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ABSTRACT

We developed a novel system for imaging and qualitatively analyzing the surface vessels using near infrared (NIR) radiation using tuned aperture computed tomography (TACT®). The system consisted of a NIR-sensitive CCD camera surrounded by sixty light emitting diodes (with wavelengths alternating between 700 nm or 810 nm). This system produced thin NIR tomograms, under 0.5mm in slice thickness. The venous oxygenation index reflecting oxygen saturation levels calculated from NIR tomograms was more sensitive than that from the NIR images. This novel system makes it possible to non-invasively obtain NIR tomograms and accurately analyze changes in oxygen saturation.

Keywords: near infrared; tuned aperture computed tomography; near infrared tomogram; venous oxygenation index.

1. INTRODUCTION

The regional vascular oxygenation level provides very important clinical information for the analysis of biological conditions. Vascular oxygenation levels need to be measured as an aid to monitor blood oxygen levels and saturation; therefore, non-invasive measurement methods under realistic biological conditions have been developed.[1-5] These are permitted by measurement method using near infrared (NIR). Systems described in the literature are based on a specific characteristic that NIR is absorbed by the hemoglobin in blood.[6] Additionally, development of noncontact sensing methods to define the location of the near surface veins holds considerable promise for aiding in obtaining of blood samples from individuals whose veins are not evident from visual inspection.[7] Such capability would be especially useful for infants and those with elevated BMI values. Since NIR can transmit through thin regions such as through a finger, vascular images can be easily acquired[8, 9] and monitoring blood oxygen saturation can be easily measured.[10] Although, using a transmission method is limited to thin regions, this study developed a novel system for the non-invasive imaging of surface vessels in thick regions where NIR imaging is not always feasible. Additionally, NIR tomograms using tuned aperture computed tomography (TACT®) were obtained, as well as measurements of the regional vascular oxygenation levels.

In this paper, we demonstrated the utility of this system, described its characteristics, and its potential future clinical applications.

2. MATERIALS AND METHODS

2.1 System

A NIR-sensitive charged-coupled device (CCD) camera (XC-EI50/50CE, Sony Corporation, Tokyo, Japan) was surrounded by sixty light emitting diodes (LED) (alternating wavelengths between 700 nm to 810 nm, VSF706C1 and LSF811C1, Optrans, Tokyo, Japan), that could only detect NIR from subcutaneous tissues (Fig. 1). The NIR was absorbed across surface vessels more than any other surrounding tissues.

2.2 TACT theory

TACT is a reconstruction method that can be used to synthesize three-dimensional representation from multiple arbitrary prerecorded two-dimensional basis images (each acquired at a different angle) of interesting region. The basic principles of TACT algorithm are derived from optical aperture theory and tomosynthesis.[11, 12] The TACT stacks the basis images, inputs locations of fiducial markers for each basis image, and reconstructs a series of arbitrary multi-planner cross-sectional images. Stability for maintaining continuity in geometric is required for the generation of three-dimensional images, such as computed tomography, at the time of collection of images. However, TACT enables an arbitrary setup of projection directions, because the position of the fiducial markers is always available. Moreover, because image reconstruction often involves only shifting and adding two-dimensional images, the process is rapidly and efficiently managed by even the simplest image-processing computers. Iterative restoration is often utilized in TACT imaging in an attempt to improve detail clarity.[13, 14] The iterative restoration algorithm works for the deblurring of TACT slices to remove out-of-focus noise. TACT has been used in the clinical application of digital mammography,[15] and oral surgery using x-ray emitting devices,[16] whereas there has been no study, that we are aware of, that reconstructed NIR tomograms.

2.3 Tomograms

To increase the image contrast of the vessels and obtain three-dimensional information, we created tomograms calculated from NIR images (basis images) using the TACT program (TACT Workbench version 0.9.43). First, for TACT series, a fiducial marker was used by attaching approximately 1 mm wire to the forearm skin within the field of view. Next, when considering the factors influencing the image accuracy of TACT,[17-19] Six concentric NIR projections of surface vessels including the marker were obtained, and reconstructed as tomograms (Fig. 2). The angular disparity was set at 30 degrees during each projection. Reconstructed images were processed by using the proprietary iterative restoration algorithm 3 times (default setting).

