

# Synthesis and characterization of breast-phantom-based gelatine-glutaraldehyde-TiO<sub>2</sub> as a test material for the application of breast cancer diagnosis

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**Abstract.** Synthesis of breast-phantom-based on gelatine-glutaraldehyde-TiO<sub>2</sub> as testing material of breast cancer diagnosis using Near Infrared-Diffuse Optical Tomography (NIR-DOT) is presented. Glutaraldehyde (GA) is added to obtain optimum breast phantom which has same elasticity modulus with mammae. First, synthesis is conducted by mixing gelatine with various amounts of 1 g, 2 g and 3 g with saline solution on 40<sup>0</sup> C temperature for 30 minutes until they become homogenous. Next, GA with concentration of 0.5 and 1.0% is added. The characterization includes FTIR test, physical test, and mechanical test used to identify group of gelatine's functions. Elasticity modulus of breast phantom of gelatine composition 2 g and 0.5% GA is obtained at 53.46 kPa which is the approximation of mammae culture elasticity. This composition is chosen to synthesise the next step. In the second step, TiO<sub>2</sub> is added with variation of 0.01 g, 0.015 g, 0.02 g, 0.025 g, and 0,03 g. With this variation, it is aimed to get a breast phantom providing image with optimum absorption. The test of this material uses Differential Scanning Calorimetry (DSC), homogeneity test, and analysis of coefficient absorption. The result shows the sample has a good thermal property in the range of 40 – 70<sup>0</sup> C with a good homogeneity and absorption coefficient of 0.4 mm<sup>-1</sup>.

## 1. Introduction

Cancer is a disease caused by abnormal cell / tissue which is malignant and grows fast, whereas breast cancer is a type of cancer mostly found in women, and the highest number of breast cancer case can be found in Indonesia [1] .Plaint or early symptoms of this disease are often unrecognized by sufferers, therefore, it needs a diagnosis method which is fast, safe, inexpensive, effective, and noninvasive. One technique for early detection of Breast cancer which is easily accessible by public is the near infrared-diffuse optical tomography (NIR-DOT). The advantage of NIR-DOT is that the radiation source used is in the form of near infrared (NIR) which is non-invasive and non-ionizing .Unfortunately, direct exposure to visible light or NIR on mammary tissue often causes concern in most women. Therefore, in an effort to build early detection equipment with NIR-DOT requires replacement material to act as tissue simulations to ensure the presence of Carcinoma mammae. For that purpose, breast phantom is used.

Phantom is defined as an object which is able to act as a tissue simulation to replicate the characteristics of human's or animal's tissue [2] This requires test material to have elastic characteristics with the corresponding value of the absorption and scattering similar to those of breast. One of the materials which meet these properties is gelatine [3]



Gelatine is a natural polymer extracted from bones and skins of animals which are used extensively both in pharmaceutical and industrial fields. Gelatine swells when it absorbs water. It is capable of absorbing water 5-10 times its weight, forming a gel at 35-40° C temperature. Furthermore, it is soluble in hot water and can be reversibly changed from sol to gel [4]. In making this gelatine-based breast phantom, saline solution is used as a solvent, Copy of isotonic fluid which represents the human body fluids [5] However, gelatine has the disadvantage that it decays quickly that it is necessary to add GA as a crosslinking agent (crosslink) to keep it long lasting. Crosslink itself is a bond which connects one polymer chain with another polymer chain which can increase resistance to heat, chemical resistance, and mechanical properties such as tensile strength It can also increase the thermal stability [6]. Breast phantom GA is easily obtained from a lower toxicity than from formaldehyde Inelastic, durable breast phantom must also have optical properties whose absorption and scattering properties can be detected by the means of optical tomography. It also needs extra TiO<sub>2</sub> as scattering agents since it is nontoxic, stable, and environmentally friendly non-corrosive [7].

