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Photoacoustic Imaging for Periodontal Disease Examination

Atika Windra Sari[1], Rini Widyaningrum[2*], Mitrayana[1]

[1]Department of Physics, Faculty of Mathematics and Natural Sciences, Universitas Gadjah Mada, Sekip Utara, Yogyakarta, Indonesia
[2]Department of Dentomaxillofacial Radiology, Faculty of Dentistry, Universitas Gadjah Mada, Jl. Denta, Sekip Utara, Yogyakarta, Indonesia

***Correspondence to**
Rini Widyaningrum,
Email: rinihapsara@ugm.ac.id

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Abstract
Introduction: After caries, periodontal tissue inflammation (periodontitis) is the most common oral health problem. Photoacoustic imaging (PAI) is a new technique that uses simple components such as a diode laser and a condenser microphone. This study aimed to evaluate the performance of a simple PAI system in periodontal disease imaging by using an animal model.
Methods: Normal periodontal and periodontitis tissues were obtained from Sprague–Dawley rats categorized as the control group, treatment group 1 (7 days of periodontitis induction), treatment group 2 (11 days of periodontitis induction), and treatment group 3 (14 days of periodontitis induction). The PAI system was controlled by LabVIEW and Arduino IDE software from a personal computer.
Results: Results revealed that the optimal frequency of laser modulation for periodontal tissue imaging was 19 kHz with a duty cycle of 50%. The photoacoustic (PA) intensity of periodontal tissues was −68.71 dB for treatment group 3, −70.34 dB for treatment group 2, −71.69 dB for treatment group 1, and −73.07 dB for the control group. PA image analysis showed that the PA intensity from periodontal disease groups was higher than the control group.
Conclusion: This study indicates the feasibility of using a simple PAI system to differentiate normal periodontal tissues from periodontitis tissues.
Keywords: Diode laser; Laser modulation; Periodontitis; Animal model.

Introduction

Periodontal disease, also known as periodontitis, is a chronic inflammatory illness that affects tooth-supporting tissues[1,2] and is caused by infection from accumulating pathogenic bacteria, which induce gum inflammation (gingivitis) and the progressive loss of the periodontal ligament and alveolar bone.[3,4] When not treated effectively, periodontitis can lead to systemic diseases such as coronary heart disease, stroke, and peripheral artery disease.[2]

Clinical and X-ray radiographic examinations are used to diagnose periodontal disease. The latter is preferred for hard tissues but has limitations for soft tissues. Photoacoustic imaging (PAI) is an innovative technology based on the photoacoustic (PA) effect, the emission of acoustic signals from materials exposed to laser or other electromagnetic waves.[4] PAI is an effective technique for soft tissue imaging and thus shows potential for periodontal disease examination.[5,6]

In the last two decades, various non-invasive PAI systems have been developed for biomedical research.[6-10] PAI is a future biomedical imaging modality that combines the merits of optical resolution with the depth of acoustic penetration. This imaging technique can be used to obtain structural, functional, molecular, and kinetic information from various tissues and has been developed for clinical applications, including breast cancer, dermatological, vascular, carotid artery, musculoskeletal, gastrointestinal, adipose, dental and other tissue imaging.[8,11,12]

PAI is a non-invasive and low-cost imaging technique and does not produce ionizing radiation.[13] A laser is commonly used as its electromagnetic source. The PA effect occurs when the optical energy of a laser interacts with the medium, and then it is absorbed and converted into heat. Thermal expansion in the medium subsequently produces a pressure wave that spreads in the tissues and then propagates as acoustic waves, which can be detected by a condenser microphone. These acoustic waves, labeled as PA intensity, are then reconstructed as PA images in the computer.[14] Lasers are widely used in the medical and dentistry fields.[6] Several chromophores, such as melanin and hemoglobin, are present in periodontal tissue.[15,16] In this study, the diode laser employed to image periodontal tissue has a wavelength of 532 nm. Several chromophores in biological tissues absorb light effectively at these wavelengths, including melanin and hemoglobin,

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which have absorption coefficients of 750 cm^{-1} and 230 cm^{-1} respectively.[17]

This study aimed to assess the performance of a simple PAI system based on the diode laser and the condenser microphone for periodontal disease imaging. Comparison was conducted among the obtained PA images to differentiate between normal (healthy) periodontal and periodontitis tissues from animal models.

