THE INFLUENCE OF HOST BONE SUBSTRATE IN TITANIUM MESH CRANIOPLASTY

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Reconstructive surgery of bone defects in the calvarium makes use of a multitude of biological and artificial materials. Due to the increased number of such medical casuistry in the recent years, a special attention was dedicated to the biocompatibility and osteointegrative properties of various types of biomaterials. Titanium emerged to be a promising cranioplasty material due to its excellent mechanical properties and biocompatibility. However, the way the host calvarial bone reacts to the titanium implant has not been fully understood.

Here, we evaluate the influence of cranial bone substrate on the osteoconduction and osseointegration of titanium mesh implants. The pattern of bone tissue reaction in the areas of contact with metallic implant is analyzed by means of bone density measurements on the computer tomography images. Twenty-eight patients underwent cranioplasty with titanium mesh implants for bone cranial defects due to different aetiology. With the aid of visual analogue scales, the patients' status (osteointegration degree, comfort and cosmetics) was evaluated after 3 – 14 months since surgery (implantation).

1. Introduction

The surgical treatment of skull defects is one of the oldest neurosurgical procedures, and until recently it was believe to date back 2300 years to ancient, when Paracas Indians first used a gold plate to correct a large frontal cranial defect produced by trephination [1,2]. Recently, discoveries emerged arguing an earlier history of this type of surgical techniques, with a much wider geographical area [3,4]. For instance, historical proofs suggested that early Danubians were performing cranial surgery in 3000 BC [3]. The procedure known as cranioplasty is using different materials such as bone grafts from human or non-human donors, bioinert metals (including gold, silver or tantalum), cements, and more recently biosynthetic materials such as resins, ceramics, and titanium [5]. Currently, titanium, in the form of meshes with different sizes and thicknesses is one of the most used material for cranioplasty implants, due to its excelent biocompatibility and mechanical performance [6,7]. Special surface treatments could lead to its bioactivation, and to exhibit osteoconductive properties promoting the osteogenesis by across the implant [8–10].

Defects in the calvarium are the result of various medical casuistries: trauma, congenital pathologies, or therapeutic consequences (in cases of tumours or infections that imply the removal of the affected bone) [11]. It is known that the quality of the bone itself is an important factor in osteogenesis [7]. The aim of this study is to analyse the influence of the etiology of the skull bone

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defects on the process of osteoconduction and osteogenesis after cranioplasty with titanium meshes (TiM).

2. Experimental

In this study we analyzed the biological behaviour of surface TiM implants used for calvarium defects reconstruction. The study comprised of a series of 28 patients who underwent cranioplasty surgery for cranial bone defects of various etiologies between 2008 and 2011 in our clinic (Prof. Dr. N. Oblu" Clinical Emergency Hospital, Iasi, Romania). The indications for cranioplasty included defects as a result of traumatic bone destruction, congenital defects, and iatrogenic defects. We conducted a comparative analysis between the etiological subgroups looking at the osteoinductive and osteointegrative characteristics of this type of implants.