Based on the background the above, this research aims to create gelatine-glutaraldehyde-TiO<sub>2</sub> synthesized breast phantom glutaraldehyde with saline solvent. Characterization applied in this research is FTIR test, and physical characterization includes ease of samples when removed from the mould and durability against environmental sample, press test, DSC test, homogeneity test, and analysis of the absorption coefficient.

## 2. Research methods

Materials needed in this research were gelatine, glutaraldehyde, TiO<sub>2</sub>, NaCl, and distilled water. Equipment used included digital balance, beakers, thermometers, pipettes, stirrers, magnetic stirrer, stirrer bar, and plastic pots. The tools used for sample characterization included FTIR, DSC set of test equipment, tensile strength equipment, and a set of optical tomography.

Synthesis of breast phantom began with a saline solution made of 0.9 g of NaCl dissolved in 100 ml of distilled water and 0.5% of glutaraldehyde solution preparation and 1%. of Breast phantom was synthesized with ratio of saline and gelatine used was 1:10 [8] The next step was making variation of gelatine of 1 g, 2 g, and 3 g, or making gelatine solutions of 10% (w / v), 20% (w / v), and 30% (w / v). The materials used in the first stage before varied by TiO<sub>2</sub> are presented in Table 1.

**Table 1.** Materials for First Stage

Sample	Gelatine (g)	Glutaraldehyde (%)
A	1	0.5
B		1
C	2	0.5
D		1
E	3	0.5
F		1

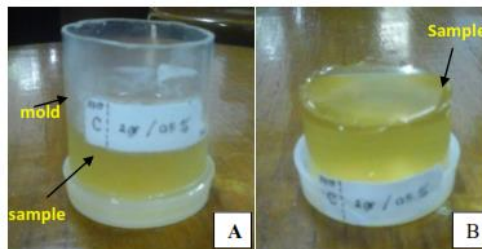
Gelatine was mixed with saline solution at 40° C for 30 minutes until becoming homogeneous. Stirring was done with a minimum speed to reduce bubbles in the sample. After 30 minutes, the gelatine solution and glutaraldehyde were added into the sample at 1:2 ratio [6] Then, the sample was poured into a plastic pot and cooled in the refrigerator for 24 hours. Samples with the best variation that were printable and durable and had similar elasticity of breast tissue characterization based on the first stage next were varied by TiO<sub>2</sub>. TiO<sub>2</sub> variation of 0.01 g, 0,015 g,; 0.02 g, 0.025 g, and 0.03 g [9] Next, TiO<sub>2</sub> was added to a mixture of gelatine and saline solution for 1 hour until it became homogeneous, then glutaraldehyde was added. The solution was then poured into the mould and stored in the refrigerator for 24 hours.

Characterization of the samples was done through FTIR test, physical characterization test, tap test, DSC test, and materials test, and material absorption coefficient ( $\mu_a$ ) homogeneity test. FTIR test was performed to determine the functional groups of each ingredient. The physical characterization was

performed to determine the ease of sample when removed from the mould and durability so that samples can be used optimally. Pressure test was performed to analyse the sample's modulus of elasticity. DSC test was carried out on the effect of temperature on test material to ensure that during the tomographic test, the sample was not degraded due to the heat radiation of the laser. The next test was homogeneity and optical properties test which was performed by measuring the absorption coefficient value ( $\mu_a$ ) samples using optical tomography.

### 3. Results and discussion

Result of the sample obtained shortly after synthesis process and after stored in the refrigerator for 24 hours are shown in Figure 1. The sample was gelatinous, rubbery, and transparent.



