Fundamental Imaging Properties of Transillumination Laser Computed Tomography Based on Coherent Detection Imaging Method

Tetsuya YUASA,[†,*1] Shinji TANOSAKI,[*2] Yoshiaki SASAKI,[*1] Michiaki TAKAGI,[*3] Akira ISHIKAWA,[*3] Hiroshi TANIGUCHI,[*4] Balasigamani DEVARAJ,[*5] and Takao AKATSUKA[*1]

[*1] *Faculty of Engineering, Yamagata University, 4-3-16 Jonan, Yonezawa 992-8510, Japan*
[*2] *I.T. Research Co., Ltd., 2-1-40 Takamori, 21st Century Plaza, Izumi, Sendai 981-3203, Japan*
[*3] *School of Medicine, Yamagata University, 2-2-2 Iida, Yamagata 990-0031, Japan*
[*4] *Faculty of Engineering, Iwate University, 4-3-5 Ueda, Morioka 020-8551, Japan*
[*5] *New Focus Corp., 5215 Hellyer Avenue, San Jose, CA 95138-1001, USA*

The coherent detection imaging (CDI) method uses the optical heterodyne detection technique. CW and single frequency lasers having long coherence lengths are used to exploit the maximum advantages of heterodyne detection, such as high directionality, selectivity and sensitivity. The CDI method based on optical heterodyne detection enables selective filtering of the directional coherence-retaining emergent photons, which leads to image reconstruction from projections, similar to X-ray computed tomography (CT). So far we have demonstrated the advantages and capabilities of the measurement technique for transillumination optical computed tomography in biomedicine. Here, we investigate the fundamental imaging properties of CDI method, such as its high directionality and quantitativeness, with preliminary physical phantom experiments. The results show that the CDI method satisfies the requirements for CT reconstruction under the first order approximation, and enables quantitative measurements in the sense that the relationship between estimated and actual concentration retains a satisfactory linearity.

(Received June 23, 2002; Accepted September 19, 2002)

Recently, diagnostic techniques, *e.g.*, X-ray computed tomography, radiography, ultrasonography, single photon emission computed tomography (SPECT), positron emission tomography (PET), and magnetic resonance imaging (MRI) are used widely in most hospitals to image the internal structure and to map the functional state of organs and tissues and are indispensable for modern clinical medicine. However, the conventional imaging techniques have some limitations. X-ray CT, SPECT, PET, and MRI expose us to ionizing radiation and intense magnetic fields harmful to human body. Medicine requires safer diagnostic methods to supplement or to provide an alternative, especially for infants or pregnant women. Furthermore, imaging equipments such as X-ray CT or MRI require large-scale facilities to shield from ionizing radiation or intense magnetic fields, resulting in high expense.

On the other hand, the recent explosive development of photonics is attracting the growing attention of researchers in biomedical measurements.[1,2] Using optical techniques enables us to realize a portable system at low cost. In addition, the advantageous properties of optical imaging in the visible and infrared regions with appropriate power provide a desirable biomedical measurement tool in the following area: First, light is nonionizing and nondestructive when optimally used and hence is even safer than the conventional imaging diagnostic methods, except for ultrasound imaging. Second, use of the inherent wavelength dependence of tissues results in enhanced image contrast, and then abstracts a variety of physiological functional information dependent on wavelengths from a biomedical subject. Third, light in the visible and infrared wavelength regions between 600 and 1300 nm, which are referred to as the therapeutic window, is relatively penetrable to biological samples. One can take advantage of not only lower Rayleigh and/or Mie scatterings by biological tissues, but also minimal attenuation of light by biological pigments in these regions.

In spite of these advantages, the development of optical methods for biomedical imaging had been hindered due to extremely complex interactions between light and biological tissues, which led to very low *S*/*N* signals. Currently, various optical measurement techniques are being developed based on different physical principles to overcome the difficulties with respect to light interaction with biological tissues.[3] Optical techniques used for biomedical imaging can roughly be categorized into time resolved methods, frequency domain methods and coherent detection methods.[3] Although fundamental detection principles are different, the basic idea of most measurement methods is to select and detect the minimally scattered on-axis photons emanating from tissue, since the highly directional photons still have their original properties even after traversing through biological tissues with highly scattered nature, and therefore contain maximum image information.