2.4 Venous oxygenation index

Multiple NIR images (six projections in total) of surface vessels on the forearm were obtained before and after the loading test, that is, using a blood pressure cuff on the upper arm at each wavelength in accordance with optical aperture theory[11, 12] during the first second. We held the cuff pressure at more than 140 mmHg to occlude vessels. Then, tomograms were created using the TACT program, and the venous oxygenation index (VOI) was calculated from the image signal intensities at each wavelength (Equation 1), which is an indicator of the oxygen saturation level.[20]

$$VOI = \frac{I_{700}}{I_{810}} \quad , \qquad (1)$$

where I_{700} and I_{810} are the signal intensities of the vessels for the 700 nm and 810 nm images, respectively. Figure 3 shows the measurement procedure for the calculation of VOI. Moreover, the VOI was compared to the oxygen saturation (SpO_2) using a pulse oximeter. The study was performed in 5 healthy volunteers after informed consent was obtained from each human subject.

2.5 System characteristics

Correlation between the current supplied to the LED and the signal intensity of the NIR images was investigated, because signal intensity of NIR image is relative value. When the current to the LED at each wavelength respectively was slowly increased to the maximum value, NIR images of LED light were obtained by CCD camera, and the signal intensities of these images were measured.

In addition, we evaluated the effective slice-thickness of our system using a chart, which is a specially designed apparatus for the measurement of tomographic slice-thickness. This chart was placed at an angle 11°32’ relative to the tomographic plane. Six concentric projections of chart images were obtained and reconstructed as tomogram using the TACT program. Slice-thickness property was evaluated visually by one of the authors.

2.6 Statistical Methods

The Wilcoxon signed-rank test was used to assess for difference in VOI and SpO_2 before and after loading test. Multiple linear regression analysis was used to assess the relation between the current supplied to the LED and the signal intensity of the NIR images.

3. RESULTS

Our system was capable of acquiring several projections for the tomograms within a few seconds in thick regions that cannot transmit [Fig. 2(a)], and easily reconstructs a tomogram using TACT program [Fig. 2(b)].

VOI was good correlated with SpO_2 in this system during loading test using blood pressure cuff (Fig. 4). Both VOI with TACT and SpO_2 after loading test were significantly lower than those before loading test (*P* value = 0.0431, *P* value = 0.0431), but VOI without TACT was not significant difference (*P* value = 0.345) (Fig. 5).

There was a high correlation between the signal intensity of NIR images and the current supplied to the LED at each wavelength in Fig. 6 (R^2 = 0.998, *P* value < 0.001 in 700 nm, R^2 = 0.999, *P* value < 0.001 in 810nm). The effective slice-thickness of our system was 0.4 mm [Fig. 7(b)].

4. DISCUSSION

A transmitted beam is generally used for NIR imaging,[8, 9] but this system would obtain NIR images in thick regions that cannot transmit [Fig. 2(a)]. Some methods to obtain tomograms using NIR are reported,[21, 22] but require lengthy imaging times, in the order of more than ten minutes, with the additional restraint of limited scan regions. We could obtain several projections for the tomograms within a few seconds, and easily reconstructs a tomogram using TACT and even three-dimensional images [Fig. 2(b) and (c)]. TACT is usually used in x-ray system (radiography is used as basis image).[11-19] Although there has been no study that reconstructed NIR tomograms, TACT reconstruction process in our system was similar method in x-ray system. Therefore, the number of projections needed to reconstruct the tomography, the accuracy of the method, and robustness of the method are not different between x-ray system and our system.

VOI and SpO_2 demonstrated good correlation in this system (Fig. 4). The result indicates that we can evaluate oxygen saturation of surface vessels. After the cuff pressure was released, the VOI tended temporarily to rise compared to before the loading test. It is assumed that the blood flow volume increased temporarily, as the blood flow was interrupted by the load and was rapidly effused when the cuff pressure was released. Moreover, measurement sensitivity was improved when tomograms were used for the calculation of VOI (Fig. 5), because tomograms can only evaluate the blood signals. However, the NIR image signal without TACT overlapped with the surrounding thick tissue signal. Although at least six NIR images were required to reconstruct the tomograms, all images were acquired within one second. Thereby, temporary resolution is satisfied with the loading test for evaluating the oxygenation change. We used a pulse oximeter as the gold standard to measure SpO_2, and compared these findings with VOI, since it was desired to exclusively use non-invasive methods.

To analyze VOI, it is necessary that the relationship between NIR radiation intensity and signal intensity of the images is linear, because signal intensity of NIR image is relative value. In this study, there was a linear dependency between the current supplied to the LED and the image signal intensity (Fig. 6). Because it is already known that the relationship between the NIR signal intensity and current supplied to LED is linear,[23, 24] linearity between NIR radiation intensity and image signal intensity was verified by this study in the range where VOI was measured. Therefore, we can measure VOI independently of image signal intensity.