**Figure 1.** (A) The sample after synthesis; (B) samples after being stored in the refrigerator for 24 hours

Once the samples were synthesised, it was then tested using the FTIR, physical, and compression test. Physical tests included ease of samples when removed from the mould and test on the sample's durability. The best sample based on physical tests and pressure tests were next varied with  $\text{TiO}_2$ . Variations of  $\text{TiO}_2$  used were 0.01 g; 0.015 g; 0.02 g; 0.025 g, and 0.03 g. Various results of the sample after  $\text{TiO}_2$  was added were shown in Figure 2. In Figure 2 (a) were shown differences in the samples before and after  $\text{TiO}_2$  was added. Samples after synthesis before  $\text{TiO}_2$  was added were transparent brown, whereas samples became murky brown after  $\text{TiO}_2$  was added. The greater the composition of  $\text{TiO}_2$  added, the murkier the samples' colour were. As for the absorption coefficient test sample preparation, samples were printed cylindrically flat with 2.7 cm in diameter, and they had various thickness of 0.3 cm, 1.5 cm, and 0.3 cm as shown in Figure 2 (b).



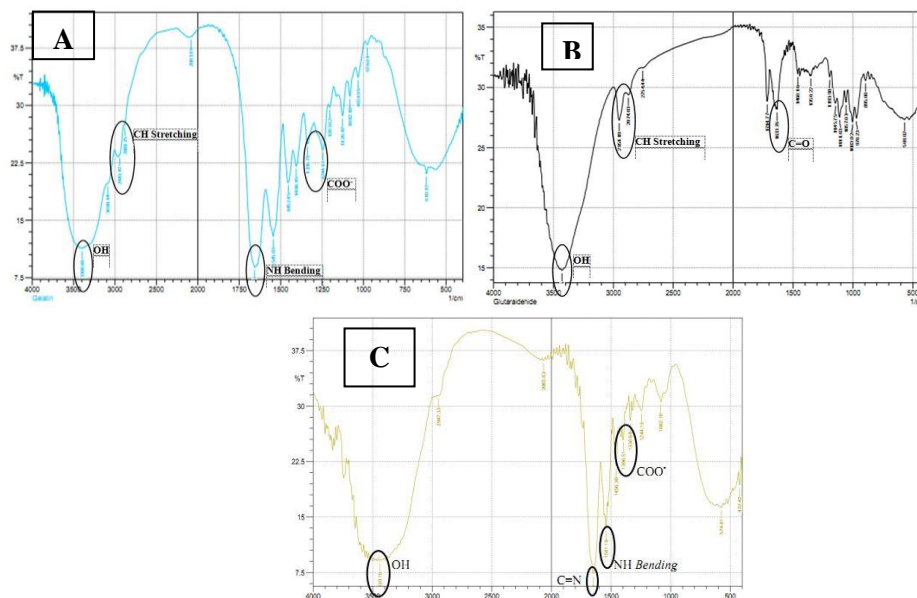
**Figure 2.** (A) The sample after  $\text{TiO}_2$  varied, (B) The test sample material absorption coefficient

#### 3.1. FTIR test

FTIR characterization test result performed on samples of gelatine, gelatine composite-GA, and GA was shown in Figure 3. FTIR analysis was performed by matching the wave absorption unique area to each functional group. Results of functional groups along with local uptake obtained by FTIR spectra were shown in Table 2.

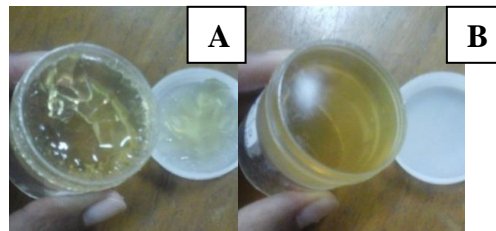
**Table 2.** Results of FTIR Spectrum Analysis

Function Group	Wave Number ( $\text{cm}^{-1}$ )		
	Materials		Sample
	Gelatine	GA	Gelatine- GA
OH	3398.69	3492.55	3439.19
NH Bending	1656.91		1541.18
CH Stretching	2881.75	2874.03	
	2943.47	2951.19	
COO <sup>-</sup>	1244.13		1338.64
	1336.71		1396.51
C=O		1633.76	
C=N			1649.19

