Clinical relevance of current materials for cranial implants
Towards an optimal patient-specific implant material
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The properties of an in vivo fractured PMMA cranioplasty after 15 years

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This chapter is based on the publication:
Properties of an In Vivo fractured Poly(Methyl Methacrylate) cranioplasty after 15 years

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ABSTRACT

Background: In 2001, a 27-year-old man was diagnosed with a meningioma with skull bone involvement. A craniectomy was performed and a CMW-3 poly(methyl methacrylate) cranioplasty was manually manufactured to reconstruct the remaining cranial defect. In 2016, he complained about progressive neurologic impairment. A CT-scan revealed that the cranioplasty had fractured into four dislocated pieces. Removal was indicated and during the same operation a poly(ether ether ketone) patient-specific implant was inserted.

Materials and Methods: The fractured cranioplasty was compared to freshly prepared CMW-3 specimens to determine whether the material properties had changed during 15 years in vivo. Gel permeation chromatography, micro-computed tomography, and flexural strength tests were performed. The fracture itself was analyzed using finite element analysis.

Results: The polydispersity index and molecular weight were not significantly different for the fractured cranioplasty and CMW-3. The fractured cranioplasty contained a total porosity of 10.7%, CMW-3 cured at atmospheric pressure 4.1%, and 0.06% when it is cured at 2.2 bar. The flexural strength of the CMW-3 cured at 2.2 bar was significantly higher than both the fractured cranioplasty and CMW-3 cured at atmospheric pressure. Finite element analysis showed stress of 12.2 MPa under a load of 100 N on a weak spot.

Conclusion: This ex vivo study shows that CMW-3 after 15 years in vivo was not influenced in molecular weight or flexural strength. However, the design of the implant and the handling of the poly(methyl methacrylate) seem important factors to improve mechanical properties of cranial reconstructions.
INTRODUCTION

After decompressive craniectomy a cranioplasty is recommended to protect the brain, improve esthetics, and increase psychosocial well-being. Most documented materials for cranioplasty are autologous bone, titanium, poly(methyl methacrylate) (PMMA), hydroxyapatite (HA), and poly(ether ether ketone) (PEEK), each with their own benefits. However, there is still no consensus on the optimal material for cranial reconstructions.

One of the most frequently used alloplastic materials is PMMA, which was developed in 1901 by Dr. Otto Röhm and was adopted early in aeronautical engineering. After several years PMMA was introduced in the clinic and was gradually applied for dental applications, hip- and knee arthroplasties, and cranial reconstructions.

Especially in cranial reconstruction, material handling has undergone a transformation in the last decade. Traditionally, PMMA powder and MMA liquid are hand-mixed and cured directly in the cranial defect. An important disadvantage of this procedure is the high temperatures reached during curing, which could inadvertently be transferred to the bone, dura, and brain. Nowadays, a 3-dimensional (3D) mold of the cranial defect can be manufactured to produce patient-specific implants (PSIs). Subsequently, PMMA is pressed into a mold and cured. After cooling down, minor adjustments can be made to the implant after which it is placed into the cranial defect. There is extensive literature available on the behavior of PMMA; however, controversy exists especially toward toxicity. An important remaining question is whether the material behavior of PMMA changes over time in nonload-bearing locations in the human body, such as the calvarium.

Advances in medical technology, such as patient-specific allogenic reconstruction, have led to an improvement of patient outcomes. Therefore, it is important to understand in vivo material behavior over time. It is also important to understand why implants fail, so the design and material may be further improved on.

In this study a 15-year-old ex vivo cranioplasty was retrieved. The chemical, structural, and mechanical properties of this fractured cranioplasty were evaluated to investigate changes of these properties in the human cranium and to find the origin of the failure.
MATERIALS AND METHODS

Case

In 2001, a 27-year-old man, with diabetes mellitus type II, visited the department of neurosurgery with complaints of sensory disturbances in the right side of his body, character changes, diminished vision, and dysphasia. Magnetic resonance imaging was performed and the patient was provisionally diagnosed with a bilateral parieto-occipital meningioma with reactive changes of the cranial bone (Figure 1). A total resection was indicated, and a direct reconstruction of the cranial defect planned.