In tomosynthesis, slice-thickness is considered to be in relation to the angular disparity of the projection geometry, as in tomography. The effective slice-thickness of our system was 0.4 mm [Fig. 7(b)]. This was considered appropriate because forearm blood vessels used for the calculation of VOI were 2 mm in diameter (Fig. 8).

However, it must be noted that there are some variables in the measurement of VOI. First, the distance between the skin and CCD camera could have an impact on the acquired image data, because the focus of the lens mounted CCD camera of this system was matched to the surface vessels. Thus, NIR repeated scattering in air could be detected by the CCD camera, which might contribute to a decrease in image contrast. In the next series of studies, a grid will be attached, which is an optical fiber bundle, between the skin and CCD camera to decrease scattering effects. The different path lengths of the NIR transmitting subcutaneous tissue might cause different signal intensity attenuations. Therefore, an attenuation correction method by the analysis of skin tissues spatial fluorescence distribution by Monte Carlo simulation is required.[25, 26] Additionally, to increase measurement precision of VOI, we need to establish a correction method of image inhomogeneous sensitivity at each wavelength.

We cannot show the advantage compared previous method on relevant NIR imaging, but it could be enhanced proposed method, because, theoretically, the summation of images increases signal-to-noise ratio and image contrast of vessels compared with single NIR image. Moreover, the ability to acquire spatial information three dimensional would increase the diagnostically useful information available over conventional two-dimensional display. Indeed measurement sensitivity was improved when tomograms were used for the calculation of VOI. Of course, further investigation in clinically relevant should be pursued in the future.

In future clinical works, we would like to apply our system to evaluate Reynaud's syndrome and torsion of the testis decreasing the regional vascular, tissue viability of skin grafts and bedsores, as well as skin inflammation due to breast radiation therapy.

4. CONCLUSION

This novel imaging system makes it possible to non-invasively obtain NIR tomograms containing three-dimensional information which can then be used to accurately analyze changes in oxygen saturation levels. There are several clinical applications for which this system will be best utilized such as to increase treatment efficacy or to detect early symptoms of the adverse effects of radiation on the sensitive tissues of the skin. Further clinical studies are required to refine the system for everyday clinical usage.

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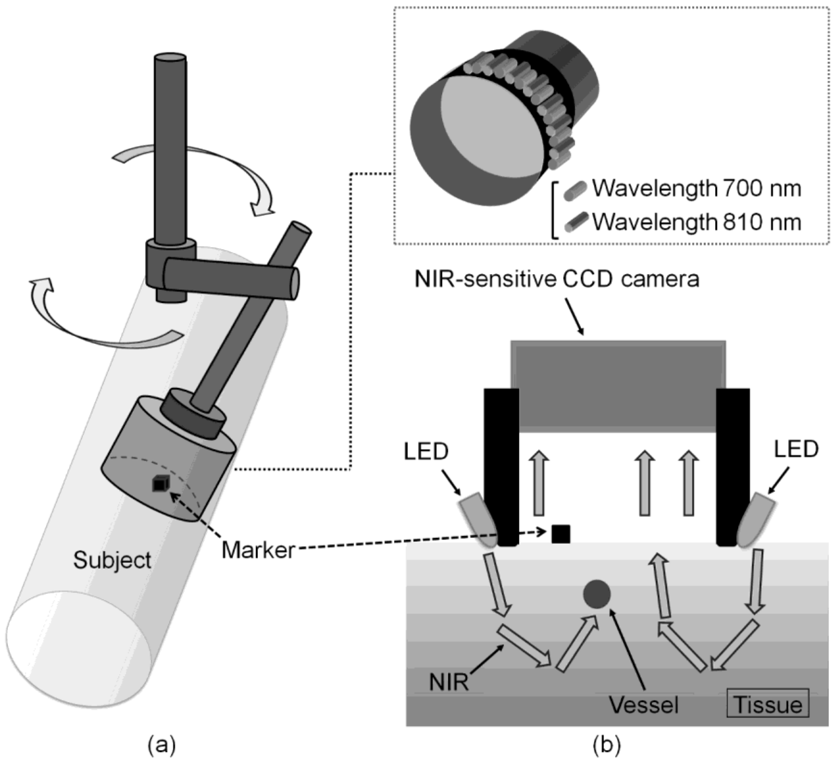


Figure 1 (a) The acquisition system and (b) schematic diagram for NIR imaging.