**Figure 3.** FTIR spectra of (A) gelatine, (B) GA, and (C) gelatine-GA

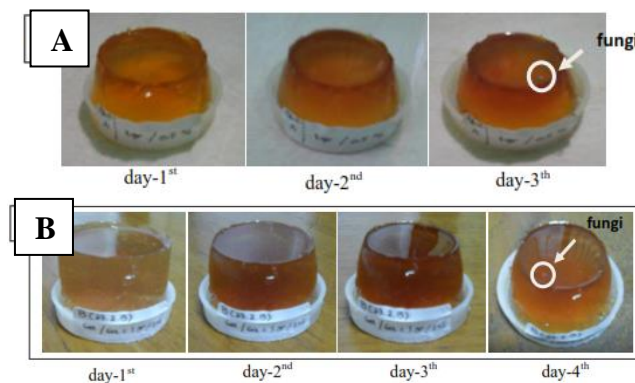
Based on the FTIR test results, each group had a specific and different absorption. Gelatine had a fairly long chain with several groups contained therein such as amines, carbonyl, and hydroxyl. Bending NH amine groups were present in the wave absorption  $1656.91 \text{ cm}^{-1}$ . Carbonyl groups shown in the FTIR spectrum were a group of COO derived from the proline in the gelatine whose absorption wavelength was  $1244.13$ ;  $1336.71 \text{ cm}^{-1}$  hydroxy 1. The OH group of gelatine was contained in uptake  $3398.69 \text{ cm}^{-1}$ . CH Stretching was on the uptake of  $2881,75$  and  $2943.47 \text{ cm}^{-1}$ . The FTIR spectrum of GA included two functional groups based on the chemical structure of the GA. The cluster functionality in the GA was CH and C = O stretching. CH Stretching on GA detected in absorption wavelength was  $2874.03$  and  $2951.19 \text{ cm}^{-1}$ . Carbonyl group C = O was contained in the uptake of  $1633.76 \text{ cm}^{-1}$ . Composite gelatine-GA that has been characterized by FTIR was known as the functional groups that represent each ingredient. FTIR spectra representing gelatine was a group of NH Bending at  $1541.18 \text{ cm}^{-1}$  absorption. OH groups were at  $3439.19 \text{ cm}^{-1}$ , and catchment area group C = N as the identity formation of crosslink and amide group C = O gelatine was at a similar wave, respectively - each was  $1690\text{-}1640 \text{ cm}^{-1}$  and  $1680\text{-}1630 \text{ cm}^{-1}$ . The composite spectrum gelatine-GA was detected in absorption of  $1649, 19 \text{ cm}^{-1}$ . This led to the formation of crosslink to the composite which could not be identified through the test FTIR.

Physical tests were conducted to determine the ease of sample when removed from the mould and samples' durability or resistance to the environment when the sample was placed at room temperature. Observations on convenience samples when removed from the mould was done by releasing the samples that have been stored in the refrigerator for 24 hours from the mould, as shown in Figure 4. Based on test results convenient samples when removed from the mould, the samples A and B were hardly removed compared to samples C, D, E, and F. This was because the gelatine concentration in the samples A and B were lower than that in other samples. 1 g of gelatine could make the sample's texture less dense because of the amount of crosslink between gelatine and GA on samples A and B was fewer than that of other samples. When samples A and B were removed from the mould, the bottom of the samples kept sticking to the mould board so that the samples were damaged in the bottom part. In contrast, the C, D, E, and F samples were easier to remove that the bottom did not stick to the mould or damaged. Samples were solid when removed from the mould as shown in Figure 4 (a) and the sample did not stick when released from the mould as shown in Figure 4 (b).



