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A Critical Investigation On Modern Artificial Skull Development Using Advanced Novel Biomaterials In Emerging Medical Industry

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Abstract

In the recent years, biomaterials used for reconstructing skull have undergone various development and researches in search of the best biomaterial which could be used. The surgical intervention used to reconstruct cranial bone defects is called cranioplasty, usually caused by injuries due to heavy falls and road accidents. In the modern field of cranioplasty considering the clinical procedures and expenses, the research for getting better reliable and comfortable biomaterials have never stopped. Cranioplasty is also employed in performing cosmetic surgeries. In the succeeding pages, the management of head injury and the process of cranioplasty as well as its complications are listed briefly. In the history of cranioplasty many different types of materials have been used and it is also being continuously evolved for betterment. An ideal biomaterial used for cranioplasty should have properties of lightweight, durability, fixable to the skull, osteoconductivity, and malleability. The principle material and the techniques are reviewed for the critical investigation on modern artificial skull development using advanced novel biomaterials in emerging medical industry. The materials being used for skull replacement are generally based on polymers, metals, ceramics, Nano materials and alloys. Each biomaterial has unique manufacturing techniques and method. The stem cell technique and autologous bones are also used in the process of bone replacement. The composition and properties of each material is explained and a comparative study of materials and techniques based on its performance and recovery of patients is done with the help of previous studies.

Introduction:

Head injuries are one among the foremost common causes of disability and death in adults. Traumatic brain injury (TBI) may be an increasing factor for mortality rate, morbidity rate, disability and socioeconomic losses in India and also it is estimated that almost 1.5-2 million persons are injured, and 1 million die per annum in India due to head injury cases [1]. Being a world's largest youthful country, a study indicated that road traffic injuries are the leading explanation for moderate and severe TBI (Traumatic Brain Injury) [2]. At 6 months, about 64% of the severe and 32% of the moderate TBI patients had died with head injury cases [2,3]. The severity of the injury varies from mild, moderate to severe supported the examining scales like Glasgow coma scale, duration of loss of consciousness, post traumatic amnesia. The injuries are classified supported with the mechanism of production as impact injuries (scalp injuries, skull fractures, cerebral contusion and laceration, epidural haematoma) and acceleration and deceleration injuries(diffuse axonal injury, subdural hematoma). Patients with these injuries are mostly provided mechanical ventilation, invasive monitoring, tracheotomy is additionally performed in certain cases. Surgical intervention (craniotomy) was performed in about 53% of severe TBI patients [1, 4]. Craniotomy is that the surgery to chop opens the skull where the bone flap is typically replaced at the top of the procedure with tiny plates and screws. The surgery where the bone flap isn't replaced is named craniectomy. The choice for surgical intervention for craniotomy depends on the injury type and therefore the patient's neurologic exam is carried out before the surgical procedure [5]. The most common neurosurgical procedures performed after brain trauma, ischemia, tumor resection or infection are Craniectomies and cranioplasty. Bone resorption rate from 4% to 22.8% and an infection rate from 3.3% to 26% are the percentile rate once after the cranioplasty surgery is performed with autologous skull bone [6]. There are concerns with their viability and therefore the potential microbial contamination was explanted for an extended period of time. No viable osteoblasts are found in cryostored skull bone flaps stored at -75 to -80 degree Centigrade beyond four month. Bacterial contamination of those cryostored flaps was 27.8% within the study conducted by David Yuen Chung Chan., et al. Bacterial culture yielded Pasteurellamultocida and methicillin resistant Staphylococcus aureus during the study carried by David Yuen Chung Chan., et al. [6].Cranioplasty is that the surgical reconstruction of cranial bone defects. Among the varied materials utilized in cranioplasty, the autologous bone grafts (from ribs, iliac bones and explanted calvarial bones) bone flap should be preserved for future re-implantation. Placing thebone under subcutaneous abdominal tissues, preserving the bone within the subgaleal space on the craniotomy's edges, or freezing the bone are the three storage options to preserve the bone flap for future surgical procedures if needed [8]. But there are cases describing an abnormal accelerated resorption of an autologous bone flap after 3 months of cranioplasty [7].

Rather than preserving the flap bone spending an excessive amount of thereon, an idea has been imagined by using an appropriate substitute for the flap bone that is been damaged during head injuries. These are the materials that can be used as substitute for replacement of flap bone in the skull they are Cortoss with Titanium and bioactive biomaterials like collagen. In the process of craniography metals like aluminium, gold, silver, tantalum were used and at the same time it has many disadvantages and due to such reasons these materials are found to be unsuitable. PolyMethylMethAcrylate (PMMA) almost adequate to the strength of the bone, titanium wire mesh was used to support the lattice PMMA placement to scale back fracture potential of the bone that is damaged.