2.1 Implant system

The implant consists of a titanium mesh with holes of different dimensions (Fig. 1a) offering multiple options in terms of positioning over the bony defect and fixation and titanium micro-screws (Fig. 1b) used for mesh fixation onto the bone. The standard mesh is a square of 90/90 mm and a thickness of 2.5 mm. The micro-screws are helically threaded with a screw head of 3 mm in diameter.
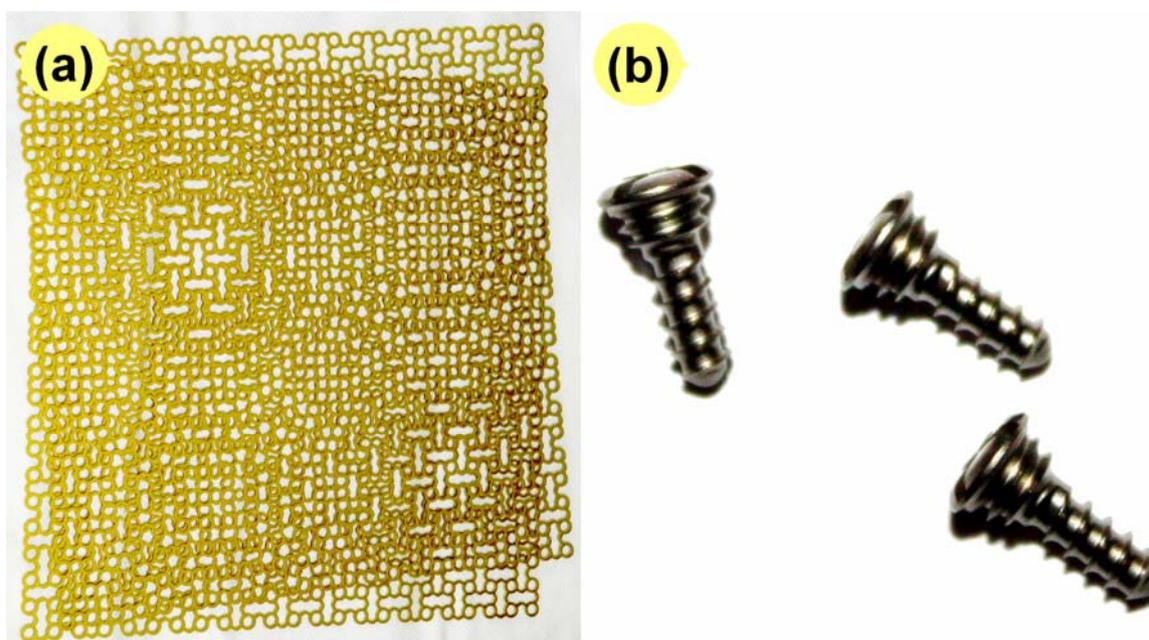
Fig. 1. Titanium implants: (a) dynamic meshes and (b) micro-screws (Stryker®, USA).

2.2 Operative technique

The patients were operated by a neurosurgical team at "Prof. Dr. N. Oblu" Clinical Emergency Hospital, Iasi, Romania. Surgical procedures were performed with patients under general anaesthesia. The patient was positioned on the operating table so that a maximum exposure of the bony defect was available to the neurosurgeon, and enough space for surgical equipment and manoeuvres was ensured.
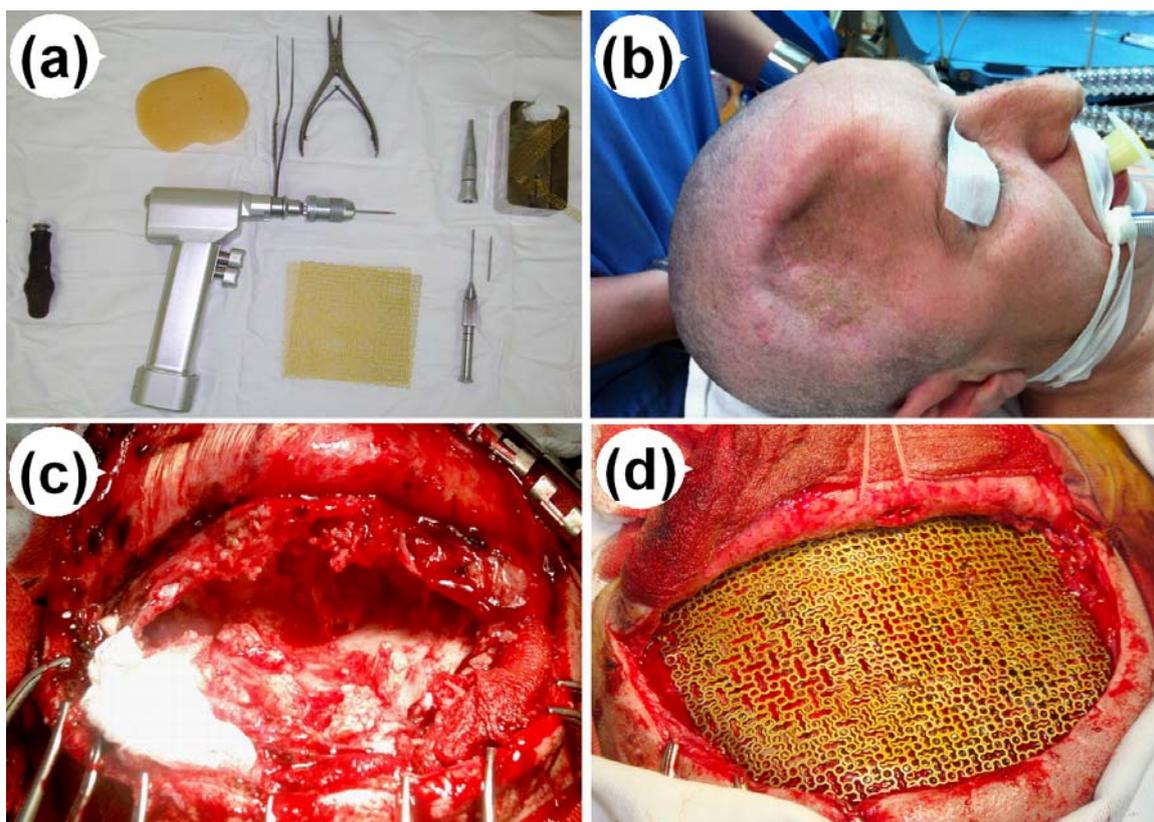
Fig. 2. Intra-operative aspects: (a) – operating instruments; (b) – head positioning; (c) – cranial defect exposure; (d) – implant fixation.