Materials and Methods

Periodontal tissues were obtained from male Sprague–Dawley (SD) rats aged 4–8 weeks and weighing 150–200 grams. The rats were divided randomly into four groups (five rats each) as indicated in Table 1.

The animals were acclimatized for 7 days and kept in a room with a constant temperature of 25°C and a 12-hour light/dark cycle prior to the treatment. The control group received no treatment. Silk ligatures were tied around the incisors of the treatment groups, which were first anesthetized by intramuscularly injecting ketamine (10 mg/kgW).[18] The method of periodontitis induction in the animal model is presented in Figure 1.

All the rats were euthanized after the treatment. The region of the incisor and supporting structures were dissected and fixed in 10% buffered formalin for 24 hours. The specimens were decalcified using EDTA 10% (pH 7.4) for 1 week at 4°C, cut in the median line, and embedded in non-biological material as a surrounding medium.

The PAI system is presented in Figure 2. The excitation source was a diode laser (Sunshine-electronics, China) with a wavelength of 532 nm and maximum output power of 200 mW in CW mode. The modulated CW laser light was focused onto a spot with a diameter of 0.2 mm on the sample to generate the PA signal, which was then detected by a condenser microphone ECM8000 (Behringer, Germany) and amplified using a UCM220HD soundcard (Behringer, Germany) connected to a personal computer. Details on the PAI system are described in our previous works.[19,20]

The study flowchart is presented in Figure 3. The samples were exposed to the laser at various frequencies (17, 18, 19, and 20 kHz) and duty cycles (10%, 20%, 30%, 40%, and 50%) to determine the optimal laser modulation for periodontal tissue imaging.

Laser power stability was examined by illuminating the sample for 15 minutes to ensure that the PAI system can be used for periodontal tissue imaging. Figure 4a shows the laser output power during sample scanning. The condenser microphone was also calibrated to ensure that the frequency given by the acoustic source was in the same frequency detected by the microphone. In LabVIEW, the frequency detected by the microphone was recorded. The results in Figure 4c confirm, by a 45° slope, the direct relationship between the frequency of the sound source (f_g) and that received by the microphone (f_m).

The characterization of the *x-y* stage is crucial to determine the accuracy of the stage shift toward the *x* and *y* direction following the number of steps inputted in the LabVIEW program. Here, *x-y* stage shifts were characterized by inputting 10, 20, 30, 40, and 50 steps in the LabVIEW program, and the length of the shifts of the *x-y* stage was measured using a digital caliper.

For image reconstruction, the modulated continues-wave (CW) laser energy was first absorbed by the periodontal tissues. The subsequent thermal expansion then produced a pressure wave that propagated as acoustic waves, which were then detected by the condenser microphone. The acoustic waves were transformed from a function of time to a function of frequency called PA intensity. This parameter was computer-processed for image reconstruction. Point-by-point linear scanning was done along the surface of the sample using the custom-built *x-y* stage in the PAI system, which moved the sample in the horizontal *x-y* plane with a 0.2 mm step size between the spots that create a repeated S line direction. In accordance with the S line direction, the sample table

Table 1. Groups of the animal model for periodontal disease

Group	N	Treatment
Control Group (C)	5	No treatment
Group (T1)	5	7 days
Group (T2)	5	11 days
Group (T3)	5	14 days

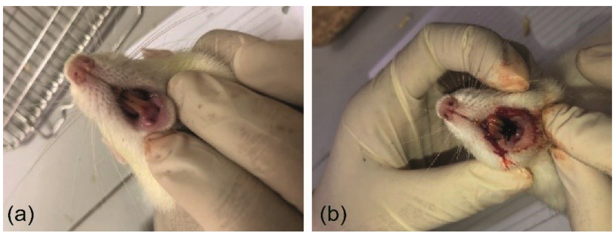

Figure 1. Teeth and Gingiva Condition of the Control Group **(a)** and Silk Ligatures Tied Around the Incisors of the Treatment Group **(b)**