Despite the benefits, it has high risk of infection, extrusion, and decomposition. It has about 23% of complication within 8 years of operation performed after the head injury [11]. PMMA is that the most generally used material and there is no complication of infection in using PMMA during surgical procedures [11, 12]. Due to its tensile strength, fracture suspectability and lack of incorporation make it difficult to use at some cases [11]. Hydroxyapatite may be a phosphate compound that is manufactured as ceramics and is used as material for replacement of flap bone during surgeries carried out after head traumatic injury or TBI. It is brittle, has low tensile strength and high infection rate, so it is been limited during cranioplasty surgery. As hard as diamond, Alumina ceramics are hard and expensive and cause 5.9% infection. Polyetheretherketone (PEEK) is semi crystalline polymer. PEEK is expensive and lack osteo-generative property, generates foreign body reaction. Titanium mesh together or with other symmetric materials is employed to strengthen prosthetics. Titanium is corrosive and non-inflammatory, has high tensile strength, and the graft infection is as low as 2.6% when compared to other materials [11].

1. Structure of skull

The skull may be a craniofacial complex made from 22 different cranial and facial bones which are of varying thickness and shapes. These flat bones are joined by sutures. The typical skull thickness for men and Women are 6.5mm and 7.1 mm, respectively. For women, the front-to-back measurement of skull is 171 mm and average width is 140mm. For men, the front-to-back measurement of skull is 176 mm and therefore the latter is 145mm.

The cranial bone may be a three layered system with two external cortical plates with a skinny layer of trabecular bone (red marrow) in between. The three layers of cranial bone are: outer cortical table – periosteal cortical plate, low density core – Dipole, Inner cortical table – endosteal cortical plate. The outer cortical table is most ordinarily used as calvarial bone graft in craniofacial reconstructions

1.1. Development of skull

Embryologically, the skull develops as Neurocranium and Viscerocranium. These are the basic forms of the bone that encloses the brain and protects it. The latter forms the facial skeleton. Neurocranium is split into chondrocranium forming the bones of base of skull and membranousneuro-cranium forming the vault of skull. The membranousneuro-craniumis made from membranous ossification of mesenchyme of neural crest cells and paraxial mesoderm. The postnatal growth of membranous bones is enhanced by apposition of latest layers within the outer surface and osteoclastic resorption from inside. At birth, the flat bones are separated from one another by narrow seamsof animal tissue namely: neural crest cells (sagittal suture) and paraxial mesoderm (coronalsuture). The wide suture at the purpose where quite two bones meet is named a fontenelle. Sutures and fontanelles allow the skull bone to mould during birth. The anterior and posterior fontanelle closes at 9-18 months and 1-2 months aged respectively. The chondrocranium is made by endochondral ossification of precordal chondrocranium (front to the rostral half sellaturcica arising from neural crest cells) and chordal chondrocranium (from occipital sclerotomes). Viscerocranium (comprising maxialla, mandible, cheekbone, malleus, incus, and stapes) is especially formed by the primary two pharyngeal arches.

Ossification of the three ear ossicles begins within the fourth month making it the primary bones to urge ossified completely.

2.1.2. Management of head injury

1.2.1. Initial management

Maintain airway, breathing, circulation of the patient

1.2.2. Initial neuro assessment

Enquire about the mechanism of injury and response at the scene. Examination of the neuro status using Glasgow coma scale (eye opening and motor response).

1.2.3. Immediate neurosurgical management

Obtain CT scan of head if,

- Patient is comatose
- GCS but or adequate to 13
- Lateralising neuro examination reveals unequal pupils and focal weakness
- Abnormal level of consciousness- they are sedated for diagnostics or treatment, if the CT scan is abnormal, neurosurgical consultation is obtained

1.2.4. Recognise and treat herniation

Look for sudden deterioration of motor response, level of consciousness and dilating pupil. If suspected, consult a neurosurgeon, hyperventilate the patient to pco2 =25 30 mm/hg, administrate i.vmannitol1g/1kg (if BP stable) and take CT scan immediately.

