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Motion Correction in Spatial Frequency Domain Imaging; Optical Property Determination in Pigmented Lesions

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ABSTRACT

Background and Objective: Spatial Frequency Domain Imaging (SFDI) is a non-contact wide-field optical imaging technology currently being used to study the optical properties and chromophore concentrations of *in-vivo* malignant melanomas and benign pigmented lesions. Our objective is to develop a motion correction procedure in order to assess the concerns of subject-motion related variables during clinical measurements.

Study Design/Materials and Methods: SFDI motion-correction is a two-part procedure which utilizes a fiduciary marker and canny-edge detection in order to reposition and align the frame-to-frame regions-of-interest (ROI). Motion-induced phase-shifts are subsequently sampled before the entire image-set is processed by a modified demodulation formula. By comparing the results of the adjusted processing method with data gathered from the current non-corrected method, we were able to systematically characterize the impact of motion variables on SFDI measurements.

Results: Motion-corrected SFDI data from moving phantom measurements and clinical patient measurements showed up to 84.58% decrease in absorption (μ_a) variance and up to 92.63% decrease in reduced-scattering (μ_s') variance. Stationary phantom test-measurements showed almost no difference between motion corrected and standard processing.

Conclusion: SFDI motion correction is necessary for obtaining high-fidelity *in-vivo* optical property measurements of pigmented lesions in a clinical setting.

1. INTRODUCTION

1.1 Diagnosis of Pigmented Lesions

Melanoma is a form of skin cancer that is often defined in medical textbooks as being a "malignant tumor of melanocytes," and while it only encompasses about 3% of all skin-cancer cases, it is also the most deadly, accounting for more than 75% of all skin-cancer related deaths around the world.⁽¹⁾ Although 3% may not seem like a large percentage, it must be kept in mind that skin cancer is by far the most common form of cancer, well ahead of the combined incidence of breast, prostate, lung, and colon cancer.⁽²⁾ More than 3.5 million cases in two million people are diagnosed annually with skin cancer worldwide⁽³⁾, and of that population, approximately 68,720 melanomas are detected, with nearly 8,650 resulting in death.⁽¹⁾

This high mortality rate for melanoma is directly related to the lack of appropriate patient screening and early detection techniques.⁽⁴⁾ In current dermatology practice, most non-invasive diagnosis of pigmented skin-lesions is done through a technique called dermoscopy in which suspicious skin-lesions are visually diagnosed by a trained specialist with a hand-held magnifier. While numerous studies demonstrate an improved diagnostic accuracy with dermoscopy compared to naked-eye examinations⁽⁵⁾, it is still an inherently subjective method of assessment. Depending on the experience and skill of the clinician, it can take anywhere from 5 to 100 lesion biopsies in order to find a single melanoma.⁽⁶⁾ The longer and more arduous a screening process, the more likely a patient will hesitate in reporting suspicious lesions.⁽⁷⁾ Because of the time-sensitive nature of melanoma treatment, there is currently a need for technologies that can accurately inform the screening process with the goal of early melanoma detection.⁽⁸⁾

One way to approach this is to characterize the optical property differences between benign and malignant lesions. A search of the literature reveals that melanoma does have a number of clinical features that may provide the basis for improved screening using an optical technology. The basis for differentiation may lie in the characteristic differences in chromophore contents including oxy- and deoxy-hemoglobin, water, and melanin.⁽⁹⁻¹¹⁾ While there are a myriad of optical imaging platforms that can be used to study melanoma, one technology of interest is Spatial Frequency Domain Imaging (SFDI).

1.2 Spatial Frequency Domain Imaging (SFDI)

Spatial Frequency Domain Imaging (SFDI) is a relatively new method of optical interrogation that allows for wide-field and non-contact probing of turbid media. Invented and currently being developed at the Beckman Laser Institute, SFDI works by combining 'structured illumination' projections with a camera-based imaging system in order to quantify subsurface absorption (μ_a) and reduced-scattering (μ_s') coefficients, which can subsequently be used to quantify chromophore concentrations of subsurface *in-vivo* tissue.⁽¹²⁾ With an average interrogation depth of about 1cm (well encompassing of the average Breslow's depth for stage I to stage V lesions⁽¹³⁾), SFDI is able to measure, over a wide and highly adjustable field of view, the concentrations of hemoglobin (total, oxy- and deoxy-forms), lipid, water, melanin, and tissue oxygen saturation.⁽¹²⁾

Fig. 1: The SFDI platform consists of three basic components: a light source, a spatial light modulator, and a CCD camera for the detection of remitted light. The liquid crystal tunable filter allows for the optical imaging of multiple wavelengths.

