



# Applications of the Poly(methyl methacrylate) (PMMA) in Cranioplasty

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**Abstract:** Cranioplasty is a surgical procedure that is used to correct any defect in skull bones after a previous decompressive craniectomy, usually made for traumatic brain injuries, with ischemic or hemorrhagic nature, or after a tumor removal. A composite for modeling on a defect in skull bones was prepared by crosslinking poly(methyl methacrylate) in the presence of barium sulfate. The crosslinking rate of methyl polymethacrylate in the presence of the benzoyl peroxide initiator, the N, N-dimethyl- $\beta$ -toluidine polymerization accelerator and the hydroquinone polymerization inhibitor allows modeling according to the location and size of the defect. Thus, the concentration of composite precursor components was optimal for this purpose. The TGA diagram shows the almost total consumption of methyl methacrylate and butyl methacrylate monomers in the crosslinking process of methyl polymethacrylate with the formation of the composite. This technical study demonstrates the efficacy of this treatment, as well as to show all the possible scenarios in such procedures.

**Keywords:** cranioplasty, poly(methyl methacrylate), composite, esthetic surgery

## 1. Introduction

The surgical procedure known as cranioplasty is an ancient procedure, as well known as its own counter-part, the cranial trephination. Its roots are found in Pre-Incas Peru, and it remains an important reconstructive procedure for modern cranio-facial surgery. The first bone graft was recorded in 1668, by J.J van Meekeren. He noted that a canine bone was good for repairing a cranial defect, and this procedure was made on a Russian man [1].

Since then, until the last decade, this procedure continued to evolve in order to improve the patient outcome. This well known procedure has an active evolution which obliges us to evaluate its progressive evolution. It is our duty to provide a customized solution applied to every different patient as well as to attack this surgical challenge with the best solution possible [2].

In its own progressive evolution, the procedure has shown great advancements, improving the neurological functions (via CSF dynamics) and cerebral blood flow. Moreover, the closing of the defects with an overlaying bone remove the atmospheric pressure effects over the already damaged brain cortex. Also, the cosmetic cranial contour restoration is very appreciated by the patient himself.

As a result, cosmetic and protective mechanical effects of cranioplasty can also protect from seizures, which is very important for the long-term quality of life. Other achievements include: Increase cerebral blood flow, brain energy metabolism and recovery of the brain tissue [3].

The cement used is conventionally radio-opaque, made of two different parts: a powder and a liquid part. When the two are mixed together, a polymerization reaction occurs, which at the end becomes a mixture.

Many different types of materials have been used through the history of the cranio-plasty procedure. However, after the oil explosion in the 1950s and the most recent discoveries in Materials Sciences, new items became available to be used in such conditions. Those materials need to have some critical features:

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It must fit the cranial defect and close it up completely, should be radio-transparent, resistant to infections, stable with temperatures changes, strong enough to resist any bio-mechanical stress, easy to shape and to use, not expensive and rapidly ready to be used in operative fields [4-5].

The correct indications, preoperative planning and Surgeons experience are critical for the clinical outcome of the cranioplastic surgery patients. In all groups of age, the most common cause of cranial defects are tumor removal or traumatic events, that required decompressive craniotomy. In children below the age of 4, with dura mater intact, cranium can achieve a self-closure. However, this does not happen in all other segments of age. The timing of the CPL is related to postoperative complications risks. The peak of incidence of infection is at 14 days after the surgical procedure. Hydrocephalus peaks at 90 days after the surgery, as well as seizures peaks at 90 days. Usually this procedure is planned in between 15-30 days, in order to have the minimum risk of infections or seizures [6-7].

Since Kim and Cheong [8], review of the historical and current approaches to CPL, a revolution has occurred in fabrication technologies (CAD software and 3-D printing) and regenerative medicine (tissue engineering). These two are complementary. Regenerative medicine can solve the problems of good integration of implants and protection of the underlying brain from infection. This procedure is however contra-indicated in cases with an already installed hydrocephalus, infections or brain edema/swelling.