1.2.5. Other conditions and pitfalls

- Control bleeding
- Orogastric tube is used rather than nasogastric tube if an anterior basilar skullfracture ormidface fracture is suspected.
- Hyperextension injury of head and neck can cause arteria carotis injury
- Systolic vital sign but 90 mmHg can cause secondary brain injury

2. CRANIOPLASTY

Cranioplasty is that the surgery performed to exchange the removed skull vault after craniectomy. It plays a crucial role in restoring CSF (Cerebro Spinal Fluid) flow dynamics, reducing the formation of pseudo-meninigiocele, enhances cerebral glucose metabolism, cerebrovascular reserve capacity and protecting vital structures. It enhances the standard lifetime of the patient post craniectomy. The procedure of craniectomy develops both psychological and physical complications in patients. Post craniectomy, the patient is emotionally disturbed by their appearance with depressed skin and sunken flap. Conditionslike hydroencephalous and sunken flap syndrome accompanied with neurological symptoms like headache, dizziness, fatigue and psychiatric changes are common after craniectomy. The indication for craniectomy decides the timing of cranioplasty. Usually the interval between craniectomy and cranioplasty is between 6 weeks to 1 year. But the neurological condition of the patient, its progression, the healing of tissue around incision, vascularization of the encompassing tissues, infection of the scalp, hydroencephalus is additionally into account .The clearance of cranial also as systemic infections are considered (using the inflammatory markers like C reactive protein, erythrocyte sedimentation rate , serial imagining) for determining the cranioplasty timing. Immediate cranioplasty is rare and performed just in case of craniectomy for neoplastic invasion of cranium. Delated cranioplasty is indicated in conditions involving intracranialinfection and refractory intracranial hypertension.

Following the choice of performing cranioplasty, the preoperative studies including computed topography supporting three dimensional reconstruction and MRI which helps within the study of structure in adjacent to the skull defect (like scalp, dura) are done.The thorough investigation of the patient is of immense importance to rule out the contradiction in surgery. Patients with conditions like hemo-dynamically unstable, bacteraemia or have persistent intracranial hypertension are postponed for surgery. The surgery of cranioplasty is sort of complicated it has many risk factors during and after the surgery. As usual, the preoperative antibiotics are administered and therefore the patient is positioned in an OT table to perform the operation. The incision follows the prior incision with care to proceed on the scar to avoid necrosis of the scalp. There is profuse bleeding found during this condition as re-incision is formed on the re- vascularized connective tissue. The scalp and muscles are reflected with the assistance of periosteal elevator. Reflection of temporal muscle with or without the attachment with flap is vital to avoid suboptimal cosmetic result. The cranioplasty flap is fashioned or replaced when the world of skull defect and therefore the soft tissues around are exposed and cleaned. The technical point of difference within the surgery is that the preferred exposure. Just in case of autologous cranioplasty, dura must be free of the inner table of thenative skull. Failure to do so prevents the bone flap from sitting correctly within the defect.But only outer cortex is exposed just in case of use of biomaterials like methyl methacrylate allowing thinner cranioplasty and proper contouring.

In occasional condition of persistent herniation through the cranial deficit caused by cerebral edema or hydrocephalus, the subsequent measures are often taken:

•A brain cannula is inserted into the ventricle to empty the CSF (Cerebrospinal fluid).
• Thinning of bone flap can also facilitate the replacement but it also increases the speed ofbone resorption.
An external ventricular drain on the contralateral side or lumbar drain could also be placed and CSF is drained just in case of replacement failure and cranioplasty are often reattempted later.
• Ventriculoperitonial shunt could also be required.

After the deficit is closed, the bone flap or the prosthesis is secured with titanium plates and screws. Conditions like epidural hematomas and postoperative epidural fluid collection are prevented by dural tack-up sutures. Small perforations made on the flap or prosthesis prevents the fluid collection beneath it. Then the soft tissue layers are closed. When the temporal muscle is separated along-side scalp flap, it need not be attached to the skull again. But, if this muscle is raised separately, it is often secured with screws to the prosthetic plate. Subgaleal draining and secure head wrap dressing prevents extensive facial swelling. Sometimes, it produces negative transluminal pressure and results in persistent bleeding from scalp arteries. In patients with CSF leakage in meningeal tissues during cranioplasty, subcutaneous drain after surgery is not advised and controversial.

Post-operative medical care and neurological status monitoring for atleast one night is useful to avoid cases of heavy bleeding from scalp edge and dura. Cases with routine cranioplasty can undergo a postoperative computed tomographic scan then placed in non- intensive care unit. The subgaleal drain could also be removed with dressing on second day after surgery.

