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A 2x2-aperture 4-tap multi-modal tissue imager for multi-band SFDI and MELSCI

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ABSTRACT

We are developing a method for simultaneous multi-band spatial frequency domain imaging (SFDI) and blood flow mapping by multi-exposure laser speckle contrast imaging (MELSCI) with a laboratory-designed 2x2-aperture 4-tap CMOS image sensor. Four-tap CMOS image sensor can capture four images synchronized with controlled illuminations and can implement flexible exposure. Although we have demonstrated SFDI with suppressing motion artifact and ambient light bias and efficient video-rate MELSCI based on a four-tap CMOS image sensor separately, simultaneous multi-modal imaging is effective for improving the accuracy of medical diagnosis. The image sensing area is divided into 2×2 regions, and each region is equipped with optical filters and an imaging lens. By using optical bandpass filters, multi-wavelength imaging and wavelength-division multiplexed imaging are realized. Using the fabricated image sensor, we observed a human wrist. 450, 550, 660nm LEDs were used for 3-band SFDI, and a 785nm LD was used for MELSCI. In order to measure a change in the blood flow speed, an examinee was measured before and after an exercise (squatting 30 times). The unit exposure duration for SFDI and MELSCI was 10ms. The pattern was generated by a DMD. The spatial frequency of the projected sinusoidal patterns was 0.1mm^{-1}. M_{DC} and M_{AC} maps for the three wavelengths by SFDI, and K^2 value maps by MELSCI were successfully obtained.

Keywords: compound-eye camera, spatial frequency domain imaging, multi-exposure laser speckle contrast imaging, multi-tap CMOS image sensor

1. INTRODUCTION

In this paper, we propose 2x2-aperture 4-tap multi-modal tissue imager. Simultaneous multi-modal image acquisition of tissue information, such as metabolism, 3D structure, and body fluid perfusion, is effective for improving the accuracy of medical diagnosis. In addition, it is desirable to be able to perform in a normal environment under the room light, not in a special environment such as a dark room. Recently, multi-tap CMOS pixels for computational imaging have been studied [1-2]. The multi-tap pixels can simultaneously capture multiple images synchronized with active illuminations and can implement flexible and functional exposure. Multi-aperture optics enables multi-wavelength imaging and wavelength-division-multiplexed imaging. The proposed imager can perform multi-wavelength spatial frequency domain imaging (SFDI) with the structured light projection [3-4] and laser speckle contrast blood flow speed imaging (MELSCI) [5] for obtaining chromophore concentration, reduced scattering, and perfusion maps. SFDI is capable to estimate absorption and reduced scattering coefficients at the same time when the assumed tissue model is reasonable. Multi-wavelength imaging enables us to estimate chromophore concentrations such us oxy-/deoxy-hemoglobin, melanin, fat, and water by fitting the measured absorption spectrum with a linear combination of their known molar absorption spectra [6-7]. Laser Doppler imaging is one of the most popular blood flow velocity imaging methods [8]. However, it has some problems such as

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contact measurement, long measurement time, size and complexity of the measurement equipment, and so on. Therefore, we use MELSCI, which is non-invasive, non-contact, has a relatively simple optical system, and can perform real-time measurements.

2. METHODOLOGY

2.1 SFDI

SFDI is based on the fact that the modulation transfer function (MTF) of a scattering medium depends on the absorption coefficient μ_a and the reduced scattering coefficient μ_s'. The modulations for two or more spatial frequencies are measured at each pixel. Then, μ_a and μ_s' are estimated by referring to a look-up table made by the Monte Carlo simulation. To measure the MTF, three sinusoidal patterns with a one-dimensional wave vector whose spatial phases differ by $2\pi/3$ are projected to the tissue and their reflection images are taken. When the pixel values of the reflection images for the three spatial phases are denoted by $I_1(x,y)$, $I_2(x,y)$, and $I_3(x,y)$, the amplitude reflections for AC and DC components, M_{AC} and M_{DC}, are calculated by Eqs. 1 and 2, respectively.