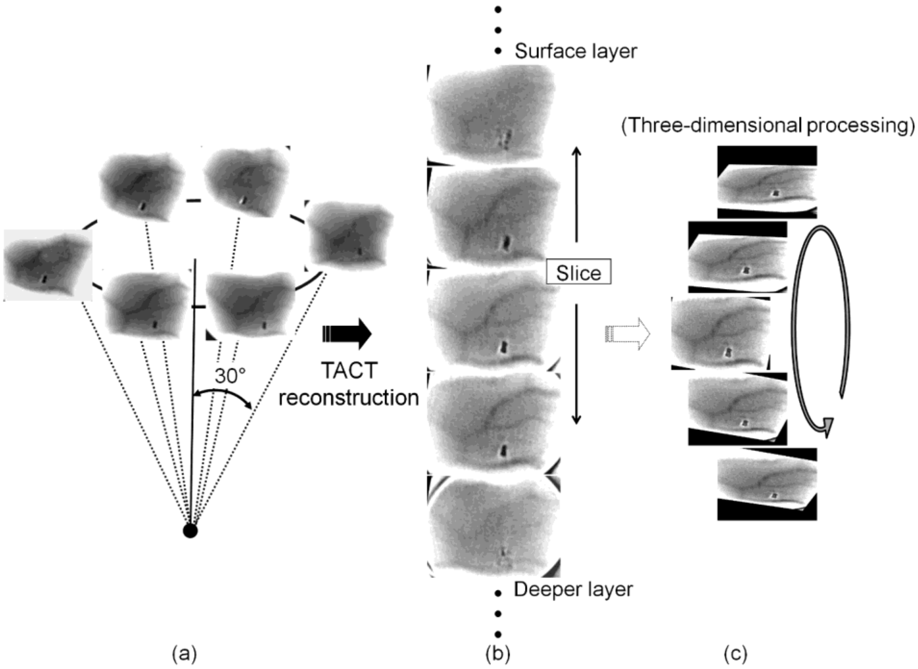


Figure 2 One example for TACT procedure. (a) NIR images (wavelengths: 810 nm) of surface vessels and projection geometry relationships between angular disparity and numbers of projections performed. (b) TACT slices reconstructed from (a). (c) Rotated three-dimensional data structures from (b).

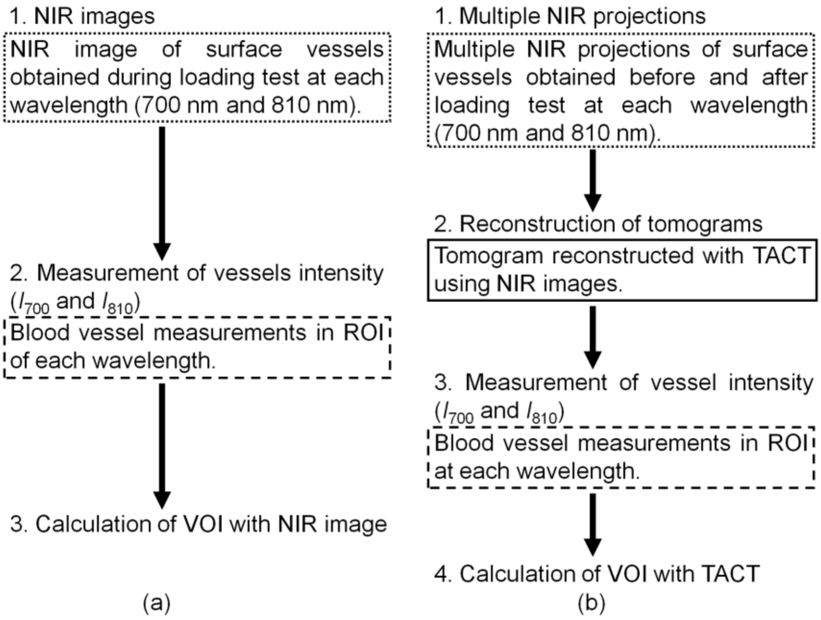


Figure 3 VOI measurement procedures (a) without and (b) with tomograms.

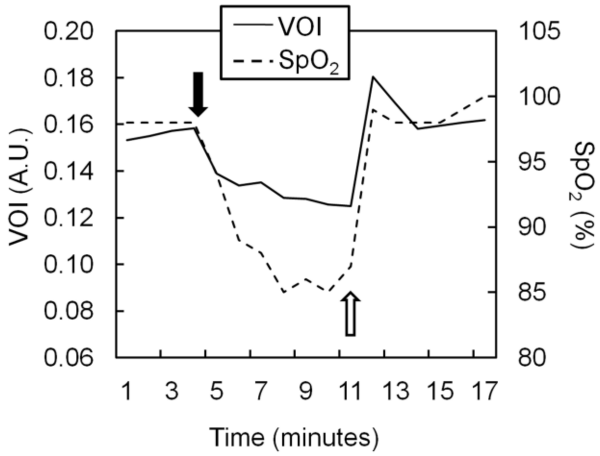


Figure 4 Change in venous oxygenation index and SpO_2 during the loading test. Black arrow showed cuff pressure on, and white arrow showed cuff pressure off. Note that there was good agreement with VOI and SpO_2. A.U.: arbitrary unit.