2.1. Pediatric cranioplasty

Apart from head injury in adults, paediatric cases involving craniosynostosis (abnormal head shape), missing bone and temporal hallowing also require cranioplasty in severe conditions. Paediatric cranioplasty features a unique set of considerations and limitations. The utilization of biomaterials rather than autologous bone is contradicted in paediatrics due to the reasons including non-flexible nature, foreign material affecting normal cranial growth, intracranial migration of biomaterial, material disintegration. Biomaterials can cause inflammatory tissue reaction and may be susceptible to fracture.

The anatomy and physiology of the dura and the skull changes rapidly initially from the birth till 8 years of age. The osteogenic properties of the dura feature a natural capacity to heal the cranial defects in patients of 0-24 months but fail to do so later in development. Further, it is crucial to avoid surgical interventions in children as they primarily affect the expansion of skull and brain. A perfect paediatric cranioplasty material should have ability to grow by integrating with the adjacent bone since the neurocranium covering the intracranial cavity enclosing the brain, grows with age in child till 6-7 yrs.

Considering the advantages of using autologous bone including decreased risk of infection,least disintegration due to high re-vascularization and integration with adjacent bone, autologous cranioplasty is preferred because it is the gold standard method in paediatric field .The cranium, ribs and ileac crest are the common donor areas of autologous bone graft [16].

3. COMPLICATIONS OF CRANIOPLASTY INFECTIONS:

Risk factors include long hospitalization, immune compromised by traumatic injuries and reoperations, length of surgical time of cranioplasty, multiplicity of head lesions, width of the cranial defect, older age, lack of pre and post-operative antibiotic therapy. It is mostly characterized by scalp tenderness with pain, redness and swelling over the implant.

3.1. Bone Resorption:

Risk factors include younger age, bone flap fragmentation, and shunt-dependent hydrocephalus. They are radiologically and clinically evident for diagnosis in 3-12 months after the cranial reconstruction.

3.2. Wound dehiscence:

It is usually caused by the utilization of hard prosthetic materials (like steel mesh, protruding metal plates) which are corrosive to the skin causing irritation. Long hospitalization in these conditions can cause saprophytic infections. They are avoided by limiting the utilization of metallic substances and providing excellent care to the surgical wound for healing.

3.3. Hematoma:

The danger factors for haemorrhage after cranioplasty include surgical injury of sentimental tissues (muscles, subcutaneous layers), high risk of cerebral lesions by dural compression of prosthesis, blood loss round the edges of skull defect, anticoagulant-antiplatelet therapy are not preventively discontinued before the cranial reconstruction Some authors reported that higher rate of hematomas (20% of patients) are found when autologous bone is employed for reconstruction [17].

3.4. Seizures:

The predisposing factors are bifrontal cranial reconstruction and adulthood [18]. Clinically, seizures are considered appearing Immediate (appearing 24 hours after surgery), Early (appear within 7 days from surgery) and Delayed (appear 7 days after surgery). When the rationale for surgery is traumatic cranial defect, the seizures appear early. Just in case of non-traumatic reasons (like tumour, haemorrhage, stroke) seizures are mostly delayed. Itis recommended to perform the surgery with care to avoid manipulation to the dura while preparing the skull edges and to not compress the brain.

3.5. Hygroma:

They are the fluid filled sacs developed over bony prominence to repeated pressure or trauma over that area. The shunt valve pressure avoids this condition if associated with pre-existing CSF shunt or dramatic intracranial haemorrhage.

3.6. CSF collection

This common complication is found in patients with traumatic damage of meningeal tissues or those that underwent several surgery procedures. This increases the danger of infection. Hence, the injury the dura matter should be prevented during cranial reconstruction.

3.7. Poor cosmetic result

The malposition of the prosthesis, sunken flap in use of autologous graft and irregular modelling of acrylic can produce poor cosmetic result. But this complication is of least importance because it does have any effect on neurological progress of the patient. It’s considered because it holds a crucial place in socially active lifetime of the patient and their satisfaction.

3.8. Nuances in cranioplasty

It is important to settle on a correct cranioplasty material for the effect and therefore the ideal cranioplasty material should be immune to infection, resistant to heat conduction, nonmagnetic, radiolucent, durability or strong to biomechanical process, easy to shape and should not be dilated with heat, inexpensive, should be tissue acceptable. Still there is no such material to satisfy of these criteria and it must fit the cranial defect and should be closed properly with plates to achieve immobility [19].