A bi-coronal incision was performed, a skin flap detached, and involved bone surgically visualized and removed. The resulting defect had a circumference of 400mm. After tumor resection and closure of the dura, a PMMA cranioplasty was prepared according to the manufacturer’s instructions using CMW-3 (DePuy International Ltd., Leeds, United Kingdom). The malleable PMMA was put into the defect for the correct size and molding, after the dura was protected with damp gauzes. After hardening small adjustments were made with a burr to create a perfect fit. After this, the cranioplasty was fixed with sutures. After closure of the skull defect a subcutaneous wound drain was placed. The total operation time was approximately 14 hours with 4.5 L blood loss. The pathologic diagnosis was as expected: meningotheliomatous (syncytial) meningioma (World Health Organization grade I) with ingrowth into the cranial bone.

Figure 1: Preoperative sagittal (left) and coronal (right) T1-weighted MR-image after intravenous gadolinium.
In the years following the initial cranioplasty the patient had multiple epileptic seizures; with the use of lamotrigine these did not recur. The patient lived by himself, was eventually permitted to drive a car, and did not have any complaints. In 2016, 15 years after the initial cranioplasty, he complained about progressive headaches, memory impairment, poor vision, inability to operate motor vehicles, and unstable gait. The patient could not recall any trauma involving the cranioplasty. On physical examination, the cranioplasty was palpable and seemed loose. A computed tomography scan with 3D reconstruction revealed that the cranioplasty had fractured into four pieces, which were dislocated (Figure 2A).

Removal of the fractured PMMA cranioplasty was indicated, and during the same operation a PEEK PSI was inserted (Figure 2B and 2C). The shards of the fractured implant were sealed in separate plastic bags, and stored at 4 °C in the dark. The PSI operation was complicated by a postoperative epidural hematoma which was surgically evacuated. After two months the patient visited the outpatient clinic and reported an improvement of his symptoms.

![Figure 2: A) 3D reconstruction (left) of the fractured cranioplasty and the remaining dislocated shards. B) PEEK cranioplasty in situ. C) Fractured CMW-3 cranioplasty in situ.](image)

Three analytical techniques, gel permeation chromatography (GPC), micro-computed tomography (µCT) and flexural strength, were used to determine whether the chemical, structural, and mechanical properties of CMW-3 had changed during 15 years in vivo. With the use of finite element analysis (FEA), the mechanical behavior of the fractured implant was analyzed to better understand the underlying reasons for failure.
Specimen preparation
The fractured cranioplasty was compared to fresh specimens of CMW-3 (PMMA). Following the manufacturer’s instructions, the PMMA particles (40.0 g) were mixed with MMA liquid (17.9 g) in a vacuum holder. The malleable CMW-3 was put into a nylon 3D printed cranial mold. One specimen was cured for 30 minutes at atmospheric pressure, another was cured for 30 minutes at a pressure of 2.2 bar.

Gel permeation chromatography
The average molecular weights and their distributions were assessed by gel permeation chromatography. Four small samples were collected from the edge of the fractured implant. To compare, 2 fresh samples of CMW-3 were retrieved. In total 6 samples were analyzed using GPC to determine the relative molecular weights. The samples of the fractured implant were washed with demi-water to remove as many blood stains as possible, and all samples were measured in duplo.

Suspensions were formed by mixing each sample in tetrahydrofuran (THF) while stirring and heating, resulting in sample concentrations of around 2 mg/mL. These suspensions were filtered to remove the present non-soluble salts and additives, and injected into the GPC column (300 x 7.5 mm, 3 µm particles, Mixed-C and Mixed-D columns connected in series (Polymer Labs, currently Agilent Technologies, Santa Clara, California, USA)). The mobile phase consisted of tetrahydrofuran at 1 mL/min and 40 °C. Ultraviolet/visible photodiode array (UV/Vis-PDA) and refractive index (RI) detectors were used to analyze the samples and were compared to polystyrene standards.