As seen in Fig. 1, the SFDI platform consists of three basic components: a light source, a spatial light modulator, and a CCD camera for the detection of remitted light. During skin imaging, a spatially-modulated illumination scheme with various spatial frequencies is projected over a large area of tissue. The remitted diffuse light is detected via a CCD camera and then demodulated in order to extract the structured AC component to the diffuse reflectance at multiple spatial frequencies.⁽¹²⁾ Due to the differential sensitivity of the diffuse reflectance to absorption and scattering at specific spatial frequencies, these two coefficients can then be reconstructed using algorithms developed in the spatial frequency domain.⁽¹²⁾ By repeating this process through different wavelengths, quantitative tissue chromophore concentrations can be generated. A more detailed explanation of this can be found in Cuccia *et al*, *Journal of Biomedical Optics*.⁽¹²⁾

While SFDI has proven to be a useful tool in various research endeavors, there is still the important challenge of developing a clinically deployable SFDI system. In particular, we are in the process of characterizing malignant melanoma in comparison to benign pigmented lesions. Part of this challenge, and the main topic of this paper, is related to the development of strategies for effective compensation of subject motion, which in turn, is critical for recording high fidelity optical properties.

1.3 Motion Correction

A typical clinical data collection requires integration of signal for several seconds for each combination of wavelength, spatial frequency, and phase. During this time, the region-of-interest (ROI) will be displaced slightly by patient

movement. The longer an SFDI measurement session takes to acquire data, the more likely the ROI will deviate from its initial position and shift the phase relation of the spatially-modulated projections. This, in turn, makes SFDI motion-correction a two-part procedure:

- 1.) *Motion Tracking and Correction*: A method for repositioning and aligning each collected image in order to maintain a consistent ROI for effective image processing.
- 2.) *Demodulation Correction*: A method for demodulation that takes motion-induced arbitrary-phase shifts into consideration for the purpose of generating high-fidelity absorption and reduced-scattering maps.

We have developed a two-part motion-correction procedure which utilizes a fiduciary marker and canny-edge detection in order to reposition and align the imaging ROI. Motion-induced phase-shifts are subsequently sampled before the entire image-set is processed by a modified demodulation equation. By comparing the non-motion corrected results with motion corrected results, we were able to systematically characterize the impact of motion variables on SFDI measurements.

2. MATERIALS AND METHOD

2.1 Instrumentation and Data Acquisition

The SFDI platform used in our experiments was developed by Cuccia *et al.* at the Beckman Laser Institute in Irvine, CA. The theories and science underlying SFDI optical-property determination can be found in greater detail in the references.^(12, 14) For the purpose of this paper, we will give a general description of the instrumentation and data acquisition in order to better understand where motion correction fits into all this.

In terms of specific instrumentation, the SFDI apparatus shown in *Fig. 1* consists of a 250W tungsten lamp connected to a Newport Corporation (Irvine, CA) power source.⁽¹⁵⁾ This light is used to illuminate the spatially modulated projections created by the 1,024 x 768 pixels DLP Developer's Kit digital micromirror device (DMD) (Texas Instruments, Dallas, TX). Sinusoidal intensity patterns for specified spatial frequencies are generated by a computer and sequentially projected via the DMD at 3 phases: 0°, 120°, 240°. Diffusely reflected light images are acquired using a Nuance Multispectral Imaging System (CRi, Inc., Woburn, MA) consisting of a liquid-crystal tunable filter capable of passing discrete 10nm bandwidth wavelengths between 650 and 1,050nm into a 1,040 x 1,392 pixel front-illuminated CCD camera. Specular diffuse skin reflectance is rejected through the incorporation of cross-linear polarizers into the optics of the camera and projection system. The measurement images were saved as binary files for post-acquisition processing.