4. TREATMENT METHODOLOGY:

The utilization of methyl methacrylate is been used for the treatment of skull during head injury and the recovery process are as follows. Large saline-soaked cotton balls are placed into the skull defect above the dura and molded until they form the acceptable contour. Thepowdered methyl methacrylate and fumes are removed using vacuum. Peroxide is added slowly and stirred, provided there is not any air bubbles formed. When the mixturereachesa thick syrup consistency, it is placed into a sterile plastic sleeve and quickly smoothed into a skinny sheet. The sleeve is placed over the skull deficit producinga chemical reaction with cortex being protected by saline soaked cotton balls. When the sides of the plate become highly transparent, the prosthesis is far away from the sleeve and dropped in cold saline. On high-speed drill, the surplus acrylic is removed. Then, the cotton balls are taken out and prosthesis is fixed within the bone deficit area of the skull.

5. ANALYSIS OF VARIOUS MATEIALS USED IN SKULL REPLACEMENT

Generally used bone replacements materials include Autologous bone (grafting), PMMA, PEEK, Hydroxyapatite, Ceramic, Cortoss, Titanium, Tantalum(coating), Cobalt-chromium Alloy, State Memory Polymer (SMP), Crystalline mineral+hydroxyapatite+(type-1) collagen, Stem cell, Nano materials (carbon). Materials to be used as skull replacements must be not conductive nor dilative of the temperature, Resistive to infection (sterilized) and biomechanical process, Malleable to suit defects withcomplete closure, Cost effective (economically feasible), Radiolucency and easy to shape.

5.1. Autologous bone

Autologous skull flap is cosmetically natural. These fresh flaps are reinserted and allowed to form a thick fusion with the encompassing bone with its inbuilt osteogenic, osteoinductive and osteoconductive properties. After re-implantation, no blood is supplied to the bone flap, resulting in ischemia. As a result an inflammatory response is initiated and blood surrounds the flap. Capillaries from the encompassing bone, dura, periosteum initiate osteogenesis to the bone flap. The primitive mesenchymal cells migrate through these capillaries and bone remodelling occurs. Necrotic bone is gradually reabsorbed. If this functional contact between the transplanted flap and surrounding bone is poor; the transplanted flaps are going to be absorbed. After craniectomy, bone is preserved either underneath the adjoining galea, subcutaneous layer of anterior wall or cryopreserved. The incidence of bacterial infections by organisms like Propionibacterium acnes, Staphylocoocusaureus and coagulase negative staphylococcus are more common in preserved autologous bone. Hence, sterile procedure should be followed in collection and preservation of the bone flap at the time of hemicraniectomy. It is suggested that the subcutaneous preservation of bone flap can increase the viability of bone. However, cryopreserved bone diminishes the danger of abdominal incision. This type of preservation has shown an increased rate of bone resorption especially in children [13]. As analternate to freezing the autologous bone flap, it is often stored in temperature aftersterilizing it in ethylene oxide gas [14].

Senapati.et.al have made a case report of a 25 year male patient who underwent right Hemispheric decompressed craniectomy for right acute subdural hemorrhage with underlying contusion and diffuse brain edema[15]. The bone flap was stored within the abdominal fat. He was discharged together with his GCS scale checked and cranioplasty was done after 2 months. The preserved bone was grafted and secured with screws. During decompressive craniectomy, laying another sheet of dural substitute over the world of exposed dura may be a maneuver which prevents adhesion between the dura and scalp. But, this adhesion can injure the underlying dura and increases the prospect of infection. The conclusion of this study was that, complications of decompressive craniectomy like sinking scalp flap, resorption of preserved bone, hydrocephalus and syndrome of the trephined are prevented by early craniectomy. Dissection of the plane of tissues was easier during this condition with no finding of profound blood loss during surgery.

5.2. PolyMethylMethAcrylate (PMMA)

PMMA is also an essential element used for bone replacement with a material composition holding two parts namely, Powder part with PMMA 84.3%, Benzoyl peroxide 2.3%, Barium Sulphate 9.6%, Gentamicin Sulphate corresponds to 1g base with 3.8%, lowviscosity and Liquid part with Butyl methacrylate, N-N dimethyl-p-toluidine, Hydroquinone (20ppm) that is used for small/medium sized cranial defects. It gets adhered to dura without reaction within the underlying tissue. As it's a chemical reaction it emits heat, to regulate that hydrogel is applied on the underlying tissues and hardened using saline water. The major properties of PMMA includes a Boiling point of 101`C, Molar mass-100.121 g/mol, Elastic modulus ranging from 2.4-3.1 GPa, Tensile Strength - 80Mpa, Density of 940 Kg/m^3 and water soluble.