Porosity and density
The porosity was determined by measuring the density and using 3D µCT. The density of the specimens was measured using a Mettler Toledo AT261 (Greifensee, Switzerland) analytical balance. Micro-CT data were acquired using a SKYSCAN 1272 (Bruker, Kontich, Belgium) with the following settings: voltage = 100 kV, current = 100 µA, exposure time = 31.2 s, pixel size = 6.7 µm, and 1200 projection angles. The porosity was determined with CTAn software (v1.7.17; Bruker, Kontich, Belgium).
In vivo fractured PMMA cranioplasty

Flexural strength
The fractured implant and the CMW-3 specimens were sawed with a 0.3-mm-wide diamond saw (Ukam Industrial, Valencia, CA, USA) into x-10-x 13-mm rectangular specimens (10 (n=10 per group) and wet ground with standard metallographic grinding paper (P500, P1000, and P1200). The specimens from the fractured cranioplasty were harvested from the center of the implant. Before testing the specimens were immersed in a water bath at 37.0 ± 1.0 °C for 50 ± 2 h. The flexural strength was determined at 37.0 ± 2.0 °C, using a three-point-bending test with a crosshead speed of 1.0 mm/min and a distance between the supports of 10.0 mm. Each specimen was tested until fracture. The ultimate flexural strength (σ) was calculated using the following equation:

\[ \sigma = \frac{3F_l}{2bh^2} \]

where \( F \) is the maximum load exerted [in newtons], \( l \) is the distance between the supports [in millimeters], \( b \) is the width and \( h \) is the height of the specimen [in millimeters].

Finite element analysis
The fractured cranioplasty (Figure 3) was visually inspected and a simplified 3D model was created to predict the stresses in the expected point of failure (Figure 4). More precisely, this point showed typical characteristics of an initial point of fracture, the so-called mirror-hackle zone \(^{19,20}\), a groove originating near the edge of the implant, and an exposed pore located at the thinnest portion of this groove. Finite Element modeling was carried out using FEMAP software (FEMAP 11.1.0, Siemens PLM Software, Plano, Texas, USA); the analyses were performed with Nastran software (NX Nastran; Siemens PLM Software, Plano, Texas, USA).
The implant and surrounding bone were modeled into a sphere-like shape with
an outside diameter of 140 mm. The thickness of the implant model was chosen
as 4.5 mm, the average thickness of the fractured implant. The dimensions of the
groove and exposed pore in the broken implant were measured using digital dial
calipers (Mitutoyo, Kawasaki, Japan). The models were composed of 17,345 parabolic
tetrahedron solid elements. The implant was fixed to the patients’ cranial bone during
surgery and held into place by surrounding tissues; therefore the interface between
the implant and the surrounding bone was designed as fixed, allowing no movement
in any direction. Material characteristics of the models were: PMMA: Young’s modulus
= 2158 MPa (experimental result of the fractured cranioplasty), Poisson ratio = 0.38;
bone: Young’s modulus = 15 GPa, Poisson ratio = 0.3. Two analyses were performed
using different loads at the outside of the implant and perpendicular to the surface.
One with a load of 100 N on the central node and one with a load of 100 N on the node
opposite to the weak spot. The material properties used in the models are shown in
Table 1.

Table 1: The maximum tensile stress (σ), in MPa, and the Young’s modulus (E), in GPa, of the materials used in the
models.

<table>
<thead>
<tr>
<th>Material</th>
<th>σ</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone</td>
<td>-</td>
<td>10</td>
</tr>
<tr>
<td>Implant</td>
<td>70</td>
<td>2.2</td>
</tr>
</tbody>
</table>

The maximum tensile stress (solid maximum principle stress) and the displacements
in the implant and surrounding bone layer were calculated. In post-processing,
the contour option ‘average elemental’, without use of the ‘corner data’, was used to
visualize the results.

The amount of absorbed energy in the implant under load was calculated as follows:

\[ E = \frac{1}{2} F tf \]

Where \( E \) is the absorbed energy [in joules], \( F \) is the applied load [in newtons], and \( tf \) is
the displacement in the direction of the applied load [meters].
In vivo fractured PMMA cranioplasty

The absorbed energy upon hitting a flat surface was calculated using the following:

\[ E = \frac{1}{2} m v^2 \]

Where \( E \) is the absorbed energy [in joules], \( m \) is the mass [in kilograms], which was assumed to be 2.25 kg, half of the mass of the patient’s head (4.5 kg) as it is supported at one side, and \( v \) is the speed [in meters per second]. Using these equations, the corresponding speed was calculated at which an impact with a flat and hard surface would cause the maximum tensile stress required for fracture.