There are many types of bone cement, as well as many providers. We included a list of them, comprising semi- acrylic bone cement, calcium-phosphate and pure acrylic bone cement. Among the many different materials used for CPL implants, some synthetic variants (such as Polyetheretherketone, polymethyl-metacrilate or titanium) present an higher primary tear resistance, while other like hydroxyapatite and autologous bone graft present good bio-mechanic properties. In short, all CPL procedures have their own advantages and disadvantages, and none of the actual currently available materials meets the all criteria required for an ideal implant, hence the choice is all up the Surgeon's preferences. While titanium showed pretty good mechanical properties, it is often very expensive and not malleable. Also, its hard structure makes it way difficult to be shaped and molded in a short window of time.

Any different patient need a personal attitude, in which the Surgeon will apply a customizable evaluation. Defects may vary significantly from patient to patient, hence the malleability of the substance is mandatory. The gold standard is a full covered bone defect, without any space left over, and the prosthetic plaque must be customized over the patient. This is done with ease using PMMA plaques. The shape of the defect is directly measured by the Surgeon intra- and extra-operatively, through cranium CT scans, craniometry and during the surgery [9, 10].

The surgeon molds the mixture by hand, shaping its 3D structure during the main operation. This process needs to be fast and it must be carried on with great attention [11]. The defect size and site should be performed both before and during the surgery, using cranio-metrics measures. Once the area of the defect is exposed intraoperatively, we have a short window of time to close the defect. This phase must be fast and prompt. The molded prosthetic will be hot (the polymerization is an exothermic reaction) and needs to be cooled down before the definitive closure [12-14]. The PMMA prosthetic is usually chosed over other competitors for some different reasons. It is safer than hydroxiapatite and more customizable than titanium. Also decreases the chance of intra operative incidents and the whole risks, general and special ones [15-17].

Our own experience in this domains, which is more than 15 years, made us choose the best solution, customizable to any patient and well tolerated by the patient. We have chosen to use radio-opaque pure acrylic bone cement because we have a limited amount of time during the operation, and needs to be non-pyogenic. Also, the material needs to be malleable and ready to use. So our choice falls over the pure acrylic bone cement. Beside this, its radio-opaque nature is very good for CT and radiographic localization [18]. Moreover, its affordability it is another chapter in favor of such substance versus its competitors [19].

The present article is a result of more than 10 years of studies and researches in the Department of Neurosurgery has been performing this procedure of cranioplasty through a decade so far. Here we

present 10 cases operated at the Department of Neurosurgery with craniotomy defects and underwent a cranioplastic surgery in the interval February 2016-March 2020. We analyzed studies, both chemical and biological, about the chemical reaction, namely the polymerization, as well as all the possible medical applications.

## 2. Materials and methods

### 2.1. Materials and equipments

The materials used in the study are of analytical purity and were taken from Sigma Aldrich: methyl methacrylate, butyl methacrylate, N, N-dimethyl-p-toluidine, hydroquinone, barium sulfate, benzoyl peroxide, gentamicin sulfate and poly (methyl methacrylate).

FTIR spectra were recorded using a Jasco FTIR-6300 (JASCO) spectrometer using an ATR (Attenuated Total Reflectance) accessory at room temperature with a scan speed of 30 scans / min with a resolution of  $4\text{cm}^{-1}$  in the range  $400$  to  $4000\text{cm}^{-1}$ . Thermogravimetric analysis was performed with a TA Q5000 (TA Instruments). The sample was heated at a rate of  $10^\circ\text{C} / \text{min}$ , from room temperature to  $700^\circ\text{C}$ , in an atmosphere of inert gas (nitrogen), with an inert flow of  $50\text{ mL} / \text{min}$ . Computed tomography analyzes were performed on a CT device - Siemens Somatom 256 slides.

