

Biosafety of Polymethyl Methacrylate as Glaucoma Drainage Plate

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Abstract

This study assesses surface roughness, biomaterial alteration and chemical compound on the polymethylmethacrylate plate of glaucoma drainage device (GDD) pre and 30 days post implantation on rabbit's eye. The implant's surface roughness was examined in 2D and 3D by Atomic Force Microscopy (AFM). The biomaterial alteration was assessed by Fourier Transform Infrared Spectroscopy (FTIR). Any tissue adhesion was also assessed since it might affect the result of the examination. Chemical compound was measured by Gas Chromatography Mass Spectrometry (GCMS). In the preimplantation assessment of surface contour, there were some sloping and rising area, but the range of amplitudo was around 28 nm. The feature of the implant in 2D was quite smooth. There were slight roughness changes of the PMMA plate after implantation and the range of amplitudo became around 22.9 nm. The elevation that was seen might be caused by the shape of the implant (curve). The FTIR assessment showed that the wavelength transmission pre and post implantation was relatively similar, which was 98,33% with frequency 3444,41 cm⁻¹ compared to 98,09% with frequency 3445,46 cm⁻¹. It means that there was no polymer degradation. There were some additional compounds found on the implant after surgery, but not a toxic compound.

Introduction

Glaucoma is the second leading cause of blindness in Indonesia, after cataract [1]. The aim of glaucoma treatment is to reduce intraocular pressure (IOP), which can be obtained through medications, laser or surgery, depends on the type and severity of glaucoma. In general, when medications has failed, filtration surgery is the next step taken [2-4]. The most common filtration surgery is trabeculectomy. Unfortunately, it cannot be done in high-degree fibrosis such as glaucoma in young people, glaucoma that caused by uveitis, trauma, neovascularisation, and other glaucoma that is grouped as refractory glaucoma. In those circumstances the alternative treatment is glaucoma implant surgery [3, 4].

Polymethyl methacrylate (PMMA) is known to be inert in the eye. It can be moulded. It has been used as ocular prosthesis and intraocular lens. There is no reported adverse reactions of PMMA [5-7].

This study was designed to evaluate the alteration on the material after utilization.

Material and Methods

The implantation was done in the faculty of veterinary medicine - Bogor Agricultural university on April-May 2015. We got

the ethical approval from the ethical committee of the university no 032/KEH/SKE/IV/2015 in accordance with the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research. The research on PMMA plate was done in Universitas Indonesia and police laboratory.

The topography of the implant surface was assessed with Atomic Force Microscopy (AFM) with contact scanning technique. The PMMA glaucoma implant was identified, along with the roughness of the surface itself.

The assessment of biomaterial alteration after implantation was done by Fourier Transform Infrared Spectroscopy (FTIR). It will assess the wavelength of the biomaterial. Any tissue adhesion was also assessed since it may affect the result of the examination.

There was possibility of compound changes of the biomaterial after the implantation. Thus the chemical compound alterations were measured by Gas Chromatography Mass Spectrometry (GCMS).

All of the examinations were done pre surgery and 30 days after the implantation in the rabbit's eye. The data will be compared based on pre and post assessment.

Results

The results of the surface contour measurement of the implant material are shown in these following charts.



Figure 1: Assessment chart of the implant's surface roughness before surgery.

On the assessment of the surface contour, there was some sloping and rising area, but the amplitude range was around 20 nm. This data shows that the implant's surface is quite smooth.