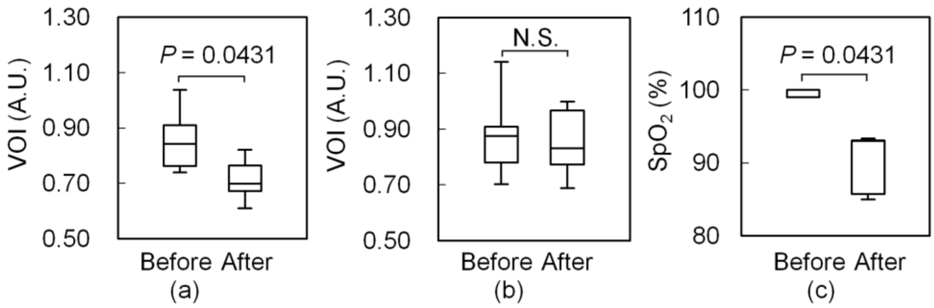


Figure 5 Change in VOI (a) with TACT and (b) without TACT, and (c) change in oxygen saturation (SpO_2) measured by pulse oximeter before and after loading test. VOI with TACT and SpO_2 after loading test were significantly greater than before. However, there was no significant difference in VOI without TACT (*P* value = 0.345). A.U.: arbitrary unit. N.S.: not significant.

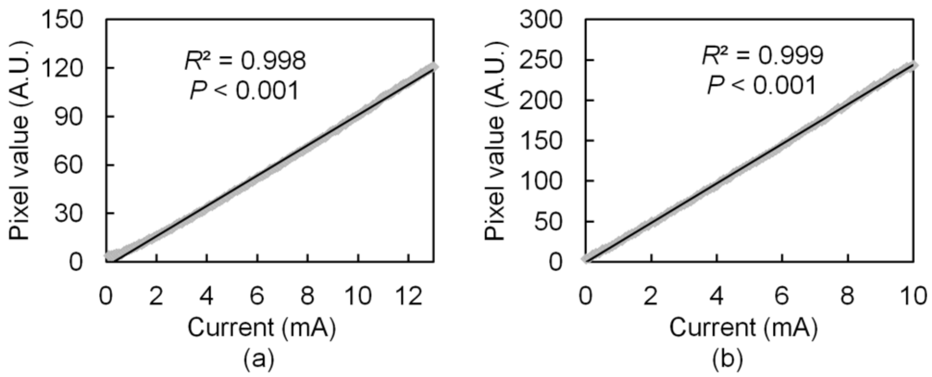
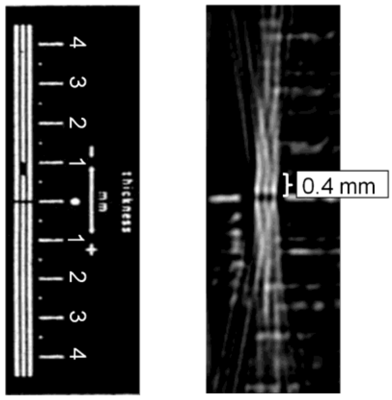


Figure 6 Relationship between the signal intensity of NIR images and current (mA) in (a) 700 nm and (b) 810 nm LED. There was a high correlation between the signal intensity of NIR images and the current supplied to the LED at each wavelength. A.U.: arbitrary unit.



(a) (b)

Figure 7 (a) Picture of chart and (b) NIR image for assessing the slice thickness of NIR with TACT. Scale corresponding to the slice-thickness of the tomogram.

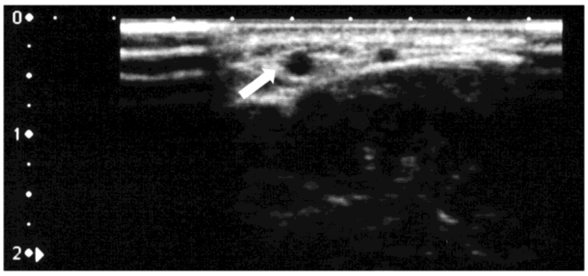


Figure 8 Forearm surface vessels image by ultrasound. White arrow shows median antebrachial vein, which is 2.0 mm in diameter. Surface to vein distance is 5.0 mm.