$$M_{AC} = \frac{\sqrt{2}}{3}[\{I_1(x,y) - I_2(x,y)\}^2 + \{I_2(x,y) - I_3(x,y)\}^2 + \{I_3(x,y) - I_1(x,y)\}^2]^{\frac{1}{2}} \quad (1)$$

$$M_{DC} = \frac{1}{3}[I_1(x,y) + I_2(x,y) + I_3(x,y)] \quad (2)$$

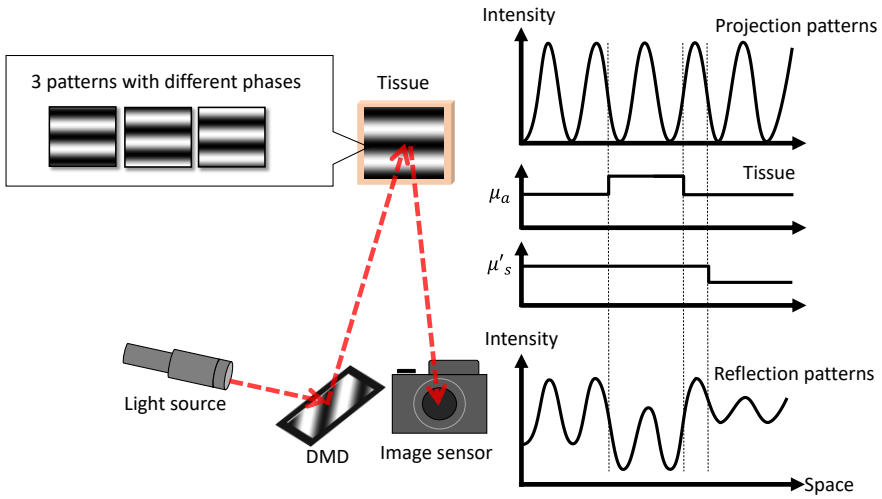

Figure 1. Spatial frequency domain imaging (SFDI).

2.2 MELSCI

MELSCI is a wide-field blood flow speed imaging method based on the bio-speckle generated by coherent illumination. Fig. 2 shows the simplified schematic of laser speckle generation. When a laser beam irradiates a scattering medium such as tissues, the reflected light interferes on the imaging plane of the camera, producing a spatially random granular light intensity distribution called a speckle pattern. When red blood cells move by the blood flow, the speckle pattern changes over time. The speed of the change depends on the flow speed. Since the speckle pattern is averaged over the exposure time of the image sensor, the faster the flow speed becomes, the lower the spatial contrast does. This is shown in Fig. 3. The square speckle contrast $K^2(T)$ is defined by the following equation, where $\langle\sigma^2(T)\rangle$ and $\langle\langle I(T)\rangle\rangle$ are the mean variance and mean average intensity, respectively, for a region of interest.

$$K^2(T) = \frac{\langle \sigma^2\,(T) \rangle}{\langle \langle I(T) \rangle \rangle} \tag{3}$$

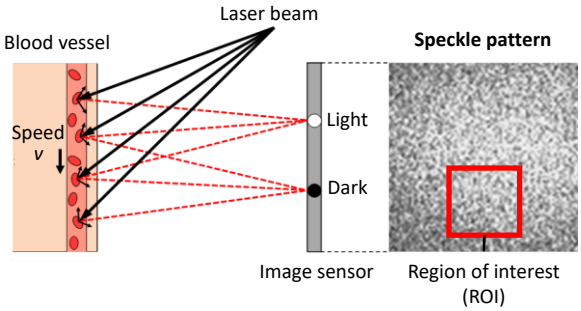

Figure 2. Simplified schematic of laser speckle generation.

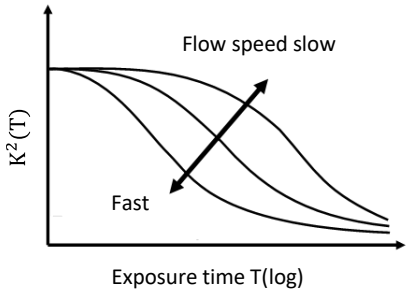

Figure 3. Exposure durations and speckle contrast squared value.

2.3 Multi-tap CMOS image sensor

Fig. 4 shows the structure of the pixel with four-taps and charge draining gates. Normal CMOS image sensor pixels provide only one pixel value for one pixel. However, multi-tap CMOS pixels output multiple pixel values at the same time because they have multiple charge transfer gates(G) and a charge detection sections(FD) in a single photodiode [9]. The multi-tap pixels can simultaneously capture the multiple images synchronized with controlled illuminations and can implement flexible exposure. Flexible exposure controllability of the multi-tap pixel is useful both for SFDI and MELSCI. We have demonstrated the SFDI with suppressing motion artifact and ambient light bias and efficient video-rate MELSCI based on a four-tap CMOS image sensor separately [10-11].