**Figure 4.** The samples when removed from the mould (A) stick; (B) does not stick

Observation on the samples' resistance or durability to environmental was done by observing the samples which were placed at room temperature once every 24 hours until the samples were damaged or mouldy. Based on the observation result, it was found that samples A, C, and E with 0.5% of glutaraldehyde concentration lasted for 3 days, while samples B, D, and F with 1% of glutaraldehyde lasted for 4 days. The result of the samples' lasting endurance test and physical test results for all samples are presented in Table 3.



**Figure 5.** (A) Sample A on days 1 to 3, (B) Sample D on days 1 to 4

Sample A on day 1 to 3 is shown in Figure 5 (a), and sample D on day 1 to 4 is shown in Figure 5 (b). Sample A on the first day had not been damaged. However, it began to shrink in the upper part on the second day. This occurred because the sample was dehydrated, in other words, the water in the sample evaporated into the air which made the top part of the sample contract. On the third day, sample A was overgrown by fungus on its surface which was indicated by the white arrow in Figure 5 (a). Meanwhile, on the third day, sample D had not been invaded by fungi, but its upper part started to shrink. On the fourth day, sample D started to be overgrown by fungi as indicated by white arrow shown in Figure 5 (b). Sample C and E experienced similar process since they had same concentration



of GA which was 0.5%. Meanwhile, sample B and F, which had similar concentration to that of sample D, experienced similar process as sample D did. Examination of the physical tests showed that samples with higher concentration of glutaraldehyde has stronger resistance to the environment, in other words, they are more durable. This indicates that the crosslink agent glutaraldehyde makes samples more durable because of its degree of crosslink among gelatine and higher GA. That also depends on the degree of density crosslinking agent

**Table 3.** Physical sample test results

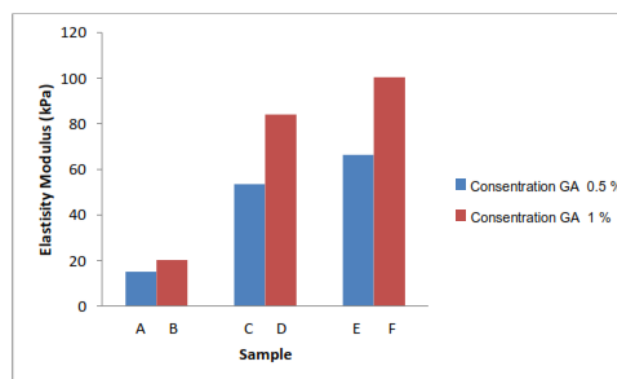
Sample	Gelatine	GA (%)	Sample removable	sample durability in room
A	1	0.5	difficult	3
B		1	difficult	4
C	2	0.5	easy	3
D		1	easy	4
E	3	0.5	easy	3
F		1	easy	4

### 3.2. Press test

Characterization of compressive strength to produce data in the form of the force (F) required to press the sample until the sample is damaged / injured. The sample used for the pressure test is a cylinder with 3.6 cm in diameter and 2 cm in height. The process was done by pressing up to a depth of 1 cm or 50% of depth on all samples. Indenter which is a cylinder with a diameter of 1.2 cm was used. The elasticity of each sample is presented in Table 4. Meanwhile, the relation between elasticity modulus and GA concentration of 0.5% and 1% is presented in Figure 6.

**Table 4.** Result of compressive strength test analysis

Sample	Gelatine (g)	GA (%)	F(N)	E(kPa)
A	1	0.5	$7.170 \pm 0.005$	$15.04 \pm 1.18$
B		1	$9.680 \pm 0.005$	$20.30 \pm 1.59$
C	2	0.5	$25.490 \pm 0.005$	$53.46 \pm 4.17$
D		1	$40.070 \pm 0.005$	$84.03 \pm 6.55$
E	3	0.5	$31.30 \pm 0.005$	$65.77 \pm 5.13$
F		1	$47.870 \pm 0.005$	$100.39 \pm 7.82$



