Value Analysis

CustomBone Service

A 25-year clinical history

Introduction

CustomBone Service (CBS) is a custom-made device for cranioplasty, manufactured from synthetic porous hydroxyapatite (HAP), whose chemical composition mimics the mineral component of human bone and whose three-dimensional porous structure resembles autologous cancellous bone. From 2000 to today, more than 9,500 devices have been implanted in 320 centers across 38 countries (7.6% pediatric / 92.4% adult – 82.8% first line / 17.2% second line). A total of 1,479 patients have been the subject of 50 indexed publications, in addition to numerous citations in reviews and meta-analyses.

Safety: Biomechanical Characteristics

The safety of CBS has been demonstrated through a mechanical resistance test carried out using an MTS Insight compression press with a 10 kN full-scale load cell. The test samples had a surface area between 66 and 170 cm². The failure test was performed applying mechanical compression of 100 N (Fig. 1) [Stefini 2013]. When comparing compression resistance with different types of human bone, CBS presents a safety profile comparable to cancellous bone (Tab. 1) [Stefini 2013].

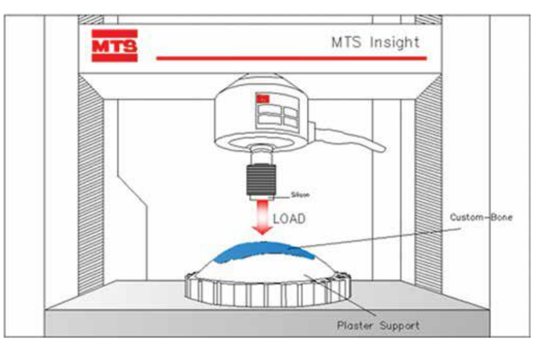

Figure 1 – Biomechanical Test

TABLE III - COMPARISON OF CHARACTERISTICS OF POROUS HYDROXYAPATITE IN RELATION TO CORTICAL BONE AND CANCELLOUS BONE (13)

Material	Porosity (Vol. %)	Compressive strength (MPa)	Elasticity (GPa)
Cancellous bone	50-80	1.6	9-32
Cortical bone	5-10	131-205	11-17
Porous hydroxyapatite	55-65	7-13