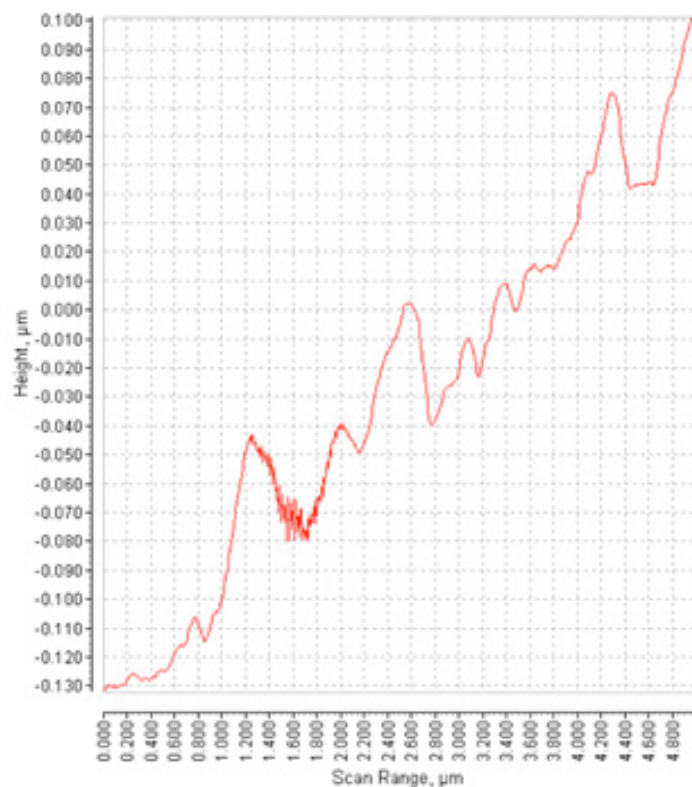


Figure 2: Assessment chart of the implant's surface roughness 30 days after surgery.

After the surgery, the amplitude range was $\pm 10-40$ nm. The cell attachment on the implant's surface could interfere with the last result. That attachment was part of body response towards foreign substance. The pattern of the chart looks different pre and post implantation, allegedly related with the placement of the material, because the implant has a certain curve. But this doesn't concern for a safety on the material, because the changes on the chart doesn't represent a significant difference on the material surface of the implant between before and after implantation.

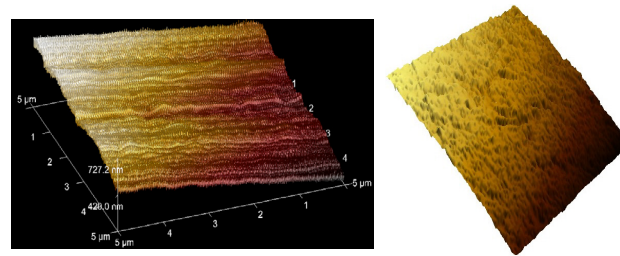


Figure 3: 3D picture of the PMMA implant before implantation

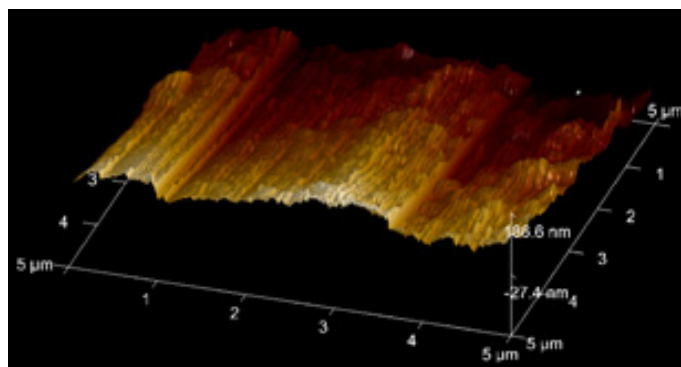


Figure 4: 3D picture of the PMMA implant after implantation.

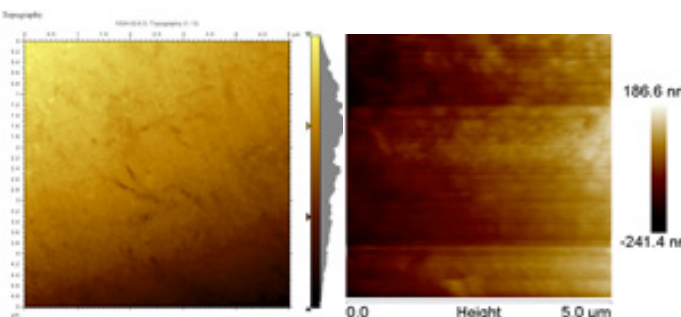


Figure 5: 2D picture of the PMMA implant's surface before (A) and after (B) surgery.

Table 1. Topography of PMMA pre and post 30th day implantation in the rabbit eye

	Pre Operation 1	Pre Operation 2	Mean Pre Operation	Post Operation
Image Rq (nm)	34.1	27.8	30.95	43.6
Image Ra (nm)	28	23.3	25.65	22.9

After the implantation, the implant is not as clear as before implantation. The attachment of tissues on the implant's surface can affect the result of the examination.

The result of AFM examination shown in table 1 that there was only slight changes. Image in Ra showed 28 nm pre surgery to 22.9 nm 30 day post implantation. The surface contour may alter the result.