Firstly, the scalp is cleared that's adhered to the dura to achieve clean curvature of the bone border and methyl methacrylate is formed. After placing the methyl methacrylate to stop heat damages from adjacent tissues it should be washed with cold water then the methyl methacrylate is placed during a cup containing physiologic serum for the aim of cooling and hardening. The material is with the assistance of mini-plates. While using titanium mesh, it is fixed with the miniplates and methyl methacrylate is poured within the sort of liquid and cooled with water [1]. It exhibits lightness, less expensive, lack of thermal conduction, malleability, radiolucency and straightforward to handle compared to metals. It was first employed by a physician zander in 1940. The preparation of the acrylic initially involves two steps firstly mold has to be made then inserted within the defect area. Then further reaction results in its malleability easily shaped to suit within the contour of the cranium. The skull plate was made by mixing polymerized methyl methacrylate (PMMA) with a liquid monomer that is composed of fine particles of prepolymerized resin mixed with methyl methacrylate. This process contains disadvantages such as, the powder mixed with the propenoic acid is not sterile and there is a chemical reaction resulting to hardening, brittleness that ends in fracture of plate and cause fragments embedded the skull.

Wael M. A. Abd El-Ghani., et al. have carried a study on 46 males and 29 females betweenthe ages of 26 to 60. The procedure was done after a year of accident and therefore the patients went through a 3d scanning for the measurement and dimension of the defect. The kit consists of liquid and powder mixture of PMMA. A homogeneous mixture was made toavoid air bubbles knead the cement with the assistance of gloves and an approximate quantity and shape of the defect was created and gel foam is applied on thedura the implantis about firm and excess cement was removed before hardening and continue with the hardening phase, irrigation is completed with saline water in natural temperature it takes 10minutes. The fixation is completed with the assistance of titanium screws and titanium mini plates. There was no material complication and excellent reconstruction was obtained. PMMA can produce chemical reaction which will cause tissue damage, but the author has used gel foam and continuous saline irrigation. The pericranial layer are often preserved permanently vascularization and healing maintaining haemostais and avoid tight wrapping for correct blood flow. PMMA may bea good cranioplastry material but should be processed with proper techniques and time to avoid complication [5].

5.3. Polyaryletheretherketone (peek)

This is the currently used plastic within the sort of polyaryletheretherketone and porous polyethylene. Until the invention of porous polyethylene, polyethylene was not used widely due to its soft nature and the pores within the porous polyethylene allow ingrowth of collagen and soft tissues. The advantages include radiolucency, stiffness, strength, non- allergic and it was originally found for the replacement of hip and spinal bone [20]. The benefits of this material was found to be easily shape-able with the assistance of warmth and limited due to its soft nature. The porous polyethelene has its good biocompatibility due to its rare case of known allergic and tissue reaction inducing vascularization followed by soft tissue in growth and deposition of collagen deposition dealing with the characteristics of vascularization. Due to its predominant features, the implant need not be removed and instead are often treated with antibiotics [19].

James k Liu., et al. have observed that the medpor porous polyethtlene, may bea biocompatible, flexible and also has surgical reconstruction of cranial base. The porous nature allows the ingrowth of sentimental tissues, implant strength and reduce the infection. A complete of 598 patients underwent in 611 procedures and 13 patients underwent bilateral methods of two different methods. The fabric is formed as smooth thick sheets or sheets of conical projections to obtain the accurate measuring of a paper template are formed. The scalpel is fixed at the sides possessing no irregularity in edges. High speed drill could also be used for fixation of implant on surrounding tissue and titanium miniplate and titanium screws are used for fixation. No further surgeries are required for the matter caused by the initial operation leading to limited operating time and donor site operation [6].

5.4. Ceramics

Generally, this possess insufficient mechanical strength [19].Phosphate ceramics is one among the fabric utilized in modern techniques of cranioplasty moreover calcium and phosphate helps in hastens the expansion of bone in 20th century and phosphate are of two types tricalcium phosphate and hydroxyapatite [20].

5.5. Hydroxyapatite

It is a hexagonal sort of phosphate , which is already present in our bone and it is believed that it helps in bone repair with Hardness-5(Mohs), Density-3.1 (g/cm3), Elastic Modulus-100 (GPa), Ultimate Tension Stress-100 (MPa) and Compression Stress-> 50 (MPa). Its durability has increased with addition of titanium mesh and therefore the osteo integrative state is increased with its porous structure. It has good osteointegration, bone repair and therefore the reaction of adjacent tissues is a smaller amount [1]. A replacement combination of hydroxyapatite with crystalline mineral and collagen is being researched and seems to be giving promising results.