Figure 3: A) The fractured PMMA cranioplasty and B) 3D models created from the computed tomography data from the shards surrounding the suspected point of failure.

Figure 4: Simplified model of the cranioplasty before fracture.
Statistical analysis
The flexural strength data were statistically analyzed using one-way analysis of variance (ANOVA) followed by Tukey’s post hoc test ($\alpha = 0.05$) in SPSS version 24.0 (IBM, Armonk, NY, USA). Student’s t-test was used to analyze the GPC data.

RESULTS
In this ex vivo study a CMW-3 PMMA fractured cranioplasty, which was part of the patient’s cranium for 15 years, was compared to fresh specimens of CMW-3 cured at 2.2 bar and at atmospheric pressure. To determine whether the chemical, structural, and mechanical properties of CMW-3 change over time GPC, μCT, and flexural strength tests were performed. The fracture itself was analyzed using FEA.

Gel permeation chromatography
All samples were analyzed using RI detection since PMMA does not contain chromophores; the UV/Vis-PDA detector therefore, did not produce useful data (Figure 5). The number average molecular weight ($M_n$), weight average molecular weight ($M_w$), Z average molecular weight ($M_z$), and polydispersity index (PDI) are comparable for each group respectively (Table 2). The PDI was not significantly different for the fractured implant and CMW-3 ($p = 0.94$). No significant difference in $M_n$ ($p = 0.76$), $M_w$ ($p = 0.70$), or $M_z$ ($p = 0.78$) was detected between the implanted material and CMW-3.
In vivo fractured PMMA cranioplasty

Figure 5: A and B) Representative gel permeation chromatography curves of the fractured PMMA cranioplasty, C and D) CMW-3. A and C depict the results from the ultraviolet/visible photodiode array detector at 254 nm, B and D depict the results from the refractive index detector.

Table 2: Representative gel permeation chromatography results of the implant and reference samples, $M_n$, $M_w$, and $M_z$ data, in g/mol, are relative to polystyrene standards.

<table>
<thead>
<tr>
<th>Material</th>
<th>Sample #</th>
<th>$M_n$</th>
<th>$M_w$</th>
<th>$M_z$</th>
<th>PDI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implant</td>
<td>1</td>
<td>90,138</td>
<td>238,850</td>
<td>488,988</td>
<td>2.65</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>96,789</td>
<td>245,156</td>
<td>504,793</td>
<td>2.53</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>87,441</td>
<td>218,874</td>
<td>404,050</td>
<td>2.50</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>87,706</td>
<td>241,354</td>
<td>487,383</td>
<td>2.75</td>
</tr>
<tr>
<td>CMW-3</td>
<td>1</td>
<td>88,232</td>
<td>234,735</td>
<td>471,701</td>
<td>2.66</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>95,322</td>
<td>245,214</td>
<td>491,876</td>
<td>2.57</td>
</tr>
</tbody>
</table>

Porosity
The density of the fractured cranioplasty was 1.147 g/cm$^3$, while the densities of CMW-3 were 1.156 (cured at atmospheric pressure) and 1.246 g/cm$^3$ (cured at 2.2 bar). This results in a macroscopic porosity of 7.9% for the fractured cranioplasty and 7.3% for CMW-3 cured at atmospheric pressure. The μCT of the fractured cranioplasty showed a total porosity of 10.7%. The specimen of the CMW-3 cured at atmospheric pressure had a porosity of 4.1% and the specimen of CMW-3 cured at 2.2 bar had a porosity of 0.06%. (Figure 6)
Chapter 4

Figure 6: A) Representative micro-computed tomography slices of CMW-3 cured at 2.2 bar, B) CMW-3 cured at atmospheric pressure, and C) the fractured cranioplasty. Pores are visualized in black and filler particles in white. Scale bar: 2 mm

Flexural strength
The results of the mechanical tests and statistical analysis are summarized in Table 3. The flexural strength of the fractured cranioplasty and CMW-3 cured at atmospheric pressure was not significantly different, however, the flexural strength of CMW-3 cured at 2.2 bar was significantly higher than both of the aforementioned groups.

Table 3: Flexural strength ($\sigma$), in MPa, of the fractured implant and control specimens.