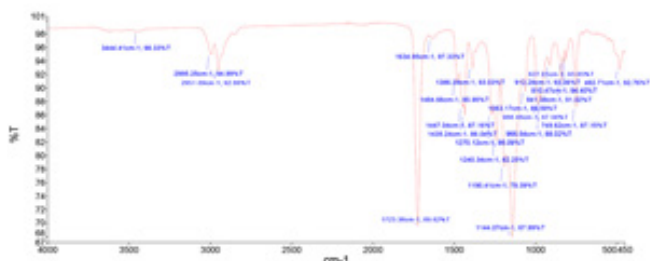


Figure 6: The result of the infrared emission of the PMMA implant before implantation

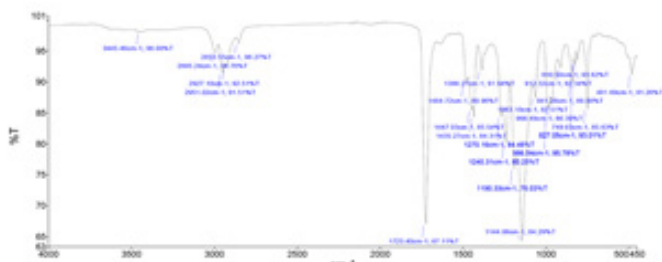


Figure 7: The result of the infrared emission of the PMMA implant after implantation.

On the table, it is shown that the wavelength transmission between before or after surgery was relatively similar. For example on number 1 (at the same point), the transmission of infrared before surgery was 98,33% with frequency 3444,41 cm-1, while after surgery the transmission of infrared was 98,09% with frequency 3445,46 cm-1.

Frequencies 1150 cm-1 until 1250 cm-1 were caused by the vibration strain C-O-C. Frequencies 986 cm-1, 1063 cm-1, and 841 cm-1 are the characteristic of vibration absorption of PMMA. Frequencies 1386 cm-1 and 749 cm-1 are the characteristic of vibration absorption of a-methyl group. Frequencies 2995 cm-1 and 2951 cm-1 are caused by vibration strain C-H (contained in PMMA). This shows that there is no polymer degradation on the implant that was already used.

GCMS measurement on the material before and after surgery shows that there was some additional compounds on the implant after surgery. Those compounds were seen on table 5 line 1, 4 and 6. Compounds on line 2 and 5 were not altered in quality and quantity. Compound on line 3 and 7 were changed in quantity only.

Table 2: The results of FTIR Examination

No.	FTIR			
	Pre-Operasi		H+30	
1	3444.41 cm ⁻¹	98.33% T	3445.46 cm ⁻¹	98,09% T
2	2995.25 cm ⁻¹	94.99% T	2995.24 cm ⁻¹	94.76% T
3	-		2853.55 cm ⁻¹	96,27% T
4	-		2927.10 cm ⁻¹	92.51% T
5	2951.09 cm ⁻¹	92.66% T	2951.02 cm ⁻¹	91.51% T
6	1723.36 cm ⁻¹	69.62% T	1723.40 cm ⁻¹	67,11% T
7	1634.95 cm ⁻¹	97.33% T	-	
8	1484.66 cm ⁻¹	90.95% T	1484.72 cm ⁻¹	89.96% T
9	1447.04 cm ⁻¹	87.16% T	1447.03 cm ⁻¹	85.54% T
10	1435.24 cm ⁻¹	86.04% T	1435.27 cm ⁻¹	84.31% T
11	1386.39 cm ⁻¹	93.03% T	1386.27 cm ⁻¹	91.94% T
12	1270.12 cm ⁻¹	86.09% T	1270.16 cm ⁻¹	84.48% T
13	1240.34 cm ⁻¹	82.25% T	1240.31 cm ⁻¹	80.25% T
14	1190.41 cm ⁻¹	78.39% T	1190.33 cm ⁻¹	76.03% T
15	1144.07 cm ⁻¹	67.99% T	1144.06 cm ⁻¹	64.29% T
16	1063.17 cm ⁻¹	89.59% T	1063.10 cm ⁻¹	87.51% T
17	986.48 cm ⁻¹	87.56% T	986.54 cm ⁻¹	85.78% T
18	912.28 cm ⁻¹	93.36% T	912.32 cm ⁻¹	92.34% T
19	966.54 cm ⁻¹	88.02% T	966.49 cm ⁻¹	86,39% T
20	841.38 cm ⁻¹	91.02% T	841.28 cm ⁻¹	89.88% T
21	827.01 cm ⁻¹	93.85% T	827.05 cm ⁻¹	98.01% T
22	810.47 cm ⁻¹	94.40% T	810.50 cm ⁻¹	93.62% T
23	749.62 cm ⁻¹	87.15% T	749.63 cm ⁻¹	85.63% T
24	482.71 cm ⁻¹	92.76% T	481.69 cm ⁻¹	91.26% T

Discussion

PMMA is a synthetic biomaterial and has been widely known as bioinert material, which means nontoxic and biologically inactive. Its uses as implant material or surgery aids on human has been done before, on ophthalmology, orthopaedic, and neurosurgery [8-11].