Our measurement technique, which is referred to as the coherent detection imaging method (CDI), belongs to the coherent detection method.[2] Originally, the CDI method based on the optical heterodyne detection technique for laser tomography of biological tissues in the transillumination mode was devised and realized by Inaba and co-workers. They had demonstrated its effectiveness for bio-

†To whom correspondence should be addressed.
E-mail: yuasa@eat72.yz.yamagata-u.ac.jp
Note: This article was prepared as a camera-ready copy.

medical imaging, and reported tomographic images of various biological samples both *in vitro* and *in vivo*.[3-11]

In this paper, we consider the fundamental imaging properties of the CDI method, not discussed sufficiently before, using a physical phantom. We first consider the high directivity of the heterodyne detection and confirm that the light power traversing through the highly scattering sample exponentially attenuates with an increase of concentration, which is indispensable for obtaining projection data. Then, we describe how the CDI method satisfies the requirements for CT reconstruction. And we demonstrate by physical phantom experiments that there exists quantitativeness in reconstructed images in the sense that the relationship between estimated and actual concentrations retains a satisfactory linearity. However, the quantitativeness still remains insufficient. Finally, we point out one factor of the hindrance.

Experimental

Imaging system

Optical heterodyne detection is a method to selectively detect a beat signal with intermediate frequency, *i.e.*, the frequency of the beat signal generated by mixing a signal light after traversing an object with a local oscillator light whose frequency is slightly different from that of the signal light. We denote the frequencies of the signal and the local oscillator light by ω_s and ω_l, respectively. Hence, since the signal and the local oscillator light are represented as $E_s = E_{s0}\exp(i\omega_s t)$, $E_l = E_{l0}\exp(i\omega_l t)$, where E_{s0}, and E_{l0} are their amplitudes and their polarizations are neglected, the output current from the detector is given as

$$|E_{s0}\exp(i\omega_s t) + E_{l0}\exp(i\omega_l t)|^2 = |E_{s0}|^2 + |E_{l0}|^2 + 2|E_{s0}||E_{l0}|\cos(\omega_s - \omega_l)t \quad (1)$$

Applying the band-pass filter at intermediate frequency ($\omega_s - \omega_l$), the absolute amplitude of the signal light, $|E_{s0}|$, can be obtained.

Figure 1 shows the schematic diagram of our experimental arrangement based on a Mach-Zehnder interferometer. A single frequency CW laser having long coherence length is used as a light source. The light beam from the laser is collimated with a pair of convex lenses and split into two beams, *i.e.*, signal and local oscillator beams. The frequencies of the local oscillator and the signal light are shifted with a pair of acousto-optic modulators by 100.0 and 110.1 MHz, respectively. The signal beam emanating from the sample is mixed with the local oscillator beam to produce the beat light at the intermediate frequency (i.f.), and then impinges on an InGaAs photodiode to generate a beat signal at the intermediate frequency of 10.1 MHz. The i.f. signal is then fed to an FFT (fast Fourier transform) spectrum analyzer that is controlled by a personal computer.

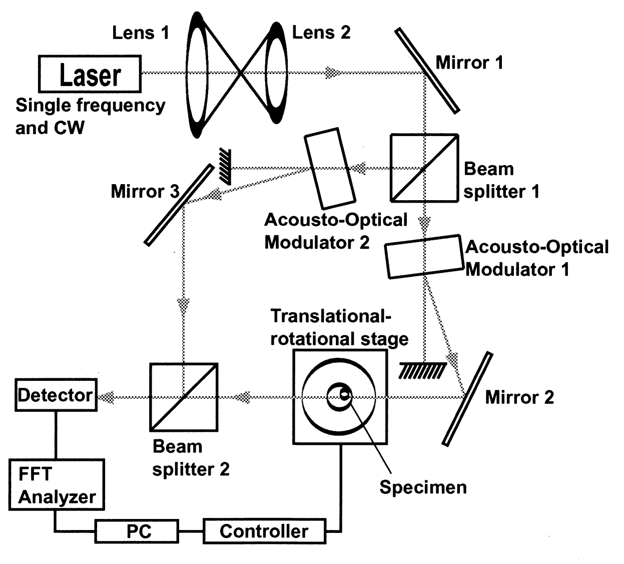

Fig. 1 Schematic of the laser transillumination imaging system.