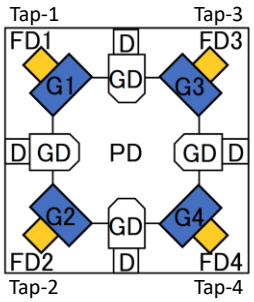

Figure 4. Pixel structure of 4-tap CMOS image sensor.

2.4 Multi-aperture multi-tap multi-modal tissue imager

Fig. 5 shows a conceptual diagram of the proposed multi-modal tissue imager based on multi-aperture optics and multi-tap CMOS image sensor. For SFDI, the light source with multiple wavelengths illuminates a digital micromirror device (DMD) to project a sinusoidal pattern onto the tissue. For MELSCI, a 785 nm LD is used for planar illumination. The wavelength assignment can be customized as desired to suit the measurement target. The image sensing area is divided into multiple regions, and each region is equipped with optical filters and an imaging lens. Each region is separated by the image separator to avoid image overlapping. By using a band-pass filter, wavelength-division multiplexed imaging of multi-wavelength SFDI and MELSCI is possible for estimating chromophore concentrations, scattering, and blood flow speed.

Fig. 6 shows an example timing chart of pixel operation. In SFDI, three patterns are projected sequentially, which are assigned to the taps-1 to -3. Tap-4 detects the ambient light. By shortening the unit exposure time and repeating the exposure, motion artifact in the measured optical property is suppressed while the captured image brightness is kept the same as that for moderate exposure time. The exposure of the MELSCI aperture should be independently controlled because the appropriate exposure time is optimized according to the flow speed range.

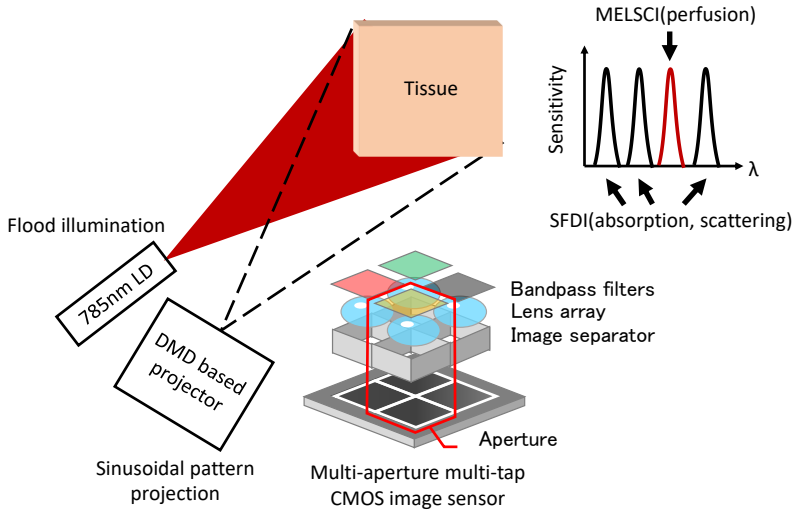

Figure 5. Multi-modal tissue imaging system.

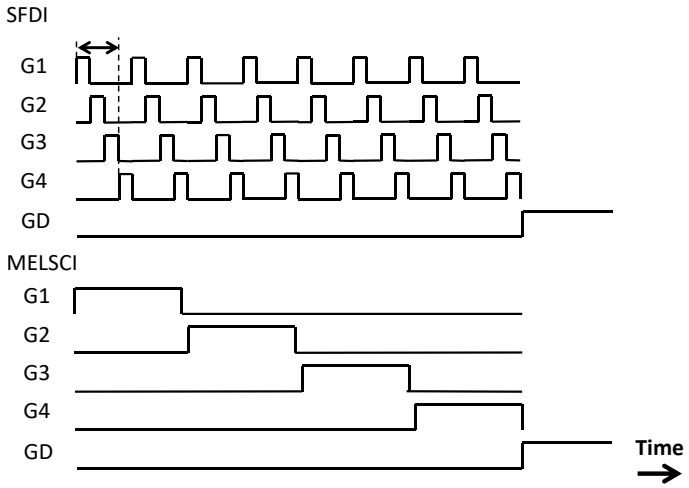

Figure 6. Timing chart.