G. Staffa., et al. have observed the high porosity hydroxyapatite. The porosity of the bone is analogous to spongy bone that has macro spores that promotes osteoblast migration.25 people were observed during this experiment regular CT scans and checkups were made for 30 months and shows excellent results. There have been no rejection, infection or fragmentation of fabric, restrictions like high cost, poor malleability and employed for stereolithography process that is made with custom made design. The biomaterial should provide mechanical support and an environment that promotes new bone formation with the assistance of 3D CT images and constructing epoxy mold including 3D stereolithography. A skinny layer of laser solidifies the liquid resin in touch, because the 3D virtual provides a model of skull that is formed for the patient layer by layer. A model is produced just like the persons defected area and therefore the hydroxyapatite is formed because the model that's approved, apart from the 12 weeks from surgery, it gives equal biomechanical resistance as that of the bone. But, for few patients the implant was fixed with silk thread and for the remainder shape memory metal elastic like roller fix was used. Since it is still fragile micro screws and miniplates cannot be used since it can cause micro fractures within the prosthesis. The patients underwent 3D CT follow ups and found that there was no rejection, reabsorption, infection and immediate fractures. A hydroxyapatite scaffold was controlled, interconnecting porosity, biocompatible. The implant was compatible altogether the cases and showed no failures within the follow ups.

5.6. Cortoss

Cortoss contains bisglycidyl methyl methacrylate, bisphenol replacement synthetic void bone filler which has a consistency of tooth paste. For fixing there are specially designed tips with double lumen cartilage and the material is prepared after polymerization during a three dimensional network to stop leaking prolonging its hardening time along- side blood. The cortoss shows maximum polymerization at 40C and fewer chemical reactions, bioactive and has equal elasticity as that of bone. At the sites of repair peristeal and endosteal were seen and therefore the strengthening of bone cement interface continues. New bones were seen along the blood vessels adjacent to Cortoss showing high shear strength, compressive strength, bending modulus and low inflammation [19].

Bae Hyun., et al. used 2:1 randomization, vertebroplasty was performed with Cortoss on 162 patients and PMMA on 94 patients. Incidence of great device-related adverse events was 4.3% in both groups still none were life threatening. Cortoss exhibited better results for pain reduction at 3 months and for working at 24 months.

5.7. Tantalum

This material was one of the bioactive material consisting of Molar mass- 180.95 g/mol, Thermal Boiling point-5458 `C, Melting point-2996 `C and Density 16.6 g/cm^3. This exhibits higher rate to corrosion resistant and bioactive in vivo. Through the formation of a bonelike apatite layer in simulated liquid body substance Ta has been shown to be bioactive and biologically bonds to bone. In several in vitro and animal studies porous Ta metal has provided a scaffold for bone ingrowth and mechanical attachment. These porous Ta components offer a coffee modulus of elasticity, high surface frictional characteristics and excellent osteointegration properties (i.e. bioactivity, biocompatibility and ingrowth properties) it had been utilized in the times of second war and was abandoned to its high price, difficulty to get , and headache to high heat conduction [19]. Vamsi Krishna Balla., et al. experimented that the Ta coatings had cells appear cuboidal and had a three- dimensional morphology with more filopodia. After 14 days culture cells on the Ta coatings became elongated, forming a dense and confluent cellular layer. The abundant amount of extracellular matrix (ECM) is been generated on the Ta coated cell surface and this is been interpreted at an early stage of osteoblast differentiation.

5.8. Titanium

Titanium has good resistance to infection but not suitable for the cases with skin viability for instance radiotherapy, multiple operations etc. Titanium is cheaper, biocompatible with nearly no risk of infection and radiolucent after mixing with other materials but it is tough to shape. Titanium mesh is now used as a support material for mechanical strength along -side cement materials [1]. Titanium is that the only metal currently used alone or as a scaffold for cements in cranial repairs [20]. Ti alloys like Ti6Al4V, which incorporate varying amounts of other metals, like aluminium (Al) and vanadium (V), are manufactured to assist improve the properties of the bottom metal.

Mario Cabraja M D., et al. have observed 26 patients for 6-12 years who underwent cranioplasty with CAD (computer-assisted design) and CAM (computer-assisted

modelled) titanium meshes. 84% of patients experienced results without pain, 88% were satisfied and 0% had poor performance, the follow ups of 4 persons performance were suboptimal that underwent removal of meningiomas. PMMA is best for primary cranioplasty also while follow from tumour and titanium mesh are secondary choice for giant skull defect from decompressive craniectomy. The implant shows low repulsion rate and sturdiness. CAD /CAM titanium mesh have high strength, biocompatibility and are suitable for post-operative image techniques, but limited due to their high cost and there have been no implants removed after the surgery. 90% of the patients were satisfiedof the result. Hydroxyapatite and other expensive ceramics haven't any advantage over PMMA and titanium [8].

