

Cranioplasty

Introduction

Cranioplasty involves the repair of a cranial defect or deformation. The commoner causes of skull defects include trauma, neurosurgical procedures and infections. The main indications for cranioplasty are protection of the cranial contents and, in children, the provision of an intact cranial vault for normal growth and development of the brain. Aesthetic and psychosocial implications also need to be considered.

History

There is evidence of cranioplasty having been performed by several early cultures, including pre-Columbian Incans using gold or silver plates, and neolithic Celts using bone 'rondelles'.^{1,2} However, the first reported cranioplasty was probably that of a Russian nobleman who, after receiving a sword blow to the head, had the resultant defect (and his health) restored with a piece of dog's cranium (Van Meekeren, 1668). Subsequently, after he had been excommunicated from the Russian church (which could not accept the presence of animal bone on a human skull), removal of the graft was impossible due to bony union.^{1,2}

Bone graft integration

During the 19th century, when the dynamic nature of living bone was first realised, many more descriptions of cranioplasties using bone pieces and plugs appeared in the medical literature. In 1893 the histological sequence of bone replacement, termed 'creeping substitution',¹ was discovered. Survival of a bone implantation graft depends on the reaction of the surrounding tissue and on functional contact between cancellous bone and adjacent resident bone.

During the first week after grafting, capillaries from surrounding bone diploe, dura and scalp infiltrate the transplant bed. During the second week fibrous granulation tissue proliferates and osteoplastic activity occurs. Primitive mesenchymal cells differentiate into osteoprogenitor cells, a process nowadays termed osteoinduction, and subsequently these osteoprogenitor cells differentiate into osteoblasts that are capable of forming new bone to replace the necrotic bone which is gradually absorbed.³

Osteoconduction is the process whereby osteoprogenitor cells from the surrounding tissue migrate into the three-dimensional structure of bony and protein matrix. It is now understood that auto- and allo-grafts have relied on osteoconduction as the main principle of cranioplasty. It is also understood that, by contrast, in osteoinduction cells do not have to migrate from the surrounding tissues but, probably with the help of bone morphogenetic proteins, can be produced in situ.¹

Materials

The ideal material for undertaking cranioplasty should be malleable to fit precisely even complicated cranial defects; strong but lightweight; easily securable to the cranium; biocompatible and chemically inert; radiolucent; non-ferromagnetic; readily available; and inexpensive. No such material currently exists.

Natural bone is the obvious choice of cranioplasty material. Bone sources are diverse, ranging from the membranous bone of the cranium itself to endochondral bone from various other sites. Bone substitutes exist in the form of metals and non-metals.

Autologous bone has the obvious advantage of lack of immune reaction and absent risk of disease transmission. Furthermore, it is readily available and has potential to grow. On the other hand the available tissue may not readily fit the defect and usually necessitates a second operative field with associated morbidity.

The simplest form of cranioplasty is the replacement of the actual bone flap that has been removed since this provides the perfect fit. If closure of the craniotomy has to be delayed (see above) the bone flap can be stored either within the patient, for example within the abdominal wall or thigh,⁴ or extracorporeally by freezing or freeze-drying.

Intracorporeal storage maintains the viability of superficial cells and of some bone matrix, and cosmetic results and low infection rates have been encouraging.⁵ The bone may, however, be absorbed over time or may become contaminated during storage. Also, an often unsightly scar results and storage may be uncomfortable. Autoclaving or boiling of bone flaps prior to extracorporeal storage can result in destruction of bone proteins; in these circumstances the bone flap will not revitalise but will be reabsorbed. All methods of removing and storing bone are covered by the Human Tissue Act (2007) which prohibits removal and storage of human cells without appropriate consent and also specifies the need for a scheduled, qualifying purpose for all removed tissue.

The inner table of the cranium may be used as a split-graft (first described in 1890,⁶ but increasingly more popular during the 20th century⁷). For this technique the section of donor skull to be used is split and the outer table is applied to cover the craniotomy defect leaving the inner table to cover the donor site. Split calvarial grafts result in an aesthetically pleasing contour. However, they are not usually available to cover large defects and both the donor and recipient sites are less biomechanically stable than adjacent skull.¹ Allogeneic bone may be obtained as a live or cadaveric graft. Although it has the advantage of being in good supply there is the risk of disease transmission and cadaveric bone in particular carries ethical issues. Since the 1980s



Robert M Redfern undertook neurosurgical training in Liverpool and London, and since 1992 has been a consultant neurosurgeon at Morriston Hospital, Swansea. His sub-specialist interests are in pituitary surgery, and intrathecal management of pain and spasticity.



Heinke Pülhorn is a Trust Grade Registrar in Neurosurgery at Morriston Hospital, Swansea. After qualifying from the University of Erlangen, Germany, she completed her Basic Surgical Training in Merseyside before moving to South Wales. Heinke has an interest in the general management of trauma with particular emphasis on the management and outcome of traumatic brain injuries and in neuro-critical care.