3. DATA

3.1 Prototype 2x2-aperture 4-tap multi-modal tissue imager

Fig. 7(a) shows the layout of the prototype image sensor and Fig. 7(b) shows the assembled multi-modal imager with lenses and filters. As shown in Fig. 7(a), the pixel area is divided into 2 × 2, one of which is assigned to MELSCI and the other three to SFDI. The three SFDI regions and the MELSCI region are controlled separately. In SFDI, motion artifacts can be suppressed by repeated exposure with short exposure times. On the other hand, in MELSCI, the exposure time was optimized for the measured blood flow speed range. Table 1 summarizes the specifications and measured characteristics of the prototype system.

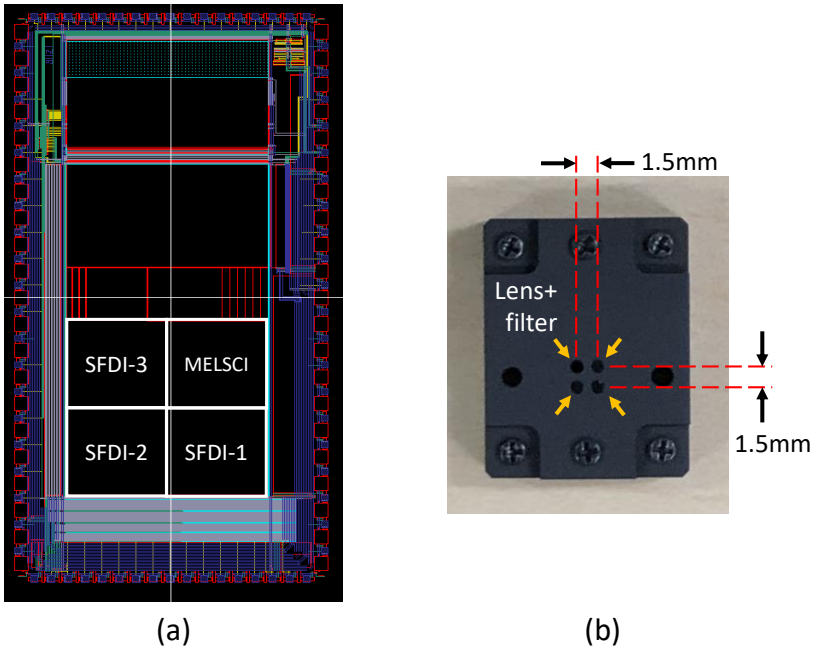

Figure 7. (a) layout of prototype sensor and (b) attached optics.

Table 1. Specifications and characteristics.

Technology	0.18μm CMOS process
Aperture count	2×2
Pixel count per aperture	132×132
Pixel size	11.2μm□
Effective imaging area per aperture	1.48mm sq.
Fill factor	17.5%(w/o MLA)
Number of taps	4 taps + drain
Frame rate	2.8fps
Charge transfer speed	<10μs
Pixel control	SFDI and MELSCI can be controlled separately.

3.2 Experimental condition

Table 2 shows the experimental condition. Using the fabricated prototype image sensor, we observed a human wrist. The spatial frequency of the projected sinusoidal pattern is 0.10mm^{-1}. The numbers of repeated exposures for SFDI and MELSCI were set to 16 and 1, respectively. The experiment was conducted in the darkness. For SFDI, 450, 550, and 660nm LEDs operated in the CW mode were used as the light sources of the DMD projector. Although near-infra-red wavelengths should be included, only visible wavelengths were selected due to low photosensitivity of the prototype image sensor. For MELSCI, a 785nm LD was used for planar illumination. In order to measure the change in blood flow speed by MELSCI, the subjects were asked to squat 30 times. The measurement was conducted before and after the exercise. Pulse rates measured by pulse oximeter were 75 bpm and 118 bpm before and after the exercise, respectively.

Fig. 8 shows the optical setup. In SFDI, three LED light sources with wavelengths of 450, 550, and 660 nm were combined by the dichroic mirrors. A polarizer and analyzer were placed to remove the surface reflection. In addition, a 785nm LD for MELSCI was used to illuminate the specimen after expanding with a lens.