While the field-of-view for the SFDI system is highly scalable, for the purpose of this study, 70mm x 95mm measurements were taken at five spatial frequencies equally spaced between 0 to 0.25mm: the first being an unmodulated zero-frequency followed by four progressively higher frequencies. Seventeen spectral wavelengths between 650 and 970nm were acquired in 20nm intervals, and the diffuse reflectance images were calibrated for system response using a 96mm x 96mm x 10mm tissue simulating phantom with known optical properties ($\mu_a = 0.0188\text{mm}^{-1}$ and $\mu_s' = 1.098\text{mm}^{-1}$ at 650nm). The phantoms were created using silicone-based polydimethylsiloxane (PDMS) with homogeneously distributed India ink as an absorber and TiO_2 as a scattering agent.⁽¹⁶⁾ Spectral absorption and reduced-scattering coefficients of the calibration phantoms were verified using two-distance frequency domain photon migration (FDPM) measurement, which is an inherently self-calibrating measurement.⁽¹⁷⁾

Data acquisition times averaged about 2.5 minutes per repetition, with a total of one repetition (5 frequencies, 3 phases, 17 wavelengths, 255 images total) measured on clinical subjects, and three repetitions measured on tissue-simulating phantoms. Depending on measurement settings and the albedo properties of the skin, data acquisition times can sometimes take up to 5 minutes, during which motion-related variables can have a large impact on SFDI measurements, as will be seen in the later sections of this paper.

2.2 Post-Processing: Motion Tracking and Correction

The first part of SFDI motion correction involves the motion tracking of the collected images and collating the set so that the ROI in each frame stays consistent throughout post-acquisition data processing. This is accomplished through the

use of a fiduciary marker and the canny edge detection function included in Matlab. The fiducial is utilized as a fixed reference point that is easily identifiable by an edge detection operator since it maintains high contrast from tissue at all NIR wavelengths imaged in this system. By tracking the frame-to-frame movement of the fiducial, motion information can be recorded and used to crop and re-position the image set for consistent data processing as seen in *Fig. 2*.

The same motion and cropping information is then applied to a calibration phantom measurement in order to sample (through sine-wave fitting the summed intensities) the motion-altered phase-shifts for later use in demodulation. The reason for sampling the calibration phantom instead of the actual subject is due to the non-uniform intensity maps induced by features found on the skin (hair, other lesions, etc...)

Fig. 2: Illustration outlining SFDI Motion Tracking and Correction. (a) A fiduciary marker (upper left) is placed near the pigmented lesion (lower right) before imaging. (b) During data processing, canny edge detection is used to mark and trace the position of the fiducial. For each individual frame, a region of interest (ROI) is specified with relation to the fiducial's position. (c) The specified ROI's are cropped and collated in order to maintain frame-by-frame consistencies during demodulation. (d) The same ROI is applied to a reference phantom measurement in order to sample ROI specific phase-shifts for later use in demodulation correction.

Fiducials can take the form of just about anything. In our case, circular or star-shaped reflective stickers worked just fine. The rational for employing a fiduciary marker instead of the actual pigmented lesion as a motion-tracking reference is due to the fact that the lesion's surface visibility decreases significantly at higher imaging wavelengths (> 800 nm) due to differential light absorption.

Canny edge detection was selected as the operator of choice because, compared to other edge detection operators such as the Sobel and Laplacian of Gaussian method, Canny was the least likely to be fooled by noise, and most likely to detect true edges due to its combination gradient and Laplacian approach to edge detection.⁽¹⁸⁾ The low error rate, localization of edge points, and single response to a single edge make Canny edge detection ideal for outlining and marking fiducial positions.

2.3 Post-Processing: Demodulation Correction

Before delving into the math behind SFDI demodulation correction, a few things must initially be understood. First and foremost, the diffusely-reflected image intensities, I , collected by the CCD camera are mathematically described as a sum of the illuminated spatially modulated AC and background planar DC components. These can be written as:

Eq. 1

$$\begin{aligned} I_1 &= M_{AC} \cos(f_x x + \phi_1^\circ) + M_{DC} \\ I_2 &= M_{AC} \cos(f_x x + \phi_2^\circ) + M_{DC} \\ I_3 &= M_{AC} \cos(f_x x + \phi_3^\circ) + M_{DC} \end{aligned}$$

Where M_{AC} is the magnitude of the spatially-modulated AC component and M_{DC} is magnitude of the DC component. $f_x x$ and ϕ respectfully represent the spatial frequency and phase-shift of the sinusoidal AC pattern.