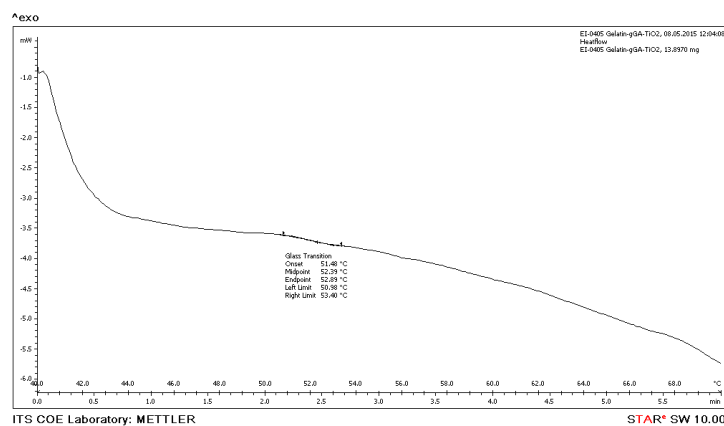
**Figure 6.** Graph on relationship between variation of the modulus of gelatine elasticity and GA concentration of 0.5% and 1%

Based on the graph in Figure 6, there is an increase modulus of elasticity along with increasing concentrations of either gelatine. This is because the resulting mechanical properties depended on density of crosslinking gen. Variations of GA gelatine at a concentration of 1% had greater elasticity modulus than that of GA 0.5%. This was because higher concentration of glutaraldehyde which affected crosslink the gelatine also increased. In other words, the higher the crosslink is, the higher the

elasticity modulus becomes [6] Based on the literature, it is known that the value of the elasticity modulus of breast tissue is 0, 167-29 kPa [10], and that means the elasticity modulus of samples A and B were included in the range of elasticity modulus of breast tissue. However, it was difficult to form samples A and B that sample C (gelatine 2 g / GA 0.5%) with a elasticity modulus of  $53.46 \pm 4.17$  kPa was the sample to be varied by  $\text{TiO}_2$  in the homogeneity test, and it was determined for its material absorption coefficient in order to make its elasticity similar to that of breast tissue.

### 3.3. Differential scanning calorimetric test (DSC)

DSC test in this study aims to determine an acceptable temperature samples and ensure the samples were not degraded when irradiated by the laser. In this DSC test, 13.897 mg of sample was used and heated at 40-70°C temperature, and the temperature was raised 5° C per minute. Temperatures used in DSC test was based on the characterization of laser in which laser output generates temperatures of 20°C every 10 minutes and the test process is performed for  $\pm 10$  minutes for one sample. DSC thermogram of synthesized gelatine-GA- $\text{TiO}_2$  is shown in Figure 7.

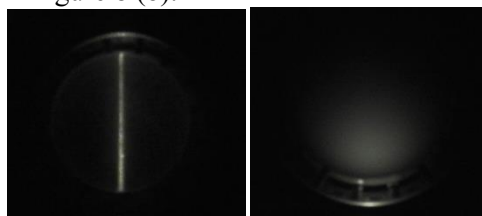


**Figure 7.** DSC thermogram gelatine composite-GA- $\text{TiO}_2$

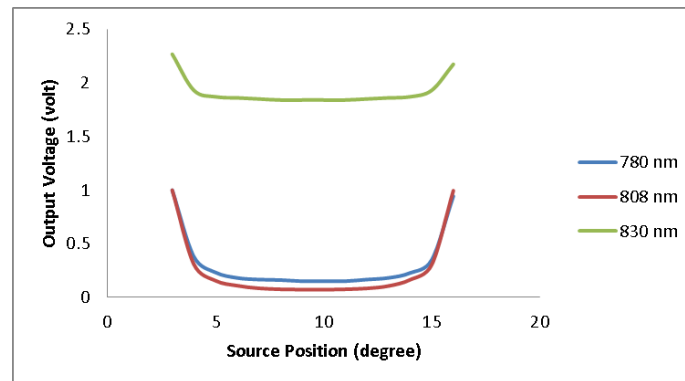
Based on the thermogram above, it can be seen that in the temperature range test neither endothermic nor exothermic occurred which illustrates that the sample did not emit or absorb heat (stable). The glass transition temperature ( $T_g$ ) occurred at of 51,40- 53,40°C temperature, and it shows a sample on balance. The result of DSC test analysis above shows that the sample was quite stable and did not undergo degradation in the temperature range 40-70°C in the optical tomography test.