In Fig. 2 the main surgical stages are graphically presented. The first stage of surgery aims at a clear exposure of the bone defect margins. This exposure has to be large enough to ensure that TiM covers the entire defect and there is enough room for the micro-screws' fixation. A preformed mesh is placed over the defect and points of anchorage to the bone are established. Usually, the mesh anchorage to the bone is made through at least four attachment points. If the defect is larger, supplementary fixation points are devised in order to ensure a good rigidity of the implant and optimum geometry. Using an electric gun drill, holes for the micro-screws' insertion were made into the bone in the pre-set positions. Fixation is achieved through self-anchoring screws (Fig. 1b).

2.3 Image analysis

All patients have been followed postoperatively by cranial direct fluoroscopy and Dyna-CT (Computed Tomography) with 3D reconstruction at 1, 3, 6 and 12 months, respectively. The radiological images were obtained using an AXIOM Artis dFC Angiography machine from Siemens AG. The images were transferred via a hospital network to workstations as DICOM data. Using E-Film, developed by Merge Healthcare, the osteoinductive properties of each implant were analyzed. The software allows tomodensitometric analysis of each anatomical area scanned based on tissue density measured on Hounsfield unit (HU) scale. For each patient three regions of interest were selected on fluoroscopy (Fig. 3c) and Dyna-CT images (Fig. 3a,b,d). The three regions were established from the edge to the centre of the plate (edge, interjacent and centre) (see Fig. 3 – bottom images). A 3D skull computed tomography was performed for the evaluation of the aesthetic results. We recorded the changes of the bone in-growth surface area around the three regions, as captured by tomography images.
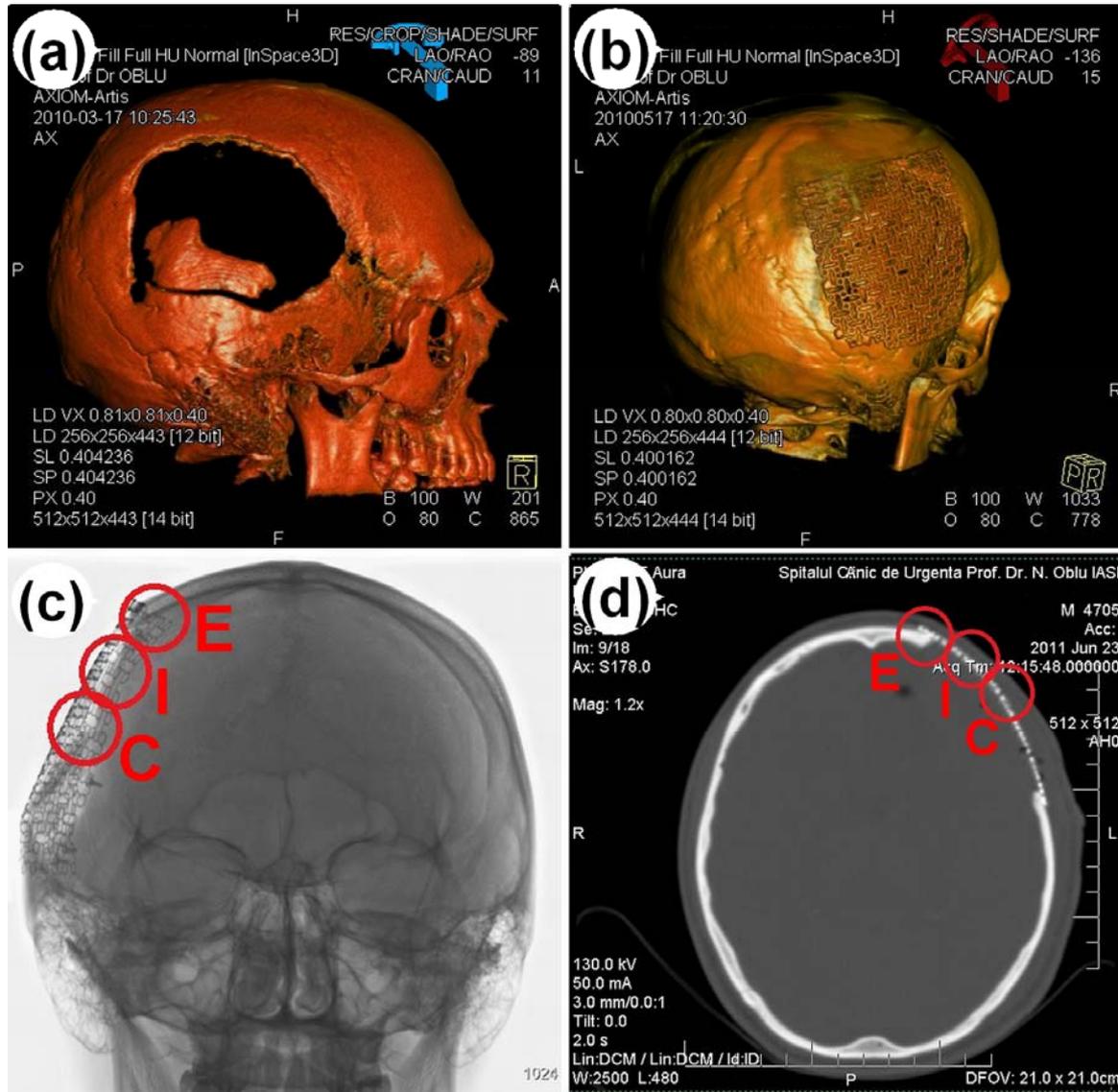
Fig. 3. 3D cranial reconstruction (a,b) and demarcation of osteoinduction and osteogenesis monitoring areas (c,d).