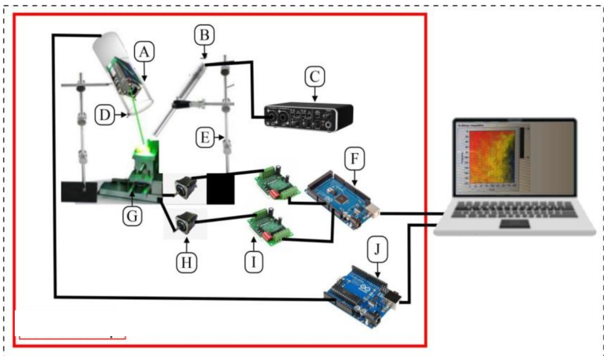

Figure 2. Experimental Setup for Photoacoustic Imaging. A. Diode laser, B. Condenser microphone, C. Soundcard, D. Lens, E. Stative, F. Arduino mega, G. Sample, H. Motor stepper, I. Motor driver, and J. Arduino uno

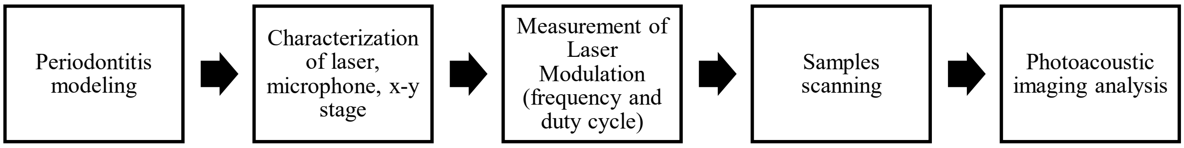

Figure 3. The Flowchart of the Study

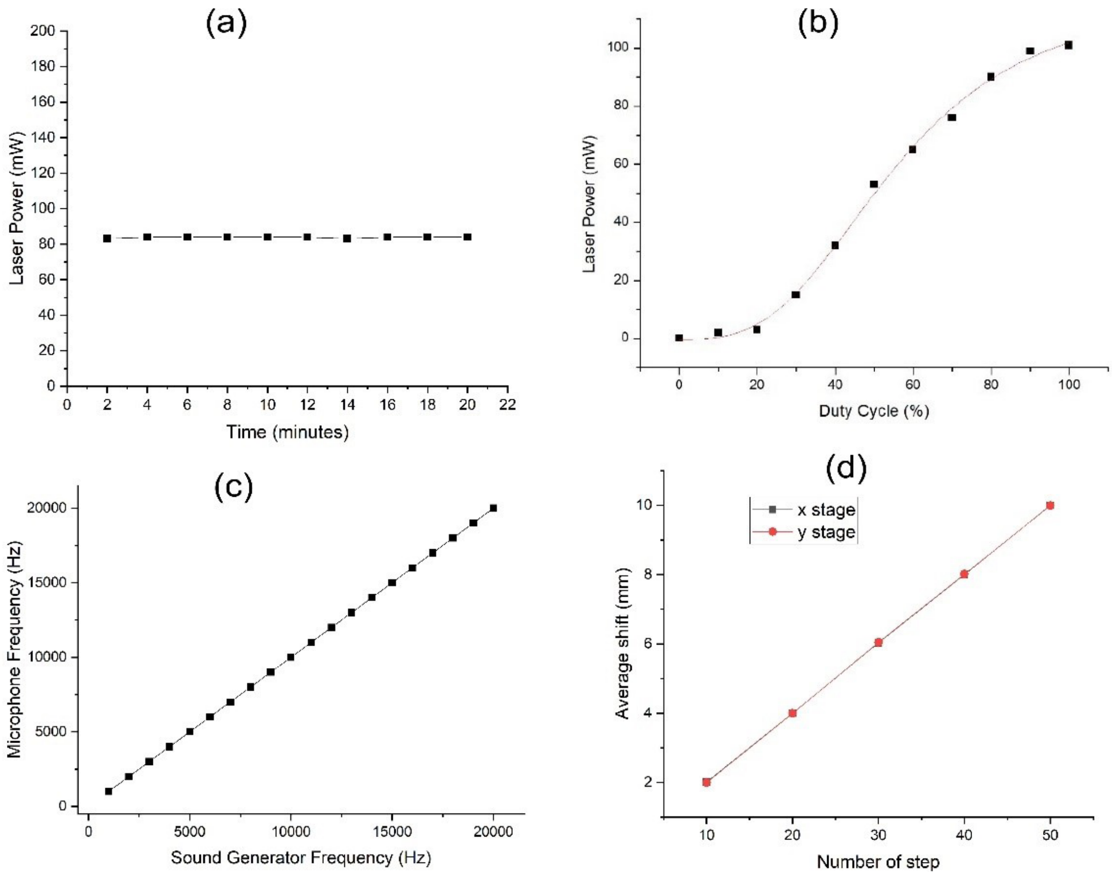

Figure 4. Characterization of the Main Component in the PAI System. (a) Laser power (mW) observed in respective interval time. (b) Laser power (mW) in the respective interval duty cycle. (c) Characterization of the main component in the PAI system: correlation of sound generator frequency (f_g) with microphone frequency (f_m). (d) Characterization of the main component in the PAI system: the average shift of the *x-y* stage step for each 0.2 mm input in LabVIEW