In order to effectively separate the AC and DC components of the diffuse reflectance for use in optical property quantization, a phase-shifting technique commonly utilized in communication systems is employed.⁽¹⁴⁾

Eq. 2

$$(I_1 - I_2)^2 + (I_2 - I_3)^2 + (I_3 - I_1)^2$$

The equation above explains why SFDI involves the imaging of three sinusoidal patterns with varying phase-shifts. By subtracting the diffusely-reflected image intensities with one another, the DC component consisting of average-image noise, digitization offset, ambient lighting, and potential spatial-calibration errors are intrinsically removed.⁽¹²⁾ Also, when the phase-shifts are symmetrical at exactly 0°, 120°, and 240°, the equation amiably reduces into $9/2 * M_{ac}^2$, thus allowing AC extraction to be as simple as square-rooting and multiplying by a constant:

Eq. 3

$$M_{AC}(x_i)|_{f_{xi}} = \frac{\sqrt{2}}{3} \sqrt{(I_1 - I_2)^2 + (I_2 - I_3)^2 + (I_3 - I_1)^2}$$

While the equation above (Eq. 3) works well when dealing with large stationary subjects, symmetrical 120° phase-shifts can't always be achieved when imaging pigmented-lesions *in-vivo* in a clinical environment. Considering the small size of many pigmented lesions (~5mm) and the amount of camera-zoom required to effectively image the lesion, motion artifacts from seemingly trivial actions such as breathing and talking have the potential of altering the position of the projected phase-shifts in relation to the target which leads to the creation arbitrary and unintended phase-shift values.

This leads us to the second part of motion-correction in SFDI: modification of the demodulation equation in order to account for motion-related phase-shifts. Going back to Eq. 2, it can be shown that for arbitrary phase-shifts, the equation reduces into a value consisting of an arbitrary function, $\kappa(f_x x, \Phi)$, multiplied by the AC magnitude squared:

Eq. 4

$$\kappa(f_x x, \Phi) M_{AC}^2$$

SFDI motion correction aims to remove the $\kappa(f_x x, \Phi)$ function by dividing the equation above by a correction factor consisting of artificial image sets generated from the sampled spatial-frequency and phase-shifts found in the previous section of this paper. Using our mathematical understanding of the image set contents found in Eq. 1 and inputting the sampled spatial-frequency and phase-shift data while setting the magnitude of the AC component to an arbitrary but convenient value of 'one', we can create a correction factor to isolate our target, M_{AC} .

Eq. 5

$$\sqrt{\frac{\kappa(f_x x, \Phi) M_{AC}^2}{\kappa(f_{x,sampled} x, \Phi_{sampled})^2}}$$

The AC and DC values extracted from this method are then processed normally using the two-frequency look-up table for rapid calculation of optical properties generated from diffusion model forward predictions as described in detail by Cuccia, *et al.*⁽¹²⁾

2.4 Relationship between Demodulation and Optical Property Determination

In order to extract the absorption and reduced-scattering coefficients from the demodulated diffuse-reflectance, a rapid two-frequency look-up table approach was utilized.⁽¹²⁾ Based on the results generated from Monte-Carlo diffusion model forward predictions⁽¹⁹⁾, these look up tables correlate modeled two-spatial frequency diffuse reflectance (AC and DC) to a population of absorption and reduced-scattering combinations. All computation and processing was handled via Matlab. A graphical example of this can be found in Fig. 3:

Fig. 3: Graphical representation of a Monte-Carlo generated two-frequency (DC vs. AC) lookup table.⁽¹²⁾ Horizontal lines mark reduced-scattering values (μ_s') increasing from left to right, and vertical lines mark absorption (μ_a) values increasing from top to bottom. Each intersection represents a unique absorption and scattering optical property for each combination of AC and DC diffuse reflectance at two specific spatial-frequencies.

Compared to using other methods such as an iterative least-squares multi-frequency fitting, using a look-up table can significantly decrease computation time while maintaining an acceptable accuracy. Whereas the iterative process may take 2 hours in order to compute solutions, the look-up table based process may take only 6 minutes. Another advantage is that the look-up table does not require an initial guess of optical properties, which is especially useful when extracting from a dynamic range of *in-vivo* optical properties.⁽¹⁵⁾

3. RESULTS

3.1 Stationary Phantom Measurements

In order to assess the validity of the motion correction technique, stationary phantom measurements were conducted. Artificial tissue-simulating phantoms and test-lesions were created from silicone-based polydimethylsiloxane with homogeneously distributed India ink as an absorber and TiO_2 as a scattering agent.⁽¹⁶⁾ The spectral absorption and reduced scattering coefficients of the calibration phantoms were verified using two-distance, multi-frequency FDPM measurement, as previously mentioned.