Biomaterial has physical, chemical and biological properties. Each of these properties can be analysed through a series of examination. In this research, the examination was done for the physical and chemical properties. Chemical properties including composition, bond and atomic structure, while physical properties examination including microstructure, phase, density and material porosity [8, 12]. The surface of the implant was assessed by AFM, polymer degradation was assessed by FTIR, and chemical compound before and after implantation was assessed by GCMS.

Surface topography assessment of the implant was done through variety of examination including optic microscope, electron microscope which is scanning electron microscope (SEM) and transmission electron microscope (TEM) also scanning probe microscope (SPM) which is scanning tunneling microscope (STM) and atomic force microscope (AFM). Optic microscope and electron microscope are only able to make assessment in 2D. Electron microscope can be affected by electron beam energy. The sample could be destroyed [12].

Scanning probe microscope is able to assess in 3D with atomic resolution. STM examination usually used on material made of metal and semi conductor or even material with electronic surface structure, while AFM is used for polymer material. The advantage of AFM is it has ability to assess mechanical contact force, Van der Waals force, electromagnetic force, capillary force, chemical bond, electrostatic bond, etc [12, 13].

Table 3: Comparison of implant material's topography and the PMMA material

Type of implant	Image Ra(μm)
PMMA post implantation	0.0229
Ahmed FP7 (silicon)	1.5 ± 0.1
Ahmed S-2 (polypropylene)	1.3 ± 0.1
Baerveldt implant (silicon)	0.1 ± 0.01
Molteno implant (polypropylene)	0.07 ± 0.01

AFM is used to assess the topography of the implant. The structure was smooth on 2D examination, but on 3D examination, the implant looks not entirely flat. The surface of the implant seem fluctuating on micrometer measurement. Before surgery, the amplitude differences is around 28 nm. The implant has curvature, by using AFM, the elevation of the surface can't be seen.

Table 4: GCMS Result on PPMA Implant Material Pre-Implantation

Substances on PMMA Implant			
RT	Area (%)	Substances	Quality
4.045	10.55	Aluminium, tripropyl- SS Tripropylaluminium SS UN 2718 SS Tripropylaluminium	78
		Oxotri (isopropoxo) vanadium	64
		3-Butenoic acid (CAS) SS Vinylacenic acid SS.beta. -Butenoic acid	59
4.148	1.38	Propyl acrylate SS 2-Propenoic acid, propyl ester (CAS)	50
		2-Propenoic acid, methyl ester SS Acrylic acid methyl ester	50
		2-Propenoic acid, methyl ester (CAS) SS Methyl acrylate SS Methyl propenoate	50
4.216	87.27	2-Propenoic acid, 2-methyl-, methyl ester (CAS) SS Methyl methacrylate SS Mme	91
		2-Propenoic acid, 2-methyl-, methyl ester (CAS) SS Methyl methacrylate SS Mme	91
		2-Butenoic acid, methyl ester, (Z) - SS Crotonic acid, methyl ester, (z) -	91
4.952	0.79	2(5H)-Furanone, 3-methyl- (CAS) SS 2-Methyl-2-butenolide	93
		2(5H)-Furanone, 3-methyl- SS.alpha.-Methyl-.gamma.-crotonolactone	93
		3-methyl - 5H - furan - 2 - on	78