The detection method, referred to as the optical heterodyne detection, offers some excellent properties such as very low minimum-detectable-optical power, very wide dynamic range, and very sharp directionality and selectivity. Therefore, the CDI method can discriminate and detect very weak, but highly directional forward scattered, and coherence retaining photons that emanate from media with highly scattering nature, as investigated in the next section. The CDI measurement system has a dynamic range of 140 dB and, therefore, can easily detect extremely low optical power, to the order of 10^{-17} W.

High directionality and exponential light attenuation

In order to obtain CT images, the following two conditions must be satisfied: (i) to collect on-axis photons after traversing through a sample along the incident beam line, and (ii) for the light power to exponentially attenuate as light propagates in the sample. Such conditions are indispensable for obtaining projection data.

To verify condition (i), we imaged a test target at wavelength of 1064 nm, where five parallel and 0.5-mm wide lines with 0.5-mm interspaces are printed in black ink on a glass plate as shown in Fig. 2. The test target was placed so that the incident beam was perpendicular to the target surface. A cell full with intralipid-10% (Kabi Pharmacia AB, Sweden) solution in saline in various concentrations was placed on the upperstream side of the test target. Intralipid-10%, fat-emulsion nutrient, administered by intravenous injection, has been often employed in experiments of optical biomedical imaging as a sample simulating biological tissues. Since its absorption property is negligible compared with its scattering one, it can be regarded as a medium only with scattering nature and then is suitable for an object simulating biological tissues with highly scattering nature. The test target was scanned at the step size of 0.1 mm horizontally and/or vertically and was imaged while changing the concentration of the intralipid-10% in saline. The concentration is defined as the percentage of the volume of intralipid-10% against that of saline. The measured images are shown in Fig. 3, where the concentrations were 0%, 10%, 20%, 30%, 40%, 50%, and not diluted intralipid-10% from the top to the bottom. The image intensity is inverted to show the images with higher contrast. That is, transmitted light is more intense in black regions than in white regions. In the top image (concentration: 0%) in Fig. 3, the contours of lines are blurred and the width of lines are thinner than the actual widths. This blurring occurs because the incident beam takes a Gaussian shape with spotsize of about 0.5 mm, and the beam spotsize is comparable to the line width. From the figures, we observe that the line width is broadened with an increase of concentration. The reason is that the beam spotsize after passing through highly scattering media broadens due to multiple scattering, which induces complex phenomena entangled with reflection, refraction, and interference. However, we can delineate the lines even for intralipid-10% without dilution. The results demonstrate