The reasoning behind these phantom measurement tests was that, without induced motion, SFDI measurements would consistently maintain symmetrical 120° phase-shifts and motion-corrected demodulation (Eq. 5) would simplify into the non-corrected demodulation (Eq. 3) formula. In this case, both processing methods should become identical and produce similar results.

Fig. 4 (a-f) shows the results from one of these stationary phantom-measurements. Fig. 4 (a, b) shows the snapshots of the absorption intensity map at 650nm. The snapshots are provided in order to indicate the two ROI's. The top-square is the phantom-lesion and the bottom-square is the phantom-skin.

(a)

(b)

(c)

(d)

(e)

(f)

Fig. 4(a-f): Comparison between non-corrected (a, c, e) and motion-corrected (b, d, f) SFDI processing on a stationary phantom measurement. Phantom lesion and skin ROI's are marked in figures (a, b). "Absorption vs. wavelength" plots (c, d) and "scattering vs. wavelength" plots (e, f) show no discernable difference between non-corrected data (left column) and motion-corrected data (right column).

Looking at the “absorption vs. wavelength” and “reduced scattering vs. wavelength” plots, it can be seen that there is no discernable difference between the non-corrected data (*Fig. 4 (c, e)*) and the motion-corrected data (*Fig. 4 (d, f)*). Variance is minuscule in the absorption plots, and the scattering plots have about a 5% variance in all plots for both non-corrected and motion-corrected results. The lack of discernable difference in the results implies that the proposed motion-correction technique does not induce artifacts into the data processing.

3.2 Clinic Measurements

After verifying that the motion-correction technique was comparable to the original non-corrected method, clinical subject measurements were conducted. The goal of these experiments was to examine the range of data variance that could occur in a clinical setting and to determine whether or not motion-correction could make significant impact on data processing.

Data was collected under IRB approved protocol HS# 2008-6307: “*Skin Imaging with Technologies in Development.*” Both the “stationary” and “talking” results presented below were collected from the same subject, a middle-aged Caucasian male with a pigmented-lesion of interest located on the upper-right portion of his back. In both measurements, the subject was instructed to lay face-down on a hospital gurney.

Fig. 5 (a, b) and *Fig. 6 (a, b)* shows the snapshots of the absorption intensity map at 650nm. The snapshots are provided in order to indicate the two ROI's. The top-square is the pigmented ROI and the bottom-square is the un-pigmented normal skin.

“Stationary” subject:

During this measurement, the subject was instructed to lie as perfectly still as possible and not make any deliberate movements. Of course, autonomic actions such as breathing and involuntary twitches were still present. Motion tracking data indicated lesion displacements of up to 0.5mm (the lesion itself was about 5mm wide).

Fig 5: Absorption intensity map at 650nm for non-corrected (a) and motion-corrected (b) SFDI processing on a "stationary" clinical subject. The top-square is the pigmented lesion ROI and the bottom-square is the un-pigmented normal skin.

Fig. 5: Comparison between non-corrected (c, e) and motion-corrected (d, f) SFDI processing on a “stationary” clinical subject. A variance decrease of up to 83.88% was observed between the non-corrected (c) and motion-corrected (d) “Absorption vs. Wavelength” plots. Similarly, a variance decrease of up to 84.29% was observed between the non-corrected (e) and motion-corrected (f) “Scattering vs. Wavelength” plots.

Looking at the “absorption vs. wavelength” and “reduced-scattering vs. wavelength” plots for the non-corrected data set (Fig. 5(c) and Fig. 5(e) respectively), it becomes apparent that even the slightest amount movement can cause a significant increase in data variance for both ROI’s, especially in the lower wavelengths (650nm to 710nm). It also becomes apparent that motion-correction minimizes the variance. For this particular “stationary” clinical subject, a variance decrease of up to 83.88% was observed between the non-corrected (Fig. 5(c)) and motion-corrected (Fig. 5(d)) “Absorption vs. Wavelength” plots, while a variance decrease of up to 84.29% was observed between the non-corrected (Fig. 5(e)) and motion-corrected (Fig. 5(f)) “Scattering vs. Wavelength” plots.

Talking Subject:

During this measurement, the subject was instructed to engage in some small-talk with the clinician during skin-imaging. The motivation was to generate motion artifacts larger than autonomic functions and represent a more extreme, yet clinically relevant, acquisition setting. Motion tracking data indicated lesion displacements of up to 7.1mm (more than an order-of-magnitude larger than the “stationary” case described earlier).