3. Results

The series included 18 males and 10 females, with age ranging from 15 to 63 years at the time of surgery. The etiology of bone defects included in this series was bone-involving tumour (four cases), trauma (fifteen cases), aesthetic deformity due to repeated craniotomies (six cases), and infection (three cases).

The follow-up ranged from 6 to 30 months postoperatively, with a mean period of 14 months. Postoperative clinical outcome has been good in all patients. None of the patients showed any evidence of foreign body reaction to the implant material or infection at the implant site. The 3D reconstruction images showed at least satisfactory aesthetic results.

Radiological analysis

None of the 28 patients showed any changes in tissue density on Hounsfield scale at 3 months after surgery. Over a period of 6 months in 5 patients with surgical craniotomies and in 11 patients with posttraumatic bone defects, changes typical to osteoinductive and osteointegration

phenomena have been noticed and documented. For all these cases, changes in tissue density on the Hounsfield scale were signalled only at the edge areas of the TiM implants (found in direct contact with the bone).

Between the 7th and the 12th month, 4 of the 11 patients with cranial reconstruction of posttraumatic bone defects, and 3 of the 5 patients with surgical craniotomies showed changes in bone tissue density on Hounsfield scale both at the edge (E) and in the interjacent (I) areas of the mesh. No patient from the other two groups ("Bone-involving tumours" and "Post-infections") demonstrated similar changes.

For the followed medical cases, no osteoinductive or osteointegrative phenomena were identified in the central (C) region of the implant at 14 months after surgery (Table 1).

Table 1. Evolution of osteoinductive or osteointegrative phenomena in the areas of interest.