Table 5. GCMS Result on PMMA Implant Post Implantation

Substances on PMMA Implant			
RT	Area (%)	Substances	Quality
2.968	2.66	-Methylamino-propylamine	78
		Amphetamine SS Aderal SS Dexedrin	43
		dl-Phenylephrine	43
3.968	12.54	Alumunium, tripropyl- SS Tripropylalumunium SS UN 2718 SS Tripropylalumunium	78
		Oxotri (isopropoxo) vanadium	64
		3-Butenoic acid (CAS) SS Vinylacenic acid SS.beta. -Butenoic acid	59
4.08	1.77	N-Propyl acrylate SS 2-Propenoic acid, propyl ester SS 1-propyl acrylate	47
		Propyl acrylate SS 2-Propenoic acid, propyl ester (CAS)	47
		2-Propenoic acid, methyl ester (CAS) SS Methyl acrylate SS Methyl propenoate	43
4.131	23.22	2-Propenoic acid, 2-methyl-, methyl ester (CAS) SS Methyl metacrylate SS Mme	91
		2-Butenoic acid, methyl ester, (Z) – SS Crotonic acid, methyl ester, (Z) –	91
		Methyl 2-butenolate SS 2-Butenoic acid, methyl ester	90
4.157	56.4	2-Propenoic acid, 2-methyl-, methyl ester (CAS) SS Methyl metacrylate SS Mme	91
		2-Propenoic acid, 2-methyl-, methyl ester (CAS) SS Methyl metacrylate SS Mme	91
		2-Butenoic acid, methyl ester, (Z) – SS Crotonic acid, methyl ester, (Z) –	91
4.396	2.42	Methyl metacrylate SS 2-Propenoic acid, 2-methyl-, methyl ester	64
		2-Propenoic acid, 2-methyl-, methyl ester (CAS) SS Methyl metacrylate SS Mme	64
		2-Propenoic acid, 2-methyl-, 2-propenyl ester SS Methacrylic acid, allyl ester	64
4.883	1	2(5H)-Furanone, 3-methyl- (CAS) SS 2-Methyl-2-butenolide	91
		2(5H)-Furanone, 3-methyl- SS.alpha.-Methyl-.gamma.-crotonolactone	90
		3-methyl - 5H - furan - 2 - on	91

AFM surface contour measurement on the implant that has been implanted on rabbit's eye for 30 days shown slight changes. It thought to be related with the tissue reaction on the implant and the manipulation during surgery. AFM has ability to assess any changes on the surface in nanometer. Rabbit's tissue attached to the implant or the procedure of the surgery may affect the result of the examination. This changes need to be considered due to polymer degradation, even though it has been widely known that PMMA is a nonbiodegradable material [14].

Fourier Transform Infra Red (FTIR) Spectroscopy was used to prove any changes on the implant, which is by polymer degradation or chemical compound alteration. FTIR uses wave by modulating interferometric. The signal will be captured and recorded on interferogram. The result will be calculated mathematically and the interaction between infrared radiation and natural vibration of the atom in the material will be assessed [15].

In this study, the frequency before and after surgery is similar. Chart 3 and 4 and also Table 2 shows the similarity between infrared transmission before and after surgery. Vibration on PMMA pictured with frequency 986 cm^{-1} , 1063 cm^{-1} and 841 cm^{-1} . These frequencies was from sequenced of atom on PMMA compound which contains group of C-H, C=O, CH_3 and $-\text{OCH}_3$. The result of this study is consistent with an experiment which was done by Ramesh¹⁶ et al, below:

Table 6: Vibrations and Frequencies on PMMA

Description of Vibrations	Wavenumbers (cm^{-1})
C-H stretching	2927-2986
C=O stretching	1700-1744
CH_3 stretching	1439
$-\text{OCH}_3$ stretching	1195

It concluded by FTIR results that the slight changes on the AFM examination was not related with the PMMA. It probably because of manipulation during the surgery.

Chemical compound on PMMA material before and after implantation was assessed with GCMS. Molecular weight was also assessed. Examination using GCMS start with changing PMMA solid structure into gas which will be ionised and fragmented into ion fragment. These ion fragment will be assessed on mass spectrometer.15 Based on the results, we could conclude although there was alterations but non toxic compounds were found.

The polymethylmethacrylate has toxic monomer in the form of liquid and gas. In a study in the rat, after exposure to methyl methacrylate concentrations of 0, 90, 437 or 2262 mg/m^3 (0, 21, 104 or 538 ml/m^3) by inhalation, 10 % to 20 % of the substance was deposited in the lower respiratory tract and metabolized there (EU 2002). Irritation of the upper respiratory tract

and eyes and possible CNS effects were reported in humans after exposure to methyl methacrylate concentrations of up to 250 ml/m³ [17]. This study did not find this monomer with this high concentration.

Conclusions

There were slight roughness changes of the PMMA plate after the implantation. The wavelength transmission pre and post implantation was relatively similar. Some additional chemical compounds were found after the implantation, but not a toxic compound.

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