### 3.4. Homogeneity test

In optical tomography test, one of the parameters observed in the sample is the scattering coefficient [11]. Therefore, the samples varied with  $\text{TiO}_2$  as light scattering agent that samples scatter light beam was given and could be detected by all detectors. Samples were already varied with  $\text{TiO}_2$  when irradiated with laser as shown in Figure 8 (b).



**Figure 8.** The sample when irradiated with laser (a) before the varied with  $\text{TiO}_2$ , (b) after varied with  $\text{TiO}_2$

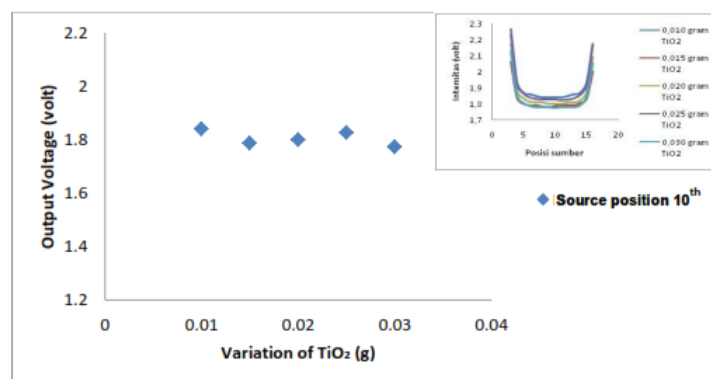


**Figure 9.** Graph of the relations between the output voltage at the source position on each wavelength (sample C / 0.01 g  $\text{TiO}_2$ )

In this homogeneity test used samples C with varied  $\text{TiO}_2$  namely 0.01; 0,015; 0.02; 0,025; and 0.03 g. The laser with 3 variations NIR wavelength that is 780 nm, 808 nm and 830 nm are launched to this sample. Based on sample homogeneity test results obtained by the graph the relationship between the output voltage at the source position number for each of the various wavelengths. Results for samples C with a concentration of 0.01 g  $\text{TiO}_2$  is presented in Figure 9.

In this study uses only one position detector which detector A. If the sample has a good homogeneity, then the position of sources that have the same distance to the detector A to produce the same output voltage. Under these conditions, the graph of the output voltage generated by the source position has had a trendline or a U-shaped pattern in Figure 9 can be seen that for all variations of wavelengths have a trendline or a similar U-shaped pattern.

NIR laser with a wavelength of 830 nm produces the highest intensity that can be detected NIR laser detector compared with the wavelength of 780 and 808 nm, so that the fund would be used 830 nm laser absorption material to the analysis phase. The material to be used for the absorption of the test will be selected based on the absorption of the material at each variation of  $\text{TiO}_2$  (in the NIR laser wavelength of 830 nm). Determination is done by creating a linear graph for the lowest voltage at each sample variation of  $\text{TiO}_2$  based on sample homogeneity test. The lowest voltage present in 9th place and 10th which is the farthest position from the position detector, so that made a graph of the output voltage with a variation of  $\text{TiO}_2$  in a position to source 10 shown in Figure 10.