will shift to the left x times, then down and to the right x times. The scan will be repeated $\frac{y}{2}$ times for inputs x and y, where x and y are integers representing the sample sizes (even integers). The PA intensity generated from the sample was used to reconstruct the PA image. High PA intensity was displayed as red in the PA image, medium PA intensity as yellow, and low PA intensity as blue.[19,20]

Results

Sprague–Dawley rats were used as the animal model. Their periodontal tissues can be induced using a simple method, and therefore, they are suitable to mimic periodontitis in humans.[21] Treatment with a silk ligature was conducted to induce inflammation in periodontal tissue. Following the removal of the silk ligature from the incisor teeth of the rats, periodontal pockets were observed in the T1, T2, and T3 treatment groups. In the normal/healthy group, no periodontal pockets were present.

The PAI system was built by integrating a pulsed laser as an electromagnetic wave source into an ultrasound transducer as a detector.[9] Acoustic signals were generated by using a modulated CW laser as an electromagnetic wave source.[19] Modulated excitation on CW lasers was carried out by periodically regulating the duty cycle and pulse width at a single frequency using the pulse duration modulation technique. This method reduces the average power delivered by an electrical signal by effectively dividing it into discrete parts. The pulse duration modulation technique was applied to obtain fluctuating laser radiation in this study.[11,19]

When a duty cycle of a laser is modulated, the laser emission becomes discontinuous. Nonstationary radiation, also known as modulated radiation, is electromagnetic wave radiation that has been organized in such a way that it becomes discontinuous. Non-stationary pulses cause thermal expansion in the sample, resulting in an acoustic signal. Here, the frequency of resulting acoustic signals was the same as that of laser modulation and directly proportional to the absorbed energy. The duty cycle of laser modulation was proportional to the intensity of the thermal expansion generating the acoustic signals.[14]

Figure 4a displays the relationship between laser output power and exposure time. After 20 minutes of scanning, the laser power output barely changed. Almost no variation in the laser power was observed during the scanning time. The laser power output is stated to be steady at about 84 ± 0.4 mW. Hence, the laser exposure was assumed as stable during PAI.

The relationship between the laser output power and the duty cycle is shown in Figure 4b. For 20 minutes, laser power measurements were taken at 0%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, and 100% duty cycles. The laser power values obtained for each duty cycle were 2 ± 0.3 mW, 3 ± 0.1 mW, 15 ± 0.4 mW, 32 ± 0.2 mW, 53 ± 0.1 mW, 65 ± 0.5 mW, 84 ± 0.4 mW, 90 ± 0.3 mW, 99 ± 0.4 mW, and 101 ± 0.2 mW respectively.

Microphone characterization revealed a linear relationship between the frequency received by the microphone (f_m) and that emitted by the sound generator (f_g) (Figure 4c). The input frequencies from sound generator are 1000 Hz, 2000 Hz, 3000 Hz, 4000 Hz, 5000 Hz, 6000 Hz, 7000 Hz, 8000 Hz, 9000 Hz, 10 000 Hz, 11 000 Hz, 12 000 Hz, 13 000 Hz, 14 000 Hz, 15 000 Hz, 16 000 Hz, 17 000 Hz, 18 000 Hz, 19 000 Hz and 20 000 Hz. The results of the measurement indicated that the frequency received by the microphone was identical to the input frequency. The signal detected by the microphone was in the form of a voltage, which was read by the LabVIEW program. This signal was converted from a function of time into a function of frequency by the Fast Fourier Transform in the LabVIEW program.