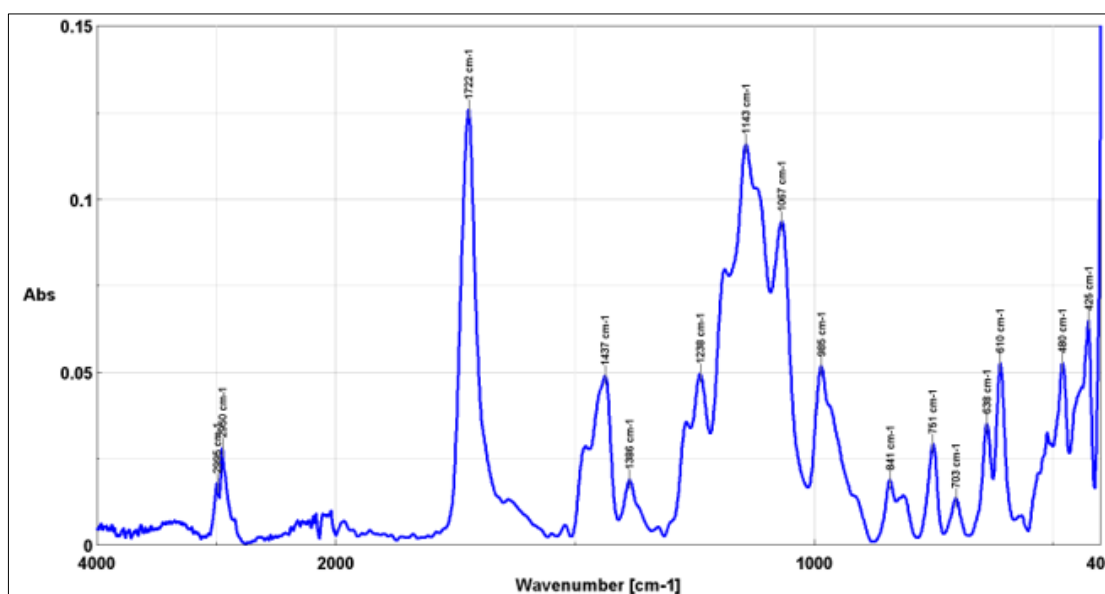
### 2.2. Methods

The preparation of the poly(methyl methacrylate) composite takes place in two stages. In the first stage, the solid phase and the liquid phase are prepared. The solid phase has the following composition: poly (methyl methacrylate) - 84.2%, benzoyl peroxide - 2.4%, barium sulfate (radio-opaque agent) - 9.6%, gentamicin sulfate -3.8%. The liquid phase has the following composition: methyl methacrylate - 85.3%, butyl methacrylate (BMA) -13.2%, N, N-dimethyl-p-toluidine (polymerization accelerator): - 1.5%, hydroquinone (polymerization inhibitor) - 20 ppm. The two phases are mixed at a solid phase / liquid phase ratio of 2.78 / 1 and heated to  $60^\circ\text{C}$  to obtain the composite precursor with an optimum fluidity to be applied.