Table 2. Experimental conditions.

Spatial frequency	0.10 mm^{-1}	
Number of repetitions	SFDI	16 times
	MELSCI	1 time
Exposure time for 1 tap	10 ms	
Ambient light	None	
Number of images taken	10 images	
Light source	SFDI	LED：450, 550, 660 nm
	MELSCI	LD：785 nm
Measurement condition	Before and after 30 squat exercises	
Examinee's pulse rates	Before	75 bpm
	After	118 bpm

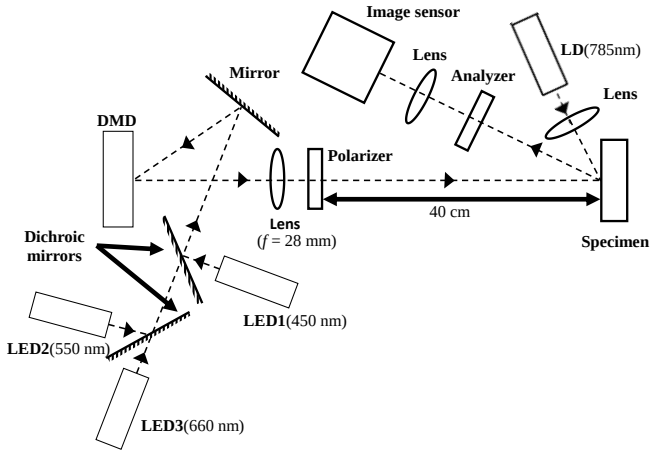

Figure 8. Optical setup.

4. RESULTS

Fig. 9 shows an example of captured images. Four images corresponding to the taps were obtained at once. Different images for the four wavelengths were embedded on a single image for each tap. The SFDI regions in tap1-3 were for the three spatial phases. The ambient light acquired by tap-4 is subtracted from the pixel values of tap1-3 to remove the bias by the ambient light if the measurement is performed in a bright place.

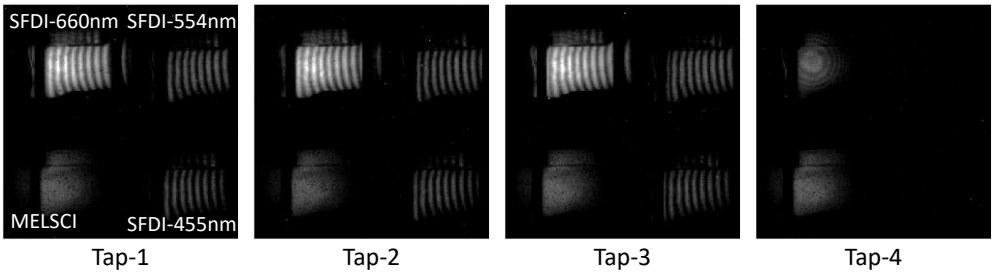

Figure 9. Captured images for before exercises (10 frames averaged, Brightness +20%, Contrast -20%).

Fig. 10 shows map of the DC and AC components of the reflectance at each wavelength. The high reflectance at 660nm reflects low absorption by tissue chromophores.

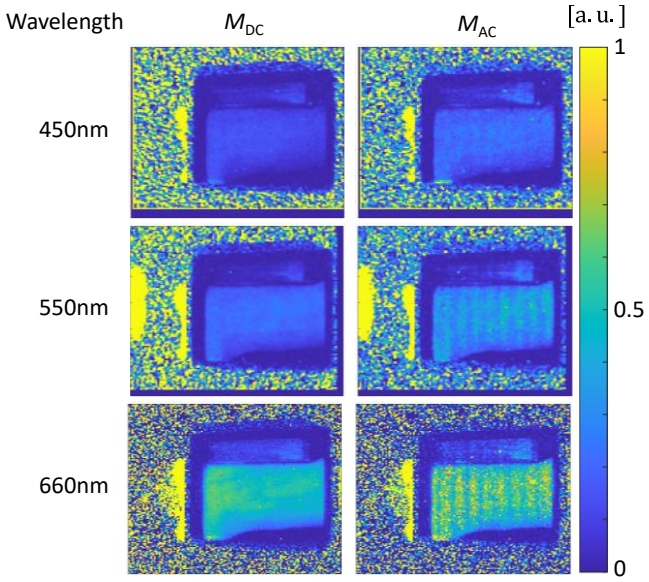

Figure 10. Measured M_{DC} and M_{AC} maps calculated from the images shown in Fig. 9.