A linear correlation was found between the step number and the input step in the LabVIEW program (Figure 4d). In the LabVIEW program, the shift input values were 10, 20, 30, 40, and 50 steps. The shifts obtained at the x stage were 2 mm, 4 mm, 6 mm, 8 mm, and 10 mm respectively. In addition, the obtained shifts at the y stage were 2 mm, 4 mm, 6 mm, 8 mm, and 10 mm respectively. Figure 4d indicates the direct relationship between the step number and the input step was linear. In addition, the input in the LabVIEW program corresponded to the shift of the x-y stage.

The laser in the PAI system was modulated to induce the acoustic signals from the samples. The energy absorbed by the sample was comparable with the PA signal. The intensity of the modulated laser light is directly proportional to the fraction of one period in a signal (known as duty cycle). The best periodontal images were obtained when the laser was modulated with optimum frequency and duty cycle to generate high PA intensity from the samples.

Figure 5a illustrates the connection between frequency difference and PA intensity for each group. The frequencies that were measured include 17 kHz, 18 kHz, 19 kHz, and 20 kHz. Based on the graph in Figure 5a, the optimal frequency for periodontal imaging was 19 kHz, with PA intensity values of -74.16 ± 0.2 dB, -72.66 ± 0.1 dB, -71.50 ± 0.3 dB, and -70.03 ± 0.3 dB for groups C, T1, T2, and T3 respectively. The optimal duty cycle measurement was performed at a frequency of 19 kHz, based on the optimal frequency that has been determined.

Figure 5b illustrates the correlation between the duty cycle difference and PA intensity for each group. The measured duty cycles are 10%, 20%, 30%, 40%, and 50%. The optimal duty cycle for periodontal imaging was 50%,

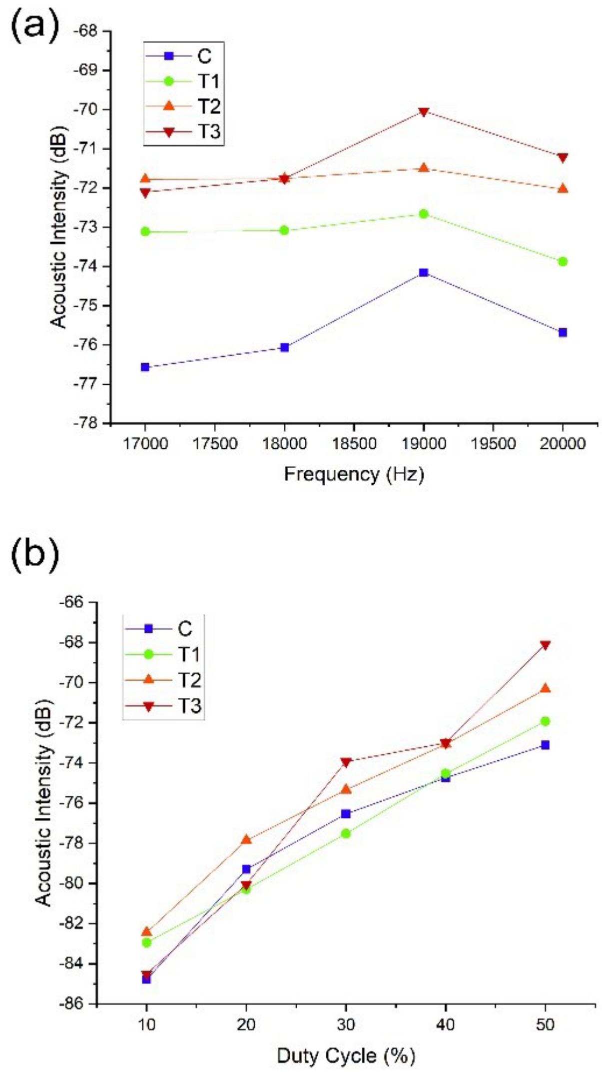

Figure 5. PA Intensity Generated From Periodontal Tissues. (a) PA intensity at 17 kHz, 18 kHz, 19 kHz, and 20 kHz laser modulation. The peak point in each group illustrates the ideal frequency to be employed in the study, which is 19 kHz. PA intensity values for groups C, T1, T2, and T3 are -74.16 ± 0.2 dB, -72.66 ± 0.1 dB, -71.50 ± 0.3 dB, and -70.03 ± 0.3 dB respectively. (b) PA intensities are 10%, 20%, 30%, 40%, and 50% during laser modulation duty cycles. The optimal duty cycle obtained was 50%, with PA intensity values of -73.10 ± 0.2 dB, -71.92 ± 0.4 dB, -70.32 ± 0.1 dB, and -68.08 ± 0.3 dB for groups C, T1, T2, and T3 respectively

with PA intensity values of -73.10 ± 0.2 dB, -71.92 ± 0.4 dB, -70.32 ± 0.1 dB, and -68.08 ± 0.3 dB for groups C, T1, T2, and T3 respectively.