The scalp was scrubbed with soap and betadine, and the entire head was shaved before the surgery. Prophylactic 3rd generation cephalosporines was given preventively to all patients, in order to prevent Staphylococcus species, because the acrylic compound is a foreign body to the patient. After general anesthesia induction, the head has been positioned according to the site of the defect, and the site usually was put parallel to the ground. We gave an injection of Adrenaline (solution 1:200.000, mixed with 10 mL of 0.5% xylene solution) in order to minimize bleeding risks at the skin level. We used the poly-methyl-metacrylate (PMMA) composite to repair the defect. As previously discussed, we mixed the powder and liquid parts, resulting in a pretty malleable substance which is shaped intraoperatively, during the surgical procedure, by hand by the Attending Surgeon in order to properly fit the defect. The Surgeon will clean the bony rims of the defects before the insertion of the PMMA prothesis. After that, the Surgeon will prepare the curvature of the prothesis, according to the site and extension of the cranial defect. The prosthetic must be cooled down with physiological serum (NaCl, 0.9%) in order to prevent heat damages (T usually is around  $60^\circ\text{C}$ ) to the adjacent brain cortex. This process is usually made in a cup filled with the Sodium chloride solution, and as soon as it cools down, it will harden enough to be installed. All the equipment that comes in contact with the bone cement during the process must be sterile, dry and kept at the room temperature, in order to minimize all risks of pre-polymerization and/or contamination with water or other substances. Also, they must be made in an inert material (non reactive, like glass or ceramics (Polyethylene instruments may be an option) to avoid any additional interface before the polymerization. It is also very important to explore any allergy or hypersensitivity to any of all the components, including eccipients, to all patients.

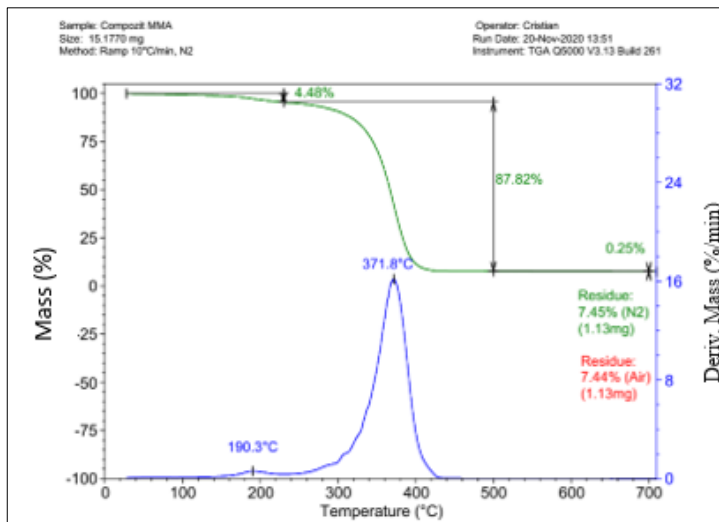
### 3. Results and discussions

The FTIR spectrum of the poly (methyl methacrylate) composite is shown in Figure 1. The FTIR ATR spectrum of the analyzed composite shows characteristic bands of the components, such as the bands from  $1067\text{ cm}^{-1}$  to  $1186\text{ cm}^{-1}$  characteristic for the sulfate group (stretching vibration). Also the vibration at  $986\text{ cm}^{-1}$  and the doublet from  $610\text{--}638\text{ cm}^{-1}$  are characteristic of the  $\text{SO}_4$  group, then the frequency of the stretching vibration of the OH group located at  $3430\text{ cm}^{-1}$  are defining elements of the inorganic part present in the composite. The organic part of the composite has as defining elements the stretching vibrations from the  $\text{CH}_3$  groups at  $2995\text{ cm}^{-1}$  and of the asymmetric methylene groups at  $2950\text{ cm}^{-1}$  and  $2846\text{ cm}^{-1}$  respectively. The most intense peak in the spectrum corresponds to the vibration of the  $\text{C}=\text{O}$  group of the ester groups of methyl methacrylate located at  $1722\text{ cm}^{-1}$ . At  $1143\text{ cm}^{-1}$  superimposed with the characteristic area of the sulfate group is found the stretching vibration of the  $\text{C}-\text{O}-\text{C}$  bond while at  $1238\text{ cm}^{-1}$  is found the stretching vibration of the  $\text{C}-\text{O}$  bond, and at  $1437\text{ cm}^{-1}$  the rocking vibration of the  $\text{C}-\text{H}$  bond. All these peaks are characteristic of the acrylic system found in the composite under analysis.