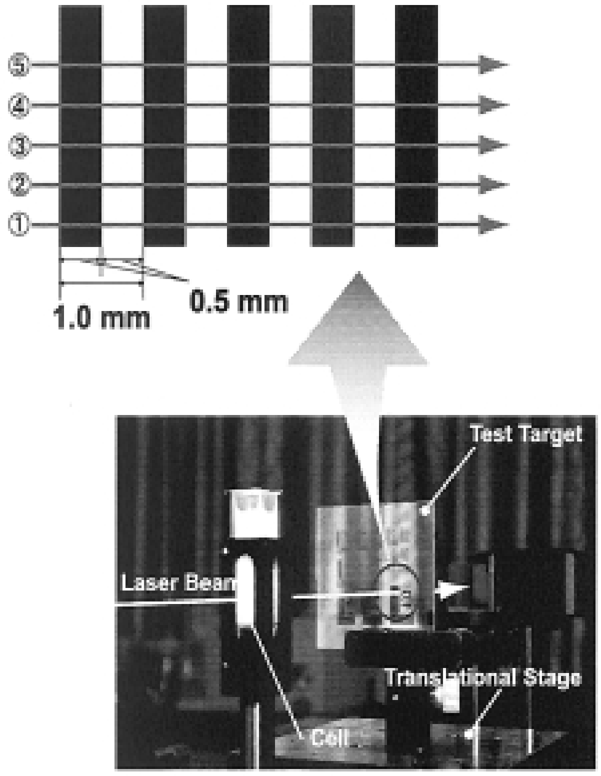

Fig. 2 Measurement of test target: The above part shows schematic diagram of the measured test target and the scanning procedures, and the lower part is the photograph of the experimental setup. The test target was first scanned horizontally with 0.1-mm step size, and after that it was displaced vertically and then scanned horizontally in a similar manner to the previous horizontal scanning. The horizontal scanning was repeated five times in order from ① to ⑤ shown in the figure.

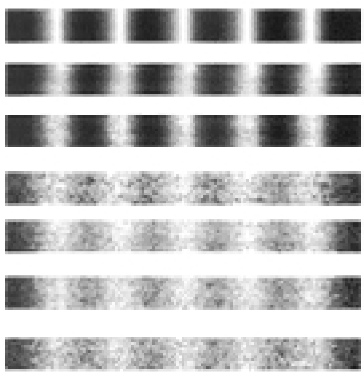

Fig. 3 Projection images of the test target through intralipid-10% solution in saline in various concentrations: From the top to the bottom, the concentrations were 0%, 10%, 20%, 30%, 40%, 50%, and not diluted intralipid-10%, where the concentration is defined as the percentage of the volume of intralipid-10% against that of saline.

that there still exists forward on-axis scattered photons bearing imaging information even after passing through highly scattered media. We can conclude that condition (i) is satisfied under the first order approximation.

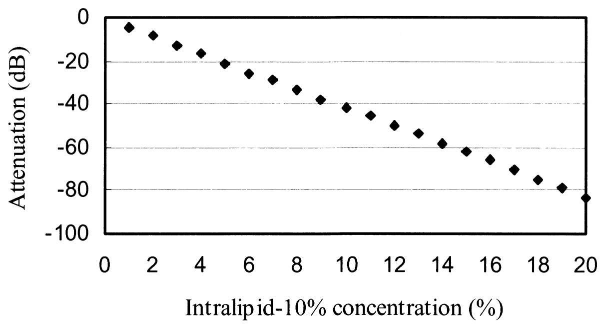

Fig. 4 Transmission characteristics of Intralipid-10% with various concentrations in saline at the wavelength of 1064 nm.

Next, we consider condition (ii). X-ray CT obtains projection data used for reconstruction from transmited light based on Beer's law, and then reconstructs 2- or 3-dimensional spatial distribution of absorption coefficients. On the other hand, the CDI-based laser CT mainly reconstructs the spatial distribution of scattering coefficients not of absorption ones. Although the light attenuation process includes both scattering and absorption, absorption is negligible compared with scattering. In fact, the absorption coefficients of biological tissues are about 1/100 to 1/1000 of the scattering one in the wavelength regions of the therapeutic window.[1,2] Therefore, to obtain tomographic images of biological tissues with highly scattering nature using the same algorithm as that of X-ray CT, for multiple scattering processes scattering coefficient and transmitted light intensity should have an exponential relationship similar to the Beer's law with respect to absorption. To confirm whether the signal light exponentially attenuates or not, we measured the light attenuation by the intralipid-10% solution with highly scattering nature. The measurements were performed on the intralipid-10% solution in saline contained in the glass cell with 10-mm thickness. Transmitted light power at the wavelength of 1064 nm were measured in various concentrations, where the definition of the concentration is the same as that in the previous experiments. The averaged attenuation characteristics at the wavelength of 1064 nm are displayed in Fig. 4. As seen in the figure, transmitted signal power exponentially decreases with an increase of the concentration. The result shows that the light exponentially attenuates due to multiple scattering, similarly to Beer's law with respect to absorption.

From these experimental results, we can conclude that under the first order approximation the CDI method satisfies the two requirements of high directionality and exponential light attenuation for reconstruction from projections, *i.e.*, computed tomography.