Discussion

A simple and low-cost PAI system was built using a condenser microphone as a detector and a modulated CW laser as an electromagnetic wave. This study aimed to differentiate healthy periodontal tissues from periodontitis tissues in terms of PA image and average PA intensity. Depending on the duty cycle of laser modulation in this study, the optical power provided to the sample ranged between 0 and 101 mW. The pulse intensity of the laser is limited to 20 mJ/cm^2 at 532 nm by the American National Standards Institute (ANSI) for the protection of humans.[22,23] Previous research has demonstrated the use of lower laser power to reduce the risk of tissue injury, with the incident light fluence on the tissue being around 15 mJ/cm^2 below the ANSI safety limit at a wavelength of 532 nm.[19] Therefore, this study recommends certain things that the previous study has.

The developed PAI system has a scan rate of 1 second per pixel. Acoustic signals were collected from the samples with a resolution of 30 x 30 pixels on average. The number of pixels can be obtained by increasing the distance on the *x-y* stage shift. Each sample was scanned for approximately 30 minutes. PA intensity data were used to create PA images. Image color was utilized to describe PA intensity produced from the PAI system, that is, blue for low PA intensity, yellow for medium PA intensity, and red for high PA intensity.[19,20] Differences in PA intensity between the control and treatment groups are shown in Figure 6.

Figure 6 displays the average PA intensity of the samples. This value was greater for the treatment group than for the control group. The average PA intensity values were −73.07, −71.69, −70.34, and −68.71 dB for the control group, treatment group 1, treatment group 2, and treatment group 3 respectively. The standard deviation of each group was 0.4 dB, 0.4 dB, 0.6 dB, and 0.2 dB respectively so that the resulting PA intensity values do not overlap among the groups of samples. Periodontal tissue inflammation alters mineral distribution in the supporting tissues of the teeth, thus creating a greater amount of PA signals for the treatment groups compared with that for the control group.[7]

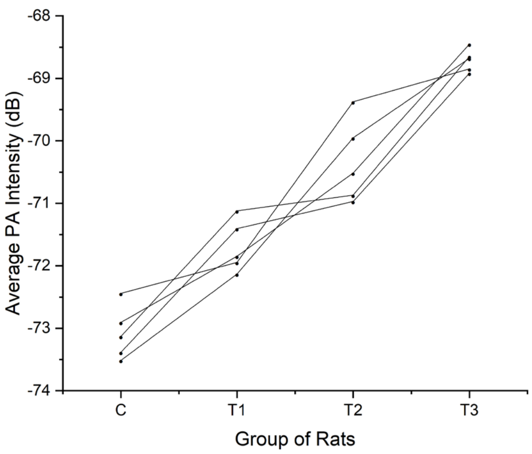

Figure 6. PA Intensity Values of Photoacoustic Images at the Frequency and duty cycle of laser modulation were 19 kHz and 50% respectively. The average PA intensity values were -73.07 ± 0.4 dB for the control group (C), -71.69 ± 0.4 dB for group 1, -70.34 ± 0.7 dB for group 2, and -68.71 ± 0.2 dB for group 3

The PA images of periodontal tissues are shown in Figure 7. Different colors indicate different PA intensities (blue: low intensity, yellow: moderate PA intensity, and red: high PA intensity). Figure 7 shows that the control group displayed a low PA intensity as indicated by the yellow color in their PA images. Meanwhile, the treatment groups showed a high PA intensity as indicated by the red hue in the PA images of periodontitis tissues.

Periodontitis is a chronic disease caused by bacterial infection. Periodontitis induction by using silk ligatures[24] can cause bacterial accumulation, which then induces inflammation and destruction in periodontal tissues, followed by demineralization.[5]

The PA intensity of periodontitis tissues in the treatment groups was higher than that of the control group as shown in Figure 6. This finding can be attributed to different mineral distributions in the tissue caused by inflammation.[6] The inflammation of periodontal tissues in the treatment groups absorbed the laser energy, resulting in a high average PA intensity.[7] There were significant variations between groups C, T1, T2, and T3 in PA intensity levels. T3 had a greater PA intensity value than the other groups, but C had a lower PA intensity value than the other groups. The order of PA intensity levels, from highest to lowest, is T3, T4, T1, and C.