Correspondence to:

Mr RM Redfern,
Consultant Neurosurgeon,
Morriston Hospital,
Swansea,
West Glamorgan,
SA6 6NL, UK.
Tel. 01792 703382
E. robert.redfern@
swansea-tr.wales.nhs.uk

Survival of a bone implantation graft depends on the reaction of the surrounding tissue and on functional contact between cancellous bone and adjacent resident bone

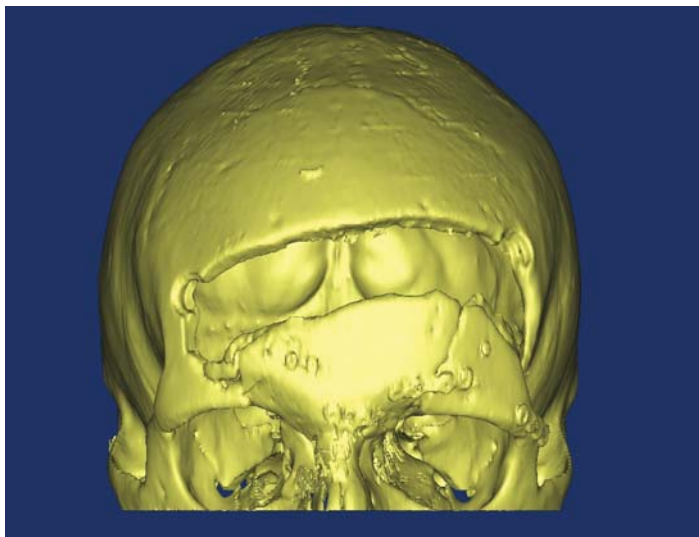


Figure 1: 3D CT reconstruction showing a bilateral frontal bone skull defect.



Figure 2: Resin model constructed from the CT data.



Figure 3: Pre-fabricated titanium plate moulded using the resin model to provide an aesthetically pleasing forehead contour. This plate is now suitable for sterilisation and implantation.

demineralised allogeneic bone matrix has become commercially available and has been used with encouraging results.⁸ Chaulking the demineralised bone powder with autologous bone paste (obtained by mixing blood and bone dust from the operative site) results in the formation of new bone throughout the cranioplasty.⁹ Furthermore, this bone paste can easily be applied to the cranial defect resulting in good cosmesis.¹⁰ Although bone donors are routinely screened for syphilis, hepatitis B and C, HIV and HTLV, the risk of disease transmission with allogeneic bone graft remains.⁹ The use of xenografts obtained from dog, goose, ape, rabbit, calf and eagle has been reported but their use has now been abandoned.

Natural bone substitutes such as temporalis fascia, fat and cartilage have also been used to cover cranial defects. However, their use is limited by a relative lack of size to cover large defects together with poor structural support. Furthermore, a tendency to reabsorption results in undesirable cosmetic results.¹

Various foreign materials have been used in cranioplasties. Metals have been widely employed but each has its shortcomings. Gold and silver are rather soft and expensive;¹¹ aluminium is epileptogenic and disintegrates over time; lead is toxic; and platinum, though very biocompatible, is prohibitively expensive. Alloys such as ticonium (first used during the 1930s) are generally cheaper than pure metals, lightweight, strong and often chemically inert.

Tantalum, a chemically inert, non-absorbable and non-corrosive material, was first successfully employed as a cranioplasty material during WW II. Unfortunately, tantalum is an excellent thermoconductor, leading to patients' complaints of headaches in extreme temperatures, and its radioopacity interferes with diagnostic radiological studies. Thus, when stainless steel (which is considerably cheaper) and acrylic compounds (which are radiolucent) were introduced, it was soon replaced.

Titanium was first used for cranioplasty in the 1940s. It is more radiolucent and less expensive than tantalum, biocompatible, non-magnetic, non-corrosive and strong. However, it is also difficult to mold intraoperatively.

Non-metals that have been used for cranioplasty include celluloid, hard rubber, plaster of Paris, gum cork and sheet mica. Due to various undesirable handling qualities and side effects none of these have gained popularity.¹²

Acrylic resins were used even before WW II as dental prostheses and since the 1940s have been employed for cranioplasty because of their good biocompatibility. Methylmethacrylate is chemically inert and, being malleable before it sets, allows for good cosmetic results. It is also lightweight, non-magnetic, non-thermoconductive and similar to bone in strength.¹³ It needs a totally dry, bloodless operative field to set, but its main drawback is the exothermic reaction produced during setting of the polymer, which can reach temperatures in excess of 100°C, with the potential for damage to underlying brain tissue - the surgeon can counteract this rise in temperature by irrigating the implant with cold saline while it sets. It is also very brittle and therefore breaks or shatters easily¹³ so that, to reduce the risk of plate breakage, it is nowadays often used with a stainless steel or titanium mesh core. Methylmethacrylate cranioplasties can be preformed, thus saving on operative time and also avoiding the hazard of intraoperative exothermic reaction during setting.