Etiliology:	Bone-involving tumours			Posttraumatic cranial defects			Aesthetic deformities due to repeated craniotomies			Post-infection		
Implantation period	**Number of patients**											
	4			**15**			**6**			**3**		
	Osteoinduction and osteogenesis monitoring areas											
	E	I	C	E	I	C	E	I	C	E	I	C
1 to 3 months	-	-	-	-	-	-	-	-	-	-	-	-
4 to 6 months	-	-	-	11	-	-	5	-	-	-	-	-
7 to 12 months	-	-	-	15	4	-	6	3	-	-	-	-
12 to 14 months	1	-	-	15	4	-	6	3	-	2	-	-

*E – edge area; I – interjacent area; C – central area.

The group of patients with cranioplasty after surgical craniotomies showed the most pronounced effect on bone in-growth (in terms of surface area), which began in the first 5 months after surgery. For comparison, the earliest sign of osteogenesis was seen at 4 months after surgery for the posttraumatic bone defect group, and at 12 months for the postinfection group. The differences became significant when this specific surgical group ("Aesthetic deformities") had an average density value of 618 HU, whereas the posttraumatic group had 486 HU, and the postinfection group only 78 HU.

4. Discussion

The search for the best bone substitute material in terms of biological integration with the host tissue in cranioplasty has led to the development of new materials which can promote the fusion with the bone edges. In our studies the titanium mesh implants showed evident signs of this particular characteristic. The ability of TiM to fuse over time in situ, and stimulate the bone in-growth, makes this kind of implant the material of choice for many neurosurgical pathologies. In addition, TiM is fairly malleable and strong enough to allow neurosurgeons to reproduce the precise contour of the calvarium, providing both good fixation and mechanical protection.

The concepts of osteointegration and osteoinduction of titanium implants are well-known and documented since 1950 by P.I. Brånemark and his collaborators [12]. They showed that the bone interface can be repeatedly formed and maintained on the surface of Ti implant for long-term use.

Long-term results of TiM in cranial defects reconstruction were also published by Mario Cabraja et al. [6]. If the importance of surface characteristics of Ti cranial implants were widely discussed in the literature [6, 8–10], the influence of "biological quality" of cranial bone defect edges is still not well documented.

Although titanium implants have a high success rate when used in cranial reconstruction, compromising conditions, such as limited capacity of the bone to heal (in patients with associated systemic pathologies, such as diabetes), local infection, tumoral invasion or prior irradiation therapy of the targeted bone can lead to a poor osteointegration which in turn leads to implant instability and ultimately implant failure.

Our clinical practice demonstrates that the ability of the bone to undergo a quick repair process is closely related to immediate or early implant osteointegration. As implant stability is essential for the prognosis of osteosynthesis and osteoinduction, osteointegration should be established as soon as possible. This makes the "biological quality" of the host bone an important factor in acceleration of the osteointegrative process of the implant.

Titanium is a nonferrous metal that is relatively radiolucent, causing no significant image artefacts on CT images or Magnetic Resonance Imaging. CT scan offers a practical approach for the non-invasive determination of new bone formation. There are several radiological methods for the measurement of bone density such as dual-X-ray absorptiometry scanning and Hounsfield scale (HUs) from computed tomography imaging. Spiral CT scanning, combined with attenuation measurements in Hounsfield units scale, can depict differences in density between implants that have induced the bone formation and those that have not. The imagistic analysis and the measurements performed in our clinical series emphasized the extent of the new bone formation.

The method of postoperative bone density measurement was demonstrated as a prognostic indicator of implant osteointegration and osteoinduction. Although this method is advocated in predicting bone density, the reliability of Hounsfield scale units is limited in providing bone-quality information. Using this method one can evaluate the bone mass/density, but with no information about the structural or chemical properties of the material can be extracted.

5. Conclusions

Although several reports have demonstrated the successful bone-titanium implant bond, based on radiological documentation,, this is among the first reports in the literature that certifies the effectiveness of such implants' integration at the cranial bone level. A dependency between the bone substrate quality, etiology and degree of osteogenesis was highlighted. However, the paucity of nowadays medical techniques and materials suggest that successful cranial reconstruction requires alternative bone formation strategies. These should involve interdisciplinary teams, with surgeons interacting with materials science researchers, engineers, biologists and imaging experts. Novel implant designs with reliable highly bioactive coatings (calcium phosphates, bioglasses), able to boost the osteointegration processes, should be envisaged and assayed in the near feature.

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