The density of certain tissues or materials also affects laser absorption in PA imaging. Chromophores are tissue components that can absorb laser light energy.[25] Several chromophores, such as hydroxyapatite, protein, and blood vessels, can be found in oral tissues.[26] Periodontal tissues have a lower mass than the teeth and therefore have higher optical absorption. The periodontal structure consists of hard and soft tissues with several blood vessels and nerves.[27] Hemoglobin is a powerful chromophore found in blood and is more abundant in periodontitis tissues than in healthy periodontal tissues. In addition to hemoglobin, periodontal tissue contains a chromophore in the form of melanin. Hemoglobin and melanin absorption coefficients, 750 cm^{-1} and 230 cm^{-1} respectively, were suitable at the wavelengths utilized (532 nm).[17]contrast of PA images was formed by differences in their PA intensity. Hence, this value can be used as an initial parameter. The PAI system can distinguish between healthy periodontal and periodontitis tissues. Figure 8 shows the different PA intensities of the

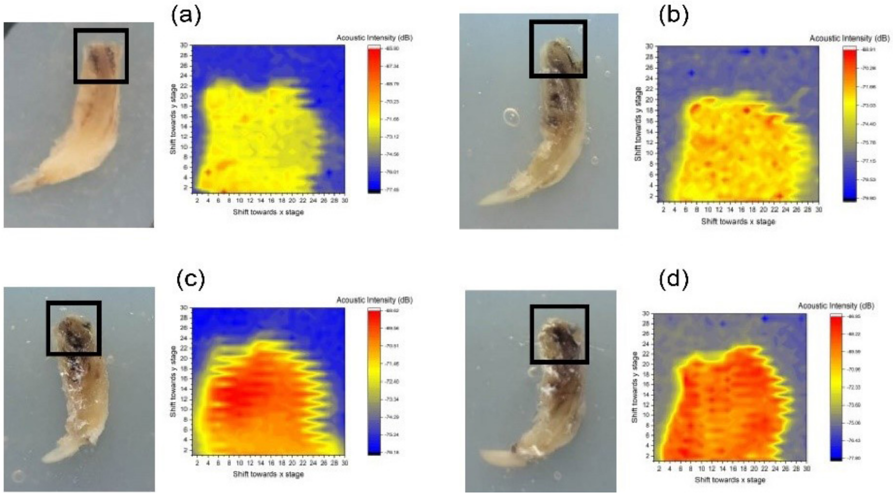

Figure 7. Incisor and Periodontal Tissue Specimens of Sprague–Dawley Rat's Periodontal Tissues and Photoacoustic Images: (a) Control group (C), (b) Group 1 (T1), (c) Group 2 (T2), and (d) Group 3 (T3). The black square in the photographs shows the area for photoacoustic imaging