**Figure 1.** FTIR spectrum of the poly (methyl methacrylate) composite

The TGA diagram of the poly (methyl methacrylate) composite is shown in Figure 2. The diagram shows a mass loss of up to 4.5% at a temperature of up to  $220^\circ\text{C}$ , probably due to the decomposition of gentamicin sulfate. The mass loss of 87.82% on the temperature range of  $220^\circ\text{C}$ – $420^\circ\text{C}$  highlights the organic phase content of the composite. The 7.45% residue represents the inorganic material content of the composite.



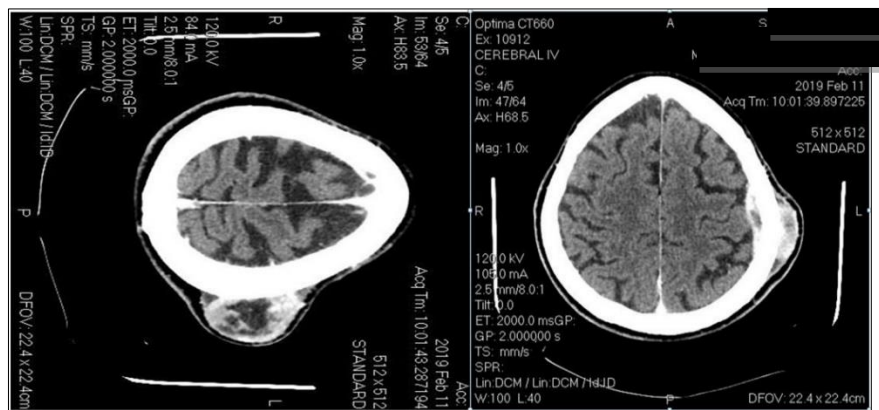
**Figure 2.** TGA diagram of the poly (methyl methacrylate) composite

We here present 3 cases of patients with an extracranial or an extra-intra cranial tumors that required a cranioplasty. These cases are the most eloquent about this procedure and why we choose such materials over others available.

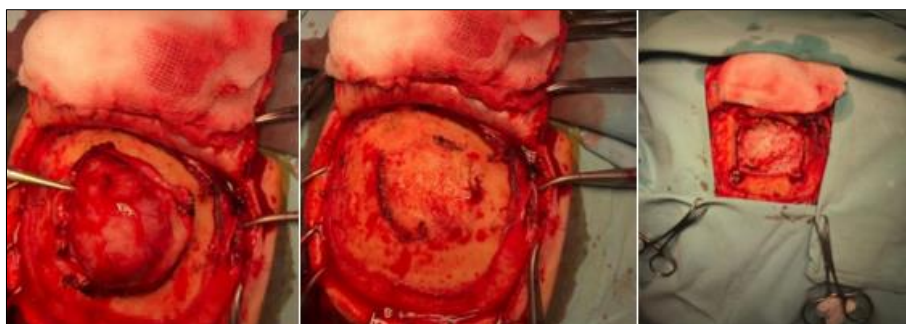
First patient was a female, 69 years of age at the surgery. The tumor was located in the left Temporo-parietal line, with extracranial invasion of the conjunctive and muscular layers of the head.

Figure 3 shows a skin incision, curved, with tumor exposed. The tumor was removed by hand macroscopically in total and (Figure 4) shows that the scalp and cranium bones were prepared for the craniotomy, namely the tiny periosteal membrane was incized, cauterized and removed.

Figure 4 also shows a left temporo-parietal craniotomy with 4 hand drill holes. The bone was removed without accidents, bleedings or dural tears.