Quantitativeness in CT reconstructed images

As shown in the previous section, since data acquired using the CDI method is similar to that acquired by X-ray CT of the first generation, or by X-ray CT using pencil beam, the reconstruction technique widely used in X-ray CT can be straightforwardly applied to the projection data acquired from the previous experimental investigations. Data processing was carried out by the filtered backprojection method (FBP) with Shepp-Logan filter used in X-ray CT image reconstruction.[13]

To confirm the quantitativity in CT measurements, we imaged a

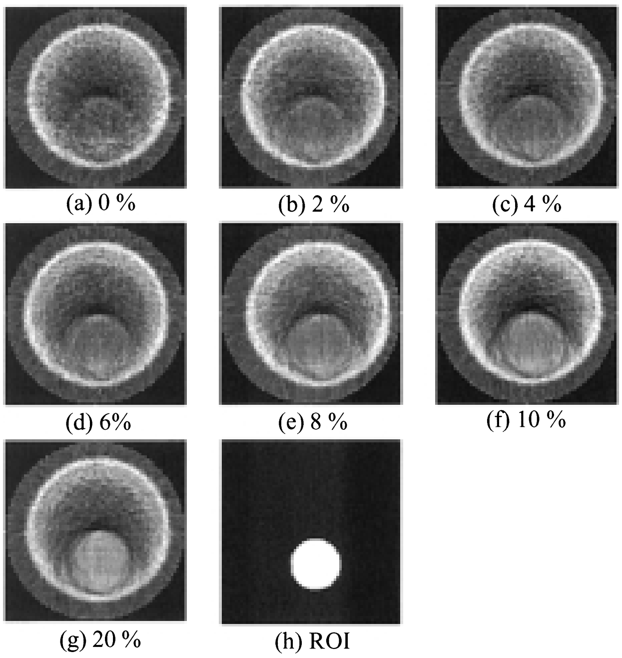

Fig. 5 Reconstructed images ((a) - (g)) of physical phantom containing intralipid-10% solution in saline in various concentrations, where the concentration is defined as the percentage of the volume of the intralipid-10% against that of saline, and the region of interest (h) used for image data processing.

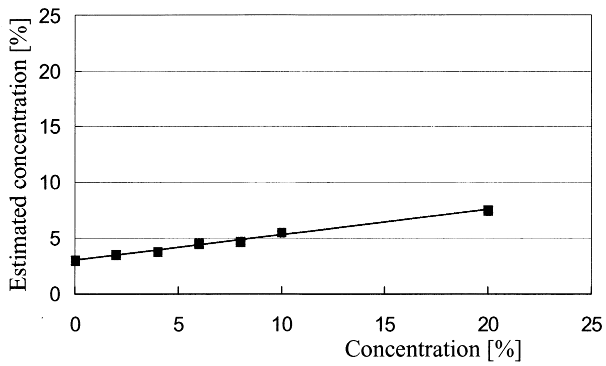

Fig. 6 Relationship between estimated and actual concentrations.

cylindrical acrylic phantom which is 15 mm in diameter and has a channel with 5-mm diameter. The channel was filledwith intralipid -10% solution in saline. The samples are mounted on a translational-rotational stepping motor stage. Each data set consists of the power of the i.f. signal for every translational step of 0.2 mm over 180 degrees at three-degree intervals. The wavelength and the power of the incident laser light were 1064 nm and 10 mW, respectively. Figures 5(a) - (g) show the reconstructed images measured in various concentrations of intralipid-10% in the channel. Note that the images are individually normalized from 0 - 255 for display, and thus, comparison of pixel intensity between different images is meaningless. Despite the highly scattering property of intralipid-10% the contrast of intralipid-10% regions seems relatively low. The reason is that intense annulus artifacts appear on the outer circumference, that is, at the boundary between air and acrylic. The cause of annulus artifacts will be discussed in the next section. In addition, the reason why the contours of intralipid-10% regions are blurred is that multiple reflection and interference occur between the outer surface of the acrylic cylinder and the inner wall of the channel. These effects are inevitable when optically homogeneous materials such as acrylic and glass are imaged, because reflection, refraction, and interference intensely occur in such materials.