**Figure 10.** Graph of the relationship between the output voltage with a variation of  $\text{TiO}_2$  in the 10<sup>th</sup> position of the source ( $\lambda = 830$  nm). Insert figure (Graph relationship with the intensity variations of  $\text{TiO}_2$ )



Based on the graph in Figure 10, it can be seen that the samples with a variation of 0.03 TiO<sub>2</sub> have the highest power absorption or low scattering power. On the concept of optical tomography, scattering power is a parameter to be considered in recording the sample shape based on the observed sample's scattering power [11]. Samples with the lowest scattering power are selected because if the low scattering power can be detected by a detector, then the larger power must also be detected. In this study, sample at 0.03 g TiO<sub>2</sub> variations was selected to be used for the analysis of absorption material.

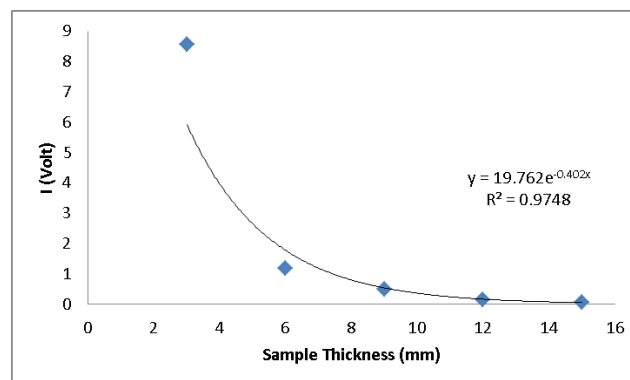
### 3.5. Results of value analysis absorption coefficient materials

Based on the sample analysis and homogeneity test, it was shown that laser with a wavelength of 830 nm which generated the highest output voltage could be detected by detector, and sample C with a variation of 0.03 g TiO<sub>2</sub> at a wavelength of 830 nm (the source position to 10<sup>th</sup>) was a sample which has the power maximum absorption. In the analysis of the absorption coefficient of this material was used sample C with a variation of 0.03 g TiO<sub>2</sub>, and an infrared laser with a wavelength of 830 nm was also used as the laser source. Absorption coefficient test results are shown in Table 5.

**Table 5.** Results of the test material absorption coefficient

Sample Thickness (mm)	I <sub>0</sub> (Volt)	I(Volt)
3	10.86	8.56
6		1.18
9		0.5
12		0.14
15		0.06

Based on Table 5 was made the logarithmic between graph intensity after getting through source material (I) and sample thickness as shown in Figure 11.



**Figure 11.** Graph o logarithmic between the intensity and sample thickness

The graph in Figure 11 shows the thicker the sample, the smaller the intensity detected by the detector. This shows the absorption of the sample events which occurred as a result of an interaction of light with matter. Based on this graph, sample thickness variations can be used to determine the absorption coefficient of the sample. Based on absorption test results which is indicated by the graph in Figure 11 and obtained  $y = 19,76e^{-0.40x}$  based on the Lambert-Beer law, it can be seen that the value of the absorption coefficient ( $\mu_a$ ) of 0.40 mm<sup>-1</sup>. Absorption range coefficient used in optical tomography process ranges from 0.01 to 1 [12]. Therefore, it can be concluded that absorption material value of 0.40 mm<sup>-1</sup> included in the range can be used in the process of optical tomography.

## 4. Conclusion

The composition of breast phantom which can result the best physical characteristics and elasticity similar to breast tissue is that of sample C. Sample C lasts for 3 days, and it is easily removed from the mould. Furthermore, its elasticity approaching is similar to that of breast tissue which is equal to 53.46

$\pm 4.17$  kPa). The homogeneity of the breast phantom is pretty good with a maximum intensity at a wavelength of 830 nm. Sample C with a variation of 0.03 g  $\text{TiO}_2$  produces maximum absorbance value in the farthest position (position 9) based on the homogeneity which is equal to 0.178 volts. Value of the absorption coefficient ( $\mu_a$ ) of breast phantom test based absorption coefficient is  $0.401 \text{ mm}^{-1}$ .

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