<table>
<thead>
<tr>
<th>Material</th>
<th>Pressure</th>
<th>$\sigma$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fractured Implant</td>
<td>Atmospheric</td>
<td>61.4 (17.4)</td>
</tr>
<tr>
<td>CMW-3</td>
<td>Atmospheric</td>
<td>72.1 (9.1)</td>
</tr>
<tr>
<td>CMW-3</td>
<td>2.2 bar</td>
<td>92.5 (4.0)</td>
</tr>
</tbody>
</table>

Values given as mean and standard deviation (SD). Identical letters indicate no significant difference between the groups. n=10 per group.
Finite Element Analysis
The maximum tensile stresses in the models under a load of 100 N in respectively the center and the weak spot in addition to the resulting translations are shown in Table 3 and Figure 7. The stress under the load of 100 N on the weak spot was 12.2 MPa. Since the material displays linear elastic behavior, a load of 503 N is needed to fracture the implant. This load corresponds with hitting a flat and hard surface at a speed of 0.42 m/s which results in a similar fracture stress.

Figure 7: Tensile stresses, in MPa, resulting from a load of 100 N perpendicular to the top surface of the implant model. The implant model is depicted from a bottom view.

Table 4: Maximum tensile stress ($\sigma_{\text{max}}$), in MPa, and the total translation (l), in mm, resulting from a load of 100 N perpendicular to the top surface of the implant model at the specified location.

<table>
<thead>
<tr>
<th>Location</th>
<th>$\sigma_{\text{max}}$</th>
<th>l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Center</td>
<td>3.8</td>
<td>0.091</td>
</tr>
<tr>
<td>Weak spot</td>
<td>12.2</td>
<td>0.159</td>
</tr>
</tbody>
</table>
DISCUSSION

This *ex vivo* study reports the material properties of a fractured PMMA cranioplasty made of CMW-3, after being part of the human cranium for 15 years, and fresh specimens of CMW-3. The following trends were observed: (I) the chemical and mechanical properties of CMW-3 did not significantly change during the 15 years *in vivo* (II) failure of the cranioplasty can be attributed to the heterogeneity in thickness and porosity (III) improvements in the mechanical properties of PMMA cranioplasties can be achieved by ensuring a consistent thickness of the cranioplasty, and by curing the implant under increased pressure.

Failed cranioplasties are generally not subjected to further investigations beyond basic microbiological evaluation in cases of infection. In our study, a single failed PMMA cranioplasty was analyzed and compared to fresh specimens of CMW-3. It is crucial to determine how the human body influences material properties of such implants over time, to ensure optimal clinical outcomes and possibly prevent further operations for the patient.

PMMA-based polymers have been used for many years in medical devices with their specific formulations and applications. It is used intra-operatively for fixation of artificial joints to bone, for dentures, and for cranial reconstructions. The information on chemical and mechanical behavior of PMMA following long-term implantation in the cranium is scant. In the literature, one patient was victim in a bicycle accident after cranioplasty which resulted in a fractured PMMA cranioplasty. Marchac et al. included 32 patients who underwent a cranioplasty with PMMA, one cranioplasty was removed because of fracture due to trauma. In another study a patient underwent a computer-based titanium mesh cranioplasty which fractured spontaneously. The authors hypothesized that the fracture of the implant occurred because of continuous pressure on the implant during the night, when the patient slept on the affected side. Fracture is more frequently described in cranioplasties manufactured from hydroxyapatite. Staffa et al. reported 25 patients who all underwent a cranioplasty of hydroxyapatite, of which one cranioplasty fractured due to trauma. Stefini et al. included 1549 patients with an hydroxyapatite cranioplasty, four were reported as fractured. The low incidence rate of fracture of cranioplastics could be due to underreporting of this complication in the literature. It is also possible that patients have no complaints and therefore do not notice the fracture.
In vivo fractured PMMA cranioplasty

The effects on molecular weight and mechanical properties for PMMA bone cements used for fixation of artificial joints is reported on in the literature. Hughes et al.\textsuperscript{27} reported a 12\% drop in molecular weight of Palacos\textsuperscript{®} (Smith & Nephew Inc., London, United Kingdom) used for fixation of the hip following 15 years in vivo. The molecular weight of Simplex\textsuperscript{®} (Stryker Howmedica Osteonics, Inc., Mahwah, New Jersey, USA), retrieved from hip fixation, was reduced by 46\% after 23 years. After 16 years no significant reduction in molecular weight was found for Simplex\textsuperscript{®} used for knee fixation\textsuperscript{27}. CMW1 cement, retrieved from hip fixation, was stable in vivo and did not show a reduction in molecular weight, even after more than 20 years. In our study the molecular weight of CMW-3 did not significantly change during 15 years in the human cranium.