5.9. Alloy of cobalt-chromium and Vitallium

Vitallium contains cobalt and chromium that was after experimenting with animals it showed compound materials shows less tissue reaction than that of pure metals. Vitallium was already utilized in dental implants and therefore the results showed less reaction, light and straightforward to shape that contains nickel and is analogous to Vitallium [19].

6. Stainless steel

It was found almost like tantalum strength, malleability, more radiolucent and cheaper in cost than tantalum. Some are incompatible and due to failure rates, non-metallic prostheseswere developed [20].

6.1. Celluloid

During the time of commercial revolution to a budget production of materials which cause the wide selection of application of starting the utilization of celluloid, the primary synthetic plastic in cranioplasty in 19th century that was famous in Germany in 1800s.Fraenkel discovered unlike other materials celluloid did not adhere to dura forming the secondary scar. Due to its tendency to react with tissues forming serosanguinous exudate which requires to be aspirated for two weeks after surgery became its limitation [20].

6.2. Stemcell technique

During this stem cell culture technique it is been identified and isolated a somatic cell population capable of skull formation and craniofacial bone repair in mice-achievinga crucial step toward using stem cells for bone reconstruction of the face and head within the future. To transplant in vitro differentiated human pluripotent somatic cell (hPSC)- derived alone or together with other cell lineages might be achieved either by direct cell transplantation, matrix embedding approaches or by more advanced in vitro tissue engineering before transplantation. Cell types which may foster cell retention, survival and repair have recently been derived from hPSC (including human embryonic stem cells (hESCs) and induced pluripotent stem cells (hPSC)) with increasing efficiencies, as demonstrated for endothelial cells, pericytes, smooth muscle cells, mesenchymal stem cellsalso as real CMs. Additionally to their potential to differentiate into essentially any vegetative cell type, PSCs have the property of unlimited proliferation at the pluripotent state when cultured under appropriate culture conditions, thus providing a perfect “raw material” for regenerative medicine [22].

7. MANUFACTURING TECHNIQUES

7.1. Addictive manufacturing (3D Printing)

In additive manufacturing technique computer aided design (CAD) or 3D object scanners is used to direct the hardware to fix the material. Further process includesdepositing alternative layers of powdered material and a liquid binder that is used an adhesive.

- SINTERING: Material is heated without being liquified. Direct metal laser sintering uses a laser on thermoplastic powder in order that the particles stay together.
- STEREOLITHOGRAPHY: Photo-polymerisation, UV laser is fixed into vat of photo polymer resin to make torque-resistant ceramic parts ready to endure heat eg: Polyethelene, polypropelene, polyamide, ABS (styrene+acrylonitride), PLA/PGA (polylactic acid/ polyglycolic acid)

7.2. Injection Molding Process

This uses molten plastics. Imagine an injection but during a huge size made from metals which could bare high temperatures. The body of the injection molded would melt the substance put into it and therefore the piston like structure pushes the melted substance into the specified mold. For an instance, Polypropelene, polyoxymehylene, polycarbonate.

Discussion

From all the above materials evaluation, Cortoss has been observed the best material for cranioplasty holding excellent properties comparatively with the manufacturing techniques. Experimentation is also done by comparing Cortoss with Simplex P acrylic in rabbits for up to 52 weeks and sheep for up to 78 weeks. As seen in scanning microscopy and histology examinations, both implant materials were surrounded by bone at late time periods, with fibrous layers of animal tissue seen in half the Simplex P specimens. Cortoss synthetic cortical bone void filler may be a good candidate material to repair implants in bone with characteristics according to long-term safety and featuresa better ability to bond to bone than Simplex P.

Conclusion

The security and efficacy of Cortoss material has been demonstrated in three U.S. clinical investigations and multiple European studies. Compared to PMMA, Cortoss material is more hydrophilic, which enables it to coat and augment the interior structure of the bone. This inter digitating characteristic resulted during a 30% reduction in material injected in comparison to PMMA during a controlled study. A Study illustrated statistically significant increase within the percentage of patients experiencing discount in short-term pain and improvement of long-term function at 24 months. The reason for choosing polymer rather than metal (titanium) because it acts more economically feasible. But, in metals, titanium with a coating of bioactive material like collagen or vantalum exhibits higher possibilities.

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