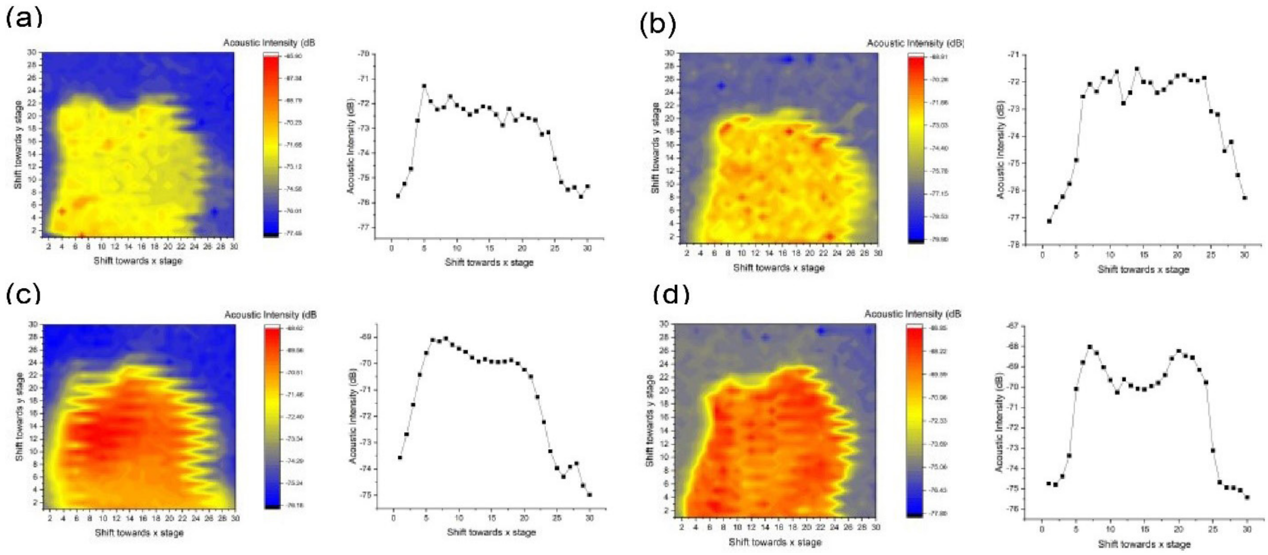

Figure 8. Differences in PA intensity between the periodontal tissue and the surrounding medium. (a) Control group (C), (b) Group 1 (T1), (c) Group 2 (T2), and (d) Group 3 (T3)

periodontal tissues and the surrounding medium. The graphs show that the PA intensity of the periodontal tissue from the 5th to the 25th steps of the *x* direction at the 10th step of the *y* direction was higher than that of the surrounding medium. Therefore, the PA images represent the differences in PA intensity between the periodontal tissues and the surrounding medium.

PAI is a hybrid imaging technique that employs acoustic detection.[13] Here, a laser excites a target that absorbs light. The target is subsequently subjected to spatially constrained heating and thermoelastic expansion which is known as PA effect. This effect generates wideband acoustic waves that can be detected by an acoustic detector or ultrasonic transducers for image generation.[28] This technique can image soft tissue and does not utilize ionizing radiation.[12,20,29] The anatomical area and extension of periodontal tissue inflammation can be determined based on acoustic intensity acquired from PA imaging.

Periodontal probing is the gold standard for measuring clinical attachment loss in periodontal disease assessment.[30] Physical probing requires the operator's experience and can cause patient discomfort, bleeding, and inaccurate measurements by penetrating inflammatory tissue.[10] In this study, the periodontal pocket was not calculated. We demonstrated that inflamed periodontal tissue (periodontitis) emitted a stronger acoustic signal than healthy periodontal tissue. The acoustic intensity served the quantitative information of the level of periodontitis. According to the result of the study, the PAI system is anticipated to be further developed as a non-invasive method for the clinical application of periodontitis detection and assessment of periodontal depth. However, since the PA system in this study utilized simple components, it needs to be modified further for clinical application.

In the field of dentistry, PAI utilizing an ultrasound detector (PA-US) has been investigated.[10,30,31] This technique employs a bulky laser source, whereas the imaging method that we devised uses a compact and inexpensive diode laser. Future work is required to address the challenges of clinical applications of PAI that are comfortable for the patient, which requires a compact excitation source combined with a portable detector.

Since this study was conducted ex vivo, in vivo research is required to build a PAI system that can be implemented on clinical examination. Signal acquisition in the study was done point-by-point, which made image reconstruction time-consuming. Advanced techniques are required to accelerate image reconstruction.

To date, studies focusing on PA imaging for periodontal disease examination are still limited. The present work quantified periodontitis using the PA intensity of the PA image. We have not found any references that used modulated CW from the diode laser for periodontal disease imaging. In summary, this research proposed a low-cost and non-invasive technique based on PA intensity that can be used for periodontal disease imaging.

Conclusion

This study proposed a PA imaging system based on the diode laser and the condenser microphone for periodontal disease imaging. The results showed that the PA intensity of the PA images of the treatment groups was higher than that of the control group. The optimal frequency of laser modulation for periodontal tissue imaging was 19 kHz with a duty cycle of 50%. This simple PA system can be further developed to build a PA tomography system.

Acknowledgment

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Conflict of Interests

The authors declare no conflict of interest.

Ethical Considerations

The research protocol was approved by the research ethics committee of the Faculty of Dentistry, Universitas Gadjah Mada, Yogyakarta, Indonesia (Ref: 00491/KKEP/FKG-UGM/EC/2020).

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