Fig. 11 shows the actual captured image and the ROI to calculate the contrast $K^2(T)$. Fig. 12 shows the contrast map obtained by synthesizing the speckle contrast captured at each tap. Fig. 13 shows the plot of the mean value of the contrast map versus the synthesized exposure time. We can see that the average contrast became lower after exercise. High pulse rate indicated that the blood flow speed increased.

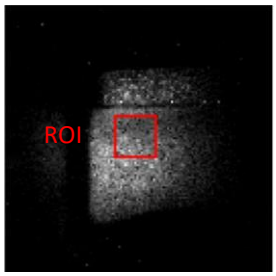

Figure 11. The ROI (20 × 20 pixels) for MELSCI.

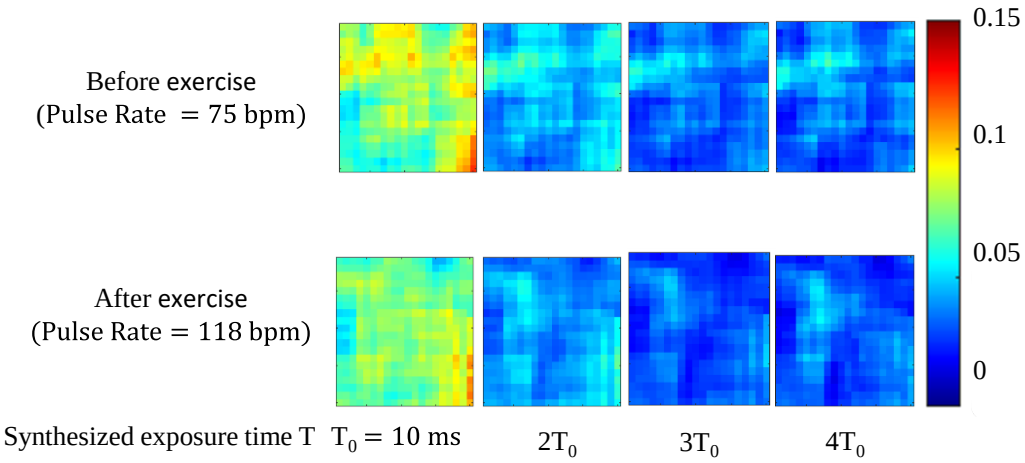

Figure 12. Measured K^2 maps for the ROI shown in Fig. 11.

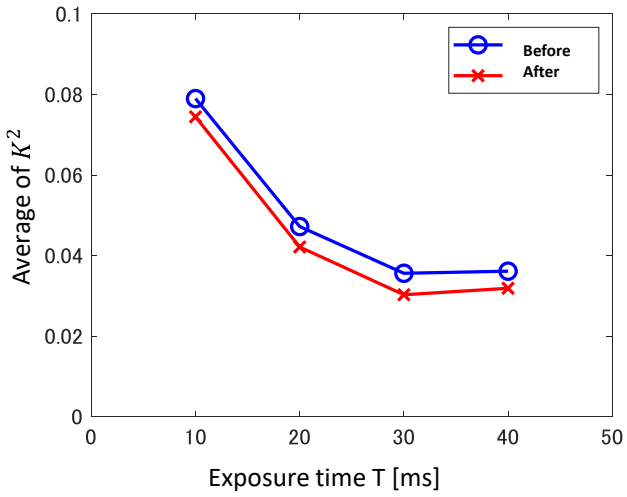

Figure 13. Average of K^2 maps for Fig. 12

5. CONCLUSIONS

A 2x2-aperture 4-tap multi-modal tissue imager for multi-band SFDI and MELSCI was proposed. From the experimental results, we realized the simultaneous measurement of different measurement methods such as multi-wavelength SFDI and MELSCI, and obtained the wide-field maps of M_{DC}, M_{AC}, and K^2 for the human wrist.

As future work, we are going to estimate the chromophore concentrations, the reduced scattering coefficients, and the blood flow speed from the obtained wide-field maps.

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