(a)

(b)

(c)

(d)

(e)

(f)

Fig. 6: Comparison between non-corrected (a, c, e) and motion-corrected (b, d, f) SFDI processing on a “talking” clinical subject. Pigmented-lesion and normal-skin ROI’s are marked in figures (a, b). The variance decrease of up to 84.58% was observed between the non-corrected (c) and motion-corrected (d) “Absorption vs. Wavelength” plots. A variance decrease of up to 92.63% was observed between the non-corrected (e) and motion-corrected (f) “Scattering vs. Wavelength” plots.

From the results found in *Fig. 6*, it can be observed that the amount of data variance further increases the more a subject moves about. Similar to the “stationary” clinical measurements found in *Fig. 5*, the “talking” clinical measurements expressed a large amount of variance, especially at the lower wavelengths (650 to 710nm)

For this particular “talking” clinical subject, a variance decrease of up to 84.58% was observed between the non-corrected (*Fig. 6 (c)*) and motion-corrected (*Fig. 6 (d)*) “Absorption vs. Wavelength” plots, while a variance decrease of up to 92.63% was observed between the non-corrected (*Fig. 6 (e)*) and motion-corrected (*Fig. 6 (f)*) “Scattering vs. Wavelength” plots.

5. Conclusion

Looking at the results found in the preceding section, it can be seen that motion-related variables do play a large role in skewing SFDI data measurements. Inconsistent ROIs for processing coupled with arbitrary phase-shift demodulation can lead to increased variability in absorption and reduced-scattering maps, which can then lead to inaccurate quantification of optical properties in pigmented lesions. This is especially true in the 650nm to 710nm wavelengths where absorption and reduced-scattering variability seemed to be the largest, possibly due to the large difference in absorption and scattering between lesion and normal skin at these wavelengths. In the presence of motion and a non-consistent ROI, the mixing of lesion and normal skin values could account for the increased variance.

By implementing motion correction with SFDI processing, a significant portion of the variance can be minimized. This is apparent in *Fig. 6* in which the motion-corrected “absorption vs. wavelength” plot (*Fig. 6(d)*) displayed up to an 84.58% decrease in variance compared to the non-corrected plot *Fig. 6(c)*, while the motion-corrected “reduced scattering vs. wavelength” plot (*Fig. 6(f)*) displayed up to a 92.63% decrease in variance compared to the non-corrected plot (*Fig. 6(e)*).

6. Discussion

In this paper, we have reported on the first motion-correction study of SFDI. While there are probably many other ways to approach the problem of motion-correction in SFDI, the method chosen for this paper was relatively direct in terms of execution. It simultaneously addresses both the motion tracking and demodulation aspects of SFDI, all while exhibiting promising results. This isn’t to say it couldn’t have been more efficient. In particular, during the phase-sampling procedure, it might have been more favorable to sample the phase-shifts from a computer-simulated virtual plane programmed with the modulations, however, due to time-constraints, this was not possible.

None the less, this implementation of SFDI motion correction was able to prove a point: motion-related variables can play a large role in shaping SFDI measurement results. The more a subject moves during imaging, the larger the data variance range increases during processing. This is especially true in terms of studying the optical properties and chromophore concentrations of pigmented lesions for the differentiation between benign and malignant nevus in a clinical setting. While a ‘talking’ clinical measurement would definitely be uncommon, a ‘stationary’ measurement in which the patient is lying as still as humanly possible would still result in skewed results. The smaller ROI that encompasses the lesion compared to the rest of the surrounding normal-skin makes it harder to obtain high-fidelity *in-vivo* optical property SFDI measurements without the use of motion correction. In the end, however, the best scenario would be a SFDI platform in which motion correction would not be even be necessary.

The main reason why motion is currently an issue is because of the acquisition time required to complete a SFDI measurement under the current system configuration. It is important to note that this is *not* a fundamental limitation of the SFDI technique, but rather a limitation of the current instrumentation. There are several ways to help improve acquisition time on the current system, such as imaging fewer frequencies at fewer wavelengths (effectively reducing the acquisition time by 60 to 73%) and by improving the light throughput of the instrument. However, when engaging in investigational studies such as this, there is a greater importance placed on acquiring more frequencies and wavelengths in order to determine which combination may be sufficient to best characterize and detect the specific targets of interest; in our case, melanoma. In these circumstances, motion must be accounted for so that collected data can hold a direct relevance to any future studies aimed at improving data-acquisition efficiency with the goal of developing a more translatable and clinically friendly instrument.

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