Next, the region of interest (ROI) was prepared as shown in Fig. 5(h), and we estimated the concentration in the ROI region of each reconstructed image. Figure 6 plots the concentration of intralipid-10% solution in saline estimated from the reconstructed image against the actual concentration. From the figure, we can observe a satisfactory linear relationship between them, where the correlation coefficient is 0.99.

Discussion

In the above experimental result shown in Fig. 3, the 0.5-mm lines with interspaces of 0.5 mm, which is a similar size to the beam spotsize, were able to be differentiated due to the high-directivity property of CDI imaging system. Since 0.5-mm structure in an object can therefore be differentiated in each projection, if a sufficient number of projections are prepared (theoretically, the number of projections should be $\pi/2$ times that of bins in a projection),[13] the spatial resolution of the CDI-based laser CT is 0.5 mm. In the experiment performed previously using biological sample, we were able to acquire signal against the biological tissues with thickness up to about 6 cm.[11] Therefore, we can conclude that the CDI-based imaging system obtains tomographic images at resolution of submillimeters for the biological samples with thicknesses up to 6 cm.

The CDI-based imaging principle is similar to X-ray CT, because the heterodyne technique detects only the highly directional emergent photons, as shown in the previous section. However, both measurement processes differ due to the conspicuous difference in the physical properties between optical radiation and X-rays. Thus far, reconstruction has been performed based on the most coarse approximation, indicating that the measurement process is the Radon transform. In terms of morphological imaging, the approximation has given satisfactory results. However, the quantitativity still remains insufficient. Actually, in the above experiment, although the relationship between estimated and actual concentrations retains a satisfactory linearity, they do not coincide in value. On the other hand, as shown in Figs. 6 (a) through (g), this approximation causes remarkable annulus artifacts due to degradation in coherence of the incident beam, reflection, and refraction as a result of the refractive index mismatch at the object boundary. These effects brings the discrepancy between the estimated and actual concentrations, since they are not incorporated in the reconstruction algorithm. Of course, these effects will also occur in biological samples in spite of highly-scattering rough surfaces, while the influence on image quality would be even less remarkable compared with optically homogeneous materials such as acrylic used in these experiments. To establish more reliable CT reconstruction, the data processing incorporating the phenomena must be developed.

As mentioned above, under the first oder approximation that the measurement process in CDI-based laser CT is similar to that in X-ray CT, we have used the FBP method, widely used in X-ray CT, for reconstruction. Apart from the FBP method, algebraic reconstruction technique is well known.[13] The algebraic reconstruction, in which a system of equations expressing the physical process is algebraically solved, is more flexible than the FBP method, because the algebraic scheme is not based on rigorous mathematics such as the Fourier slice theorem. The surface effect can easily be incorporated into the algebraic equation system. This approach is expected to improve the performance of quantitative measurement in CDI-based laser CT.

We first investigated by the experiments the high directionality of the CDI method based on the heterodyne detection, and the exponential attenuation with an increase of concentration, which are indispensable to image reconstruction from projections. We confirmed the feasibility of CT imaging by the CDI method. Then we verified by the preliminary experiments using a physical phantom quantitativeness in images reconstructed by the CDI method in the sense that the estimated and actual concentration retain sufficient linearity. However, the quantitativity still remains insufficient due to coherence degradation, reflection, and refraction as a result of the refractive index mismatch at the boundaries, which cause conspicuous annulus artifacts in reconstructed images. Future research will be conducted in order to establish the effective reconstruction algorithm including correction of the annulus artifacts.

Acknowledgements

The authors would like to thank Emeritus Professor Humio Inaba, who is a pioneer of transillumination Laser CT based on the heterodyne detection method, for appropriate advice and instruction.

This research was partially supported by Millennium Project (#12206) from the Japanese Ministry of Education, Science, and Technology. The paper was presented at the Joint Symposium on Bio-Sensing and Bio-Imaging held at Yamagata, Japan on August 2 - 4, 2001.

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