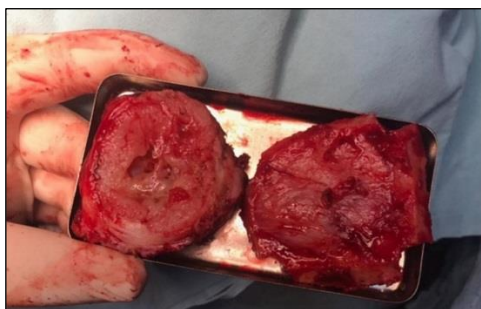


**Figure 3.** CT scans (preoperatively)



**Figure 4.** Intra-operative aspects. 4A – tumor removal. 4B preparation for the craniotomy. 4C – Craniotomy

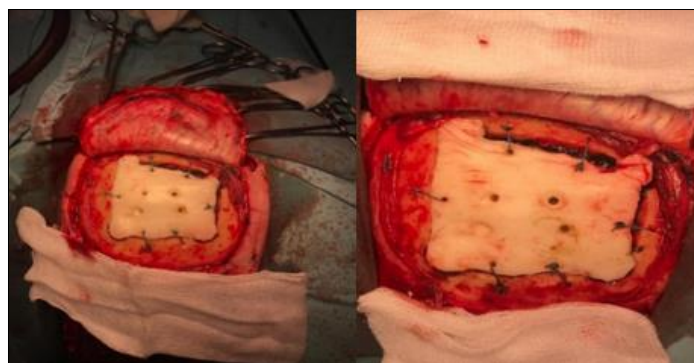
After the gross removal (Figure 5), the surgeon measured the 2 maximal distances of the squared craniotomy and prepare the mixture. The tumor had almost the same extent as the bone volet, as shown in Figure 5.



**Figure 5.** Tumor gross aspect(left) and bone volet (right)

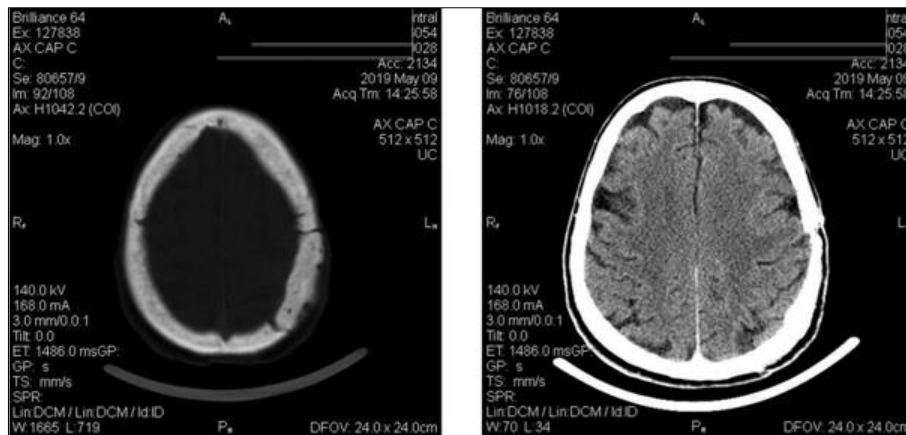
As hemostatic agents we used bone wax to prevent any bleeding risk from the bones included in the craniotomy. The tumor itself has been sent to the anatomico-pathological study to determine the nature of the tumor.

After the composite has been prepared, it is placed over the defect and then cooled (the temperature of the composite after preparation can exceed 60°C as previously discussed) to prevent any thermal damage to the brain cortex and its suturing with sutures is applied. The goal is to prevent any movement of the prosthetic plaque over the brain, which may cause severe damages, morbidity and even death of the patient.



**Figure 6.** Intra-operative aspect of a PMMA plaque

As shown in Figure 6, the PMMA composite can be modeled according to the location and size of the defect. This step can be performed manually by the surgeon during the operation. This possibility greatly facilitates the process for the surgeon, which makes this composite variant preferable to others.



**Figure 7.** Postoperative results seen at CT scan, PMMA plaque

The composite plaque is visible at both CT and MRI scans (Figure 7). It is usually well tolerated by the patient. All patients operated with CPL received a post-operative CT scan of the cephalic region. The plaque is more visible at MRI rather than CT scans.

