 kHz and (d) 120 kHz. Laser performance with the Micron Optics F-P at (e) 200 kHz and (f) 100 kHz.

3.7 Examples of sample imaging

Figure 15 shows a few sample images at different laser frequencies based on the same OFDI setup of ref. [1].

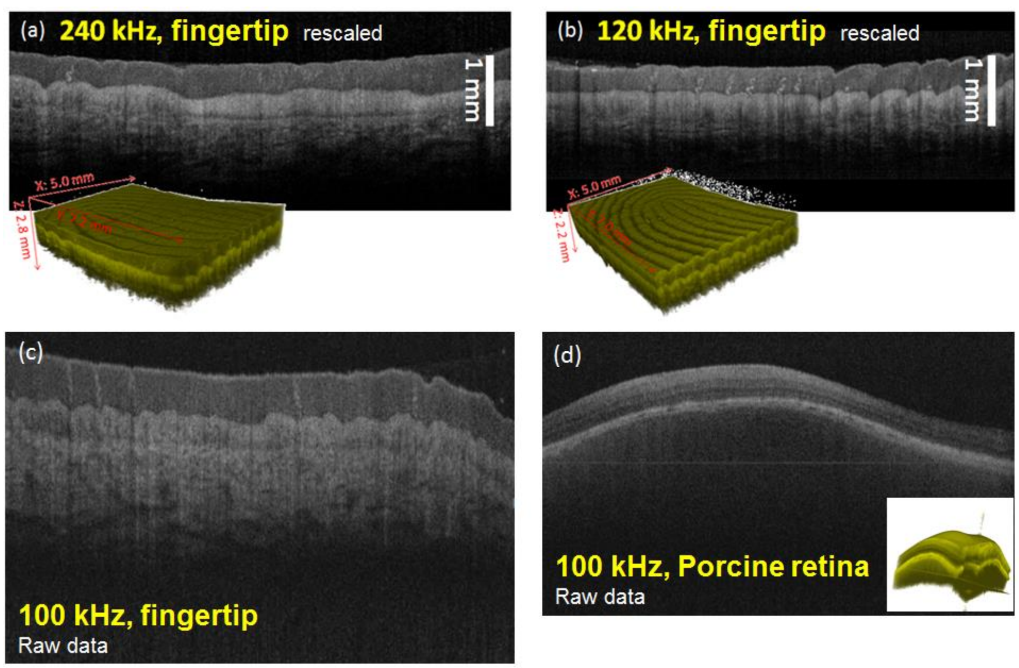

Fig. 15. Fingertip imaging at (a) 240 kHz, (b) 120 kHz and (c) 100 kHz (raw data). (d) Porcine retina imaging at 100 kHz (rat data).

4. Outlook

All-fiber, short-cavity-length wavelength swept laser based on Fabry-Perot filter was presented, including the key operation, laser build-up and sample imaging. The most significant characteristics of the laser are simplicity of assembly, low cost of materials, and robust operation without polarization control. The performance is not the best compared with the existing swept lasers, but it provides practically high performance of 100-300 kHz laser frequency with 110-150 nm sweep range, 40-100 mW average output power and ~4 mm imaging depth at 1.3 µm.

- Other wavelength band

Due to the matured technology at telecom bands, broadband (+/-50 nm) hybrid coupler/isolator is easily available at 1.3 or 1.5 µm. At ~1 µm, broadband operation with small packaging is difficult in general. The DPM photonics (TAPI-06-D-10-222-BBB-1, +/-10 nm) provides narrowband (+/-10 nm) hybrid component at 1060 nm. Its isolation is good with >40 dB over 150 nm range, but internal transmittive coating has higher loss at shorter wavelength. Combined with the ~1 µm F-P and BOA9115 (Thorlabs, 1050nm center wavelength, 57 nm@3dB ASE bandwidth, 29 dB gain), 55 nm swept laser can be built at ~1 µm. With the SOA1060 (Innolume, 1060nm center wavelength, >90 nm@3dB ASE bandwidth, 33 dB gain), >100 nm swept laser is expected at ~1 µm.

- Higher laser frequency

In all-fiber configurations, further reducing the cavity length will be challenging. Instead, using bulk optic components and higher resonance frequency of the Micron Optics F-P can achieve ~500 kHz laser frequency if required (x4 interleaving). For example, 0.3 m ×1.4676 optical ring cavity length and ~125 kHz resonance frequency can achieve ~120 nm sweep range and ~65 mW output power at 500 kHz (and 0.4 m can do 90 nm.). Even the micro-cavity version of this ring laser can be sought with proper isolation and tunable filter.

- Other swept lasers

Utilizing two FSR peaks and two SOAs, we could recently demonstrate ~230 nm swept laser at 1.3 µm, which is now under investigation about the usefulness of >200 nm swept laser. And even cheaper swept laser with high performance will be demonstrated soon.

5. References

1. C. Jun, M. Villiger, W.-Y. Oh, and B. E. Bouma, "All-fiber wavelength swept ring laser based on Fabry-Perot filter for optical frequency domain imaging," Opt. Express **22**, 25805 (2014).
2. M. Wojtkowski, "High-speed optical coherence tomography: basics and applications," Appl. Opt. **49**, D30–D61 (2010).
3. W. Drexler, M. Liu, A. Kumar, T. Kamali, A. Unterhuber, and R. A. Leitgeb, "Optical coherence tomography today: speed, contrast, and multimodality," J. Biomed. Opt. **19**, 071412–071412 (2014).
4. W. Wieser, B. R. Biedermann, T. Klein, C. M. Eigenwillig, and R. Huber, "Multi-Megahertz OCT: High quality 3D imaging at 20 million A-scans and 4.5 GVoxels per second," Opt. Express **18**, 14685–14704 (2010).
5. S. C. Schlachter, D. Kang, M. J. Gora, P. Vacas-Jacques, T. Wu, R. W. Carruth, E. J. Wilsterman, B. E. Bouma, K. Woods, and G. J. Tearney, "Spectrally encoded confocal microscopy of esophageal tissues at 100 kHz line rate," Biomed. Opt. Express **4**, 1636–1645 (2013).
6. S. Yun, G. Tearney, J. de Boer, and B. Bouma, "Removing the depth-degeneracy in optical frequency domain imaging with frequency shifting," Opt. Express **12**, 4822–4828 (2004).

Acknowledgments
The National Institutes of Health requires that investigators who use the Center for Biomedical OCT Research and Translation resources and services acknowledge that support in publications, presentations and posters. Please use the following language to cite any work that comes from utilizing the swept laser setup instructions:

This work was conducted with support from The Center for Biomedical OCT Research and Translation (National Institute of Biomedical Imaging and Bioengineering, National Institutes of Health Award P41 EB015903).