By manually manufacturing the cranioplasty during surgery, the local thickness and shape are difficult to control. The fractured PMMA cranioplasty in our study was manually manufactured and had a thickness of less than 3 mm at several locations, and point defects even up to 1.5 mm, carrying an inherent higher risk of fracture. Nowadays, this risk can be mitigated by the use of a 3D-printed nylon mold. After the mold is manufactured, it can be sterilized and used for reconstruction. During surgery PMMA can be cured following manufacturer’s instructions and put into the mold when it is moldable. Because of the mold, the PMMA can be evenly distributed with a consistent thickness, which results in fewer weak points in the implant and should therefore make it more resistant to fracture. By using a mold the high temperatures reached during polymerization do not need to be suppressed to prevent damage of the underlying tissues, leading to a final implant with a higher degree of polymerization.\textsuperscript{13–16} Preoperative, ex vivo manufacturing of a PMMA cranioplasty would allow for an even better control of the environmental conditions, especially increased pressure, during polymerization, which leads to a reduced PDI and improved mechanical and biocompatibility properties.
Macroporosity can occur when PMMA is prepared by hand due to air getting entrapped in the material. Using a vacuum system leads to a lower macro-porosity in PMMA. Similar trends are observed when reducing the speed of mixing and decreasing the amount of strokes. However, when PMMA is mixed under vacuum conditions the micro-porosity is increased as the boiling point of the liquid MMA component is lowered. Our study shows reduced porosity in the CMW-3 cured at atmospheric pressure with the use of a 3D printed mold compared to the fractured implant and a further reduction in micro-porosity when cured at 2.2 bar. As reported in the literature, the flexural strength in our study is influenced by the porosity. With increased porosity, the flexural strength is reduced. The location and distribution of the pores is important, as pores near the midline will experience lower stresses.

To understand why this PMMA cranioplasty fractured, FEA was performed. The FEA confirmed that the stresses increased from the center to the point defect under a load of 100 N. The load of fracture of 503 N will most probably not be reached in daily life as patients are assumed to be more vigilant and careful. However, hitting the head on a hard surface at a speed of 0.42 m/s might easily occur. The patient might not even remember such a minor incident, as the patient in this case could also not recall a trauma involving the cranioplasty. The FEA model is a simplified model, modelled only with the defect at the suspected weak spot and without underlying tissues. Only the bone surrounding the implant is included. The stresses and consequently the displacements are very concentrated and of such a low level away from the weak spot that detailing of the environment is not of significant influence (Figure 7). The pressure in the head in a normal healthy human ranges from 70 mm to 180 mm water column. This pressure results into an upward load distributed over the entire implant, lowering the stresses but is hardly of influence on a concentrated load of 503 N.

These combined findings suggest that fracture of a PMMA cranioplasty is more likely to occur when features such as a reduced thickness, high porosity, and pores located near the surface are situated closely together, and an impact occurs at that specific location.
Limitations of this study
This study included only one PMMA cranioplasty for analysis. To have more reliable conclusions, a larger number of fractured PMMA cranioplasties should ideally have been included. In this study tissue formation, behavior, and changes in time have not been taken into consideration. These properties may be important and may influence failure rates in clinical circumstances, as such they should be investigated in future studies.

CONCLUSION

This ex vivo study shows that a CMW-3 cranioplasty after 15 years in vivo had not resulted in a change in molecular weight or flexural strength. However, the design and the manufacturing of the PMMA cranioplasty seem to be important factors for possible improvements in cranioplasties. By curing PMMA under increased pressure, the porosity is reduced As a result the flexural strength is increased.
REFERENCES


In vivo fractured PMMA cranioplasty