Hydroxyapatite is a calcium phosphate compound that is found naturally in human bone and teeth but which, since the 1970s, can be produced synthetically by sintering, a process in which the powder is heated until its particles adhere to each other thus producing densification. It is manufactured as a paste providing ease of application and a good fit to the defect, but is now also available as granules and preformed buttons and plates. Most importantly, hydroxyapatite sets without the exothermic reaction of methylmethacrylate.¹⁴ The porosity of the compound encourages the ingrowth of fibrovascular tissue which can subsequently ossify.¹⁵ Again, however, it does not set when exposed to fluids and, compared to methylmethacrylate, is relatively expensive.¹⁶

Ceramics are relatively new materials in cranioplasties having first emerged in the 1980s. They are chemically stable and tissue compatible. They are also very strong but somewhat prone to shat-

ter. Ceramic cranioplasty plates have to be pre-formed.

Complications occurring from cranioplasty can be broadly divided into those related to the operative procedure in general and those specifically related to the particular material used (see above).

In general, mortality from cranioplasty is low at approximately 0.2%.⁷ The commonest significant complication is infection (meningitis, abscess and sinus formation) since most cranioplasty materials are foreign bodies. An infected cranioplasty generally has to be removed and prolonged treatment with antibiotics may be necessary. The infection rate is approximately 5% for methylmethacrylate but less for bone cranioplasties.⁷ Inflammatory tissue reaction, loosening of the graft and exposure of the graft through the skin may also occur (sometimes many years after implantation) but such complications are more common with bone substitutes, especially acrylic resins, than bone itself.¹⁶ Alloplastic materials can also result in erosion of the underlying bone which in turn results in a larger cranial defect.¹⁰

Unpredictable resorption of cranioplasty material is a complication when using bone, especially autoclaved bone, and can be as high as 25-40%.^{3,17} Other complications specific to bone relate to its harvest: split calvarial grafts carry the risk of intracerebral haematoma, sub-

arachnoid haemorrhage, dural tears and CSF leaks, while other sources of bone may lead to donor-site morbidities, such as pain, infection, unsightly scarring, nerve injury, hernias, fractures, bowel perforation and pneumothorax.

Future developments

The search for the ideal cranioplasty material and technique continues. Novel natural as well as synthetic materials have been used. These include natural corals which have a porous structure similar to human bone and can undergo ossification;¹² and the Norian bone cement system, a synthetic carbonated calcium phosphate compound which can be reabsorbed and replaced by human bone.¹⁸ Likewise, new techniques are being developed. Known materials are mixed, e.g. acrylic resins with titanium struts,¹¹ and their qualities improved, e.g. antibiotic coating of pre-formed plates.¹⁹ Techniques are being transferred from other surgical specialties, e.g. distraction osteogenesis with contractile polymers, or even bioresorbable dynamic implants that could be applied without transcutaneous pins.²⁰ Preforming of implants has advanced due to 3D-CT scanning, computer-assisted design^{12,21} and stereolithography.^{19,22}

In our unit we routinely use the MIMICS® (Materialise's Interactive Medical Image Control System) to prefabricate defect-specific titanium membranes for cranioplasty. A 3D-CT image of the region of interest is formatted and

a resin model is then created by fused deposition modelling. This model then acts as a template for the actual cranioplasty membrane which is fashioned preoperatively by specialised maxillo-facial prosthetic consultants.

There have also been exciting developments in 'tissue engineering' using molecular biology techniques, such as harvesting osteoblasts or bone marrow-derived mesenchymal stem cells, to seed onto the scaffold for the cranioplasty.¹² Bone morphogenetic proteins of the transforming-growth factor- β family, and various polypeptide growth factors, play a central role in fracture healing. These factors can now be manufactured by recombinant DNA techniques and potentially incorporated into implants to evoke osteoinduction.^{12,23} Furthermore, absorption of circulating endogenous or exogenous bone morphogenetic protein leads to secondary induction of bone growth²⁴ and retroviral transfection of bone morphogenetic protein-7 into periosteal cells which are then seeded onto cranioplasty matrices is now possible. This results in increased bone regeneration.²⁵ Thus, 'smart biomaterials' are the latest addition to the experimental armamentarium of cranioplasty surgery. In future, biodegradable implants could be used to provide immediate cover of the cranial defect whilst over time releasing bioactive molecules to transform the perfectly fitted implant into living bone.