The esthetical result is usually the main motivation behind a patient presentation in our service (Figure 8). Such tumors tend to be hard, fibrous, and may actually be painful, especially with big dimensions. It is mandatory to operate such lesions in a decisive manner, and all the defects resulting after the surgery must be repaired. The patient may suffer social ostracizing and may trigger depression, delusional statuses and social emargination.



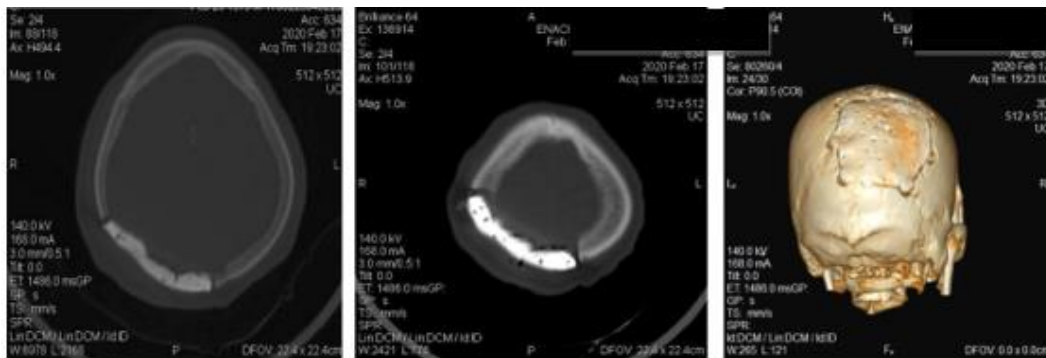
**Figure 8.** Cosmetic results, compared to before the surgery

The other case was a male, 40 years of age at the surgery. He presented a right occipital cranio-dural tumor (Figure 9). The anatomo-pathological studies identified that as a mediastinal primitive tumor metastasis.

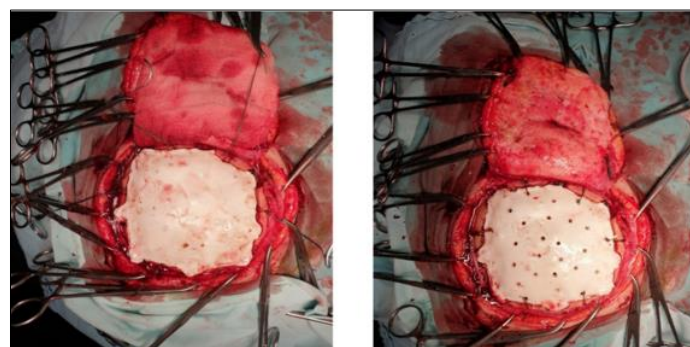


**Figure 9.** Preoperative MRI – showing another case with right occipital cranio-dural tumor

And after the surgery (Figure 10) he showed a very good esthetic and functional result (Figure 11).

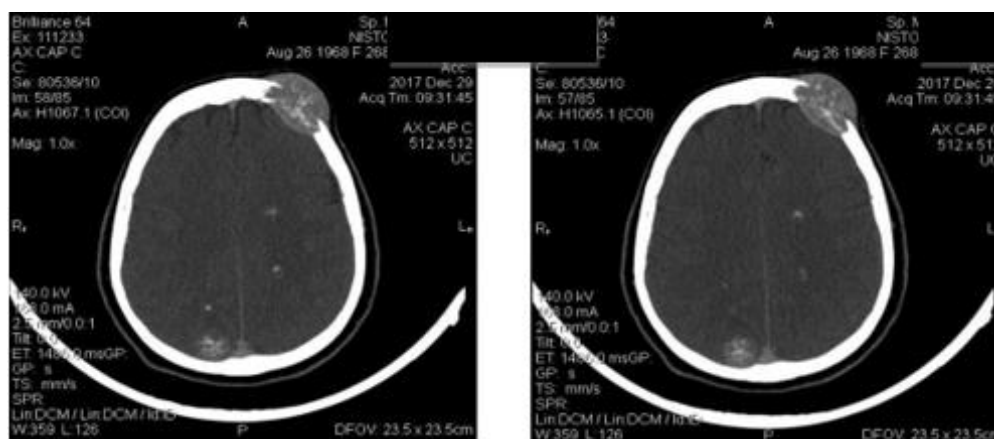


**Figure 10.** Cranial CT scan postoperative + 3D CT reconstruction



**Figure 11.** Intraoperative appearance of PMMA plaque

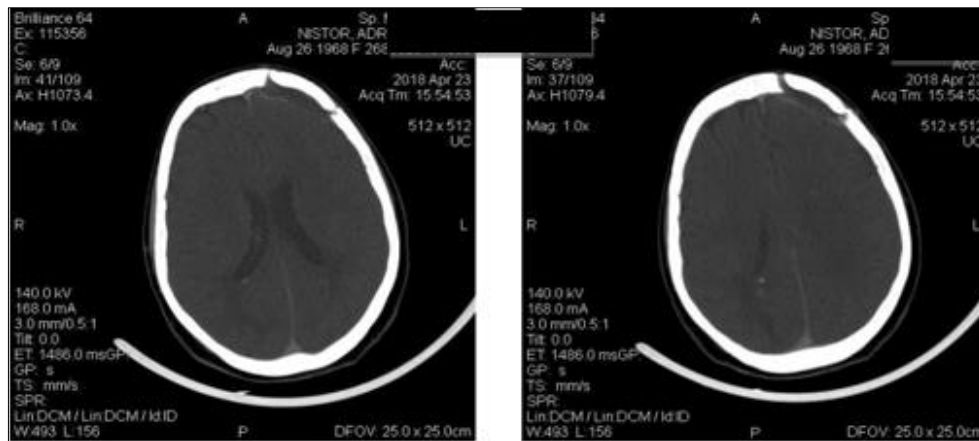
We here present a more recent case, with a 50 years old female patient with a left frontal metastasis from a primitive breast cancer (Figure 12).



**Figure 12.** Left frontal cranio-dural tumor, metastasis of a breast cancer

The operation has been scheduled few days after the MRI and the results achieved were good, both esthetically and functionally (Figure 13).





**Figure 13.** Postoperative CT scan with the PMMA prosthetic in situ

#### 4. Conclusions

Cranioplasty continues to be a challenge for surgeons who want to attack such injuries, because of the risks (pre-, intra- and postoperative) and because of the need to have a personalized response to such defects.

The crosslinking rate of poly(methyl methacrylate) in the presence of the benzoyl peroxide initiator, the N, N-dimethyl- $\beta$ -toluidine polymerization accelerator and the hydroquinone polymerization inhibitor allows modeling according to the location and size of the defect. Thus, the concentration of composite precursor components was optimal for this purpose. The TGA diagram shows the almost total consumption of methyl methacrylate and butyl methacrylate monomers in the crosslinking process of poly(methyl methacrylate) with the formation of the composite.

During the operations, the PMMA plaques have been shaped by hand by the surgeon, testing it several times before the definitive installation.

The use of PMMA plaques needs a strong collaboration, in a multi-disciplinary approach, particularly important during the bone cement procedure and during the little window of time during the polymerization.

Our series of patients showed that full recovery, with good esthetical and functional results, are possible to be achieved. The Surgeon needs to plan such operations with care and attention to the smallest details, including the dimensions of the plaques as well as the maintenance of a good cerebral blood flow and protection from the atmospheric pressure, in order to decrease the risks of seizures or other neurological complications.

#### Abbreviations

CPL – Cranioplasty

CSF – Cerebro-Spinal Fluid

CT – Computed Tomography

MRI – Magnetic Resonance Imaging

PMMA – Poly-Methyl-Metacrylate

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