In future, biodegradable implants could be used to provide immediate cover of the cranial defect whilst over time releasing bioactive molecules to transform the perfectly fitted implant into living bone

References

- Sanan A, Haines S. *Repairing Holes in the Head: A History of Cranioplasty*. Neurosurgery 1997;40(3):588-603.
- Steward T. *Stone Age skull surgery: A general review with emphasis on the new world*. Ann Rep Smithsonian Instit 1957;107: 469-591.
- Brain Surgery*. Apuzzo. 1st edition, (1993), Churchill Livingstone.
- Iwama T, Yamada J, Imai S, Shinoda J, Funakoshi T, Sakai N. *The Use of Frozen Autogenous Bone Flaps in Delayed Cranioplasty Revisited*. Neurosurgery 52(3):591-596, March 2003.
- Movassaghi K, Ver Halen J, Ganchi P, Amin-Hanjani S, Mesa J, Yaremchuk M. *Cranioplasty with Subcutaneously Preserved Autologous Bone Grafts*. Plastic and Reconstructive Surgery 2006;117(1):202-206.
- Wolf JL, Walker AE. *Cranioplasty: Collective review*. Int Abst Surg 1945;81:1-23.
- 'Neurosurgery'. Wilkins, Rengachary. 2nd edition (1996), McGraw-Hill.
- Mulliken J, Glowcki J, Kaban L et al. *Use of Demineralised allogeneic bone implants for the correction of maxillocraniofacial deformities*. Ann Surg 1981;3:366-372.
- Chen T, Wang H. *Cranioplasty using Allogenic Perforated Demineralized Bone Matrix with Autogenous Bone Paste*. Annals of Plastic Surgery 202;49(3):272-279.
- Arun K, Gosain M. *Biomaterials for Reconstruction of the Cranial Vault*. Plastic and Reconstructive Surgery 2005;116(2):663-666.
- Replogle R, Lanzino G, Francel P, Henson S, Lin K, Jane J. *Acrylic Cranioplasty Using Miniplate Struts*. Neurosurgery 1996;39(4):747-749.
- Chim H, Schantz J. *New Frontiers in Calvarial Reconstruction: Integrating Computer-Assisted Design and Tissue Engineering in Cranioplasty*. Plastic and Reconstructive Surgery 2005;116(6):1726-1741.
- Neurological Surgery*. Youmans. 3rd edition (1990), Saunders
- Maniker A, Cantrell S, Vaicys C. *Failure of Hydroxyapatite Cement to Set in Repair of a Cranial Defect: Case Report*. Neurosurgery 1999;44(6):1368-1369.
- Yamashima, Tetsumori. *Modern Cranioplasty with Hydroxyapatite Ceramic Granules, Buttons and Plates*. Neurosurgery 1993;33(5):939-940.
- Chen T, Wang H, Chen S, Lin F. *Reconstruction of Post-traumatic Frontal-Bone Depression Using Hydroxyapatite Cement*. Annals of Plastic Surgery 52(3):303-308, March 2004.
- Manson P, Crawley W, Hoopes J. *Frontal cranioplasty: Risk factors and choice of cranial vault reconstructive material*. Plast Reconstr Surg 1986;77(6):888-904.
- Baker S, Weinzeig J, Kirschner R et al. *Application of a new carbonated calcium phosphate bone cement: early experience in pediatric and adult craniofacial reconstruction*. Plast Reconstr Surg 2002;109:1789-1796.
- Taub P, Rudkin G, Clearihue W. *Prefabricated allosplastic implants for cranial defects*. Plast Reconstr Surg 2003;111(3):1233-1240.
- Guimaraes-Ferreira J, Gewalli F, David L, Maltese G, Heino H, Lauritzen C. *Calvarial Bone Distraction with a Contractile Bioresorbable Polymer*. Plastic and Reconstructive Surgery 2002;109(4):1325-1331.
- Gelaude F, Vander Sloten J, Lauwers B. *Automated design and production of Cranioplasty plates: outer Surface Methodology, Accuracies and a Direct Comparison to Manual techniques*. Computer-aided design and Applications 2006;3:193-202.
- Eppley B, Kilgo M, Coleman J. *Cranial Reconstruction with Computer-Generated Hard-Tissue Replacement Patient-Matched Implants: Indications, Surgical Technique and Long-Term Follow-Up*. Plastic and Reconstructive Surgery 2002;109(3):864-871.
- Wozney J. *Bone morphogenetic proteins*. Prog Growth Factor Res 1989;1:267-280.
- Ripamonti U. *Soluble osteogenic molecular signals and the induction of bone formation*. Biomaterials 2006;27(6):807-822.
- Breitbart AS, Grande DA, Mason J, Barcia M, James T, Grant RT. *Gene-enhanced tissue engineering: Applications for bone healing using cultured periosteal cells transduced retrovirally with the BMP-7 gene*. Annals of Plastic Surgery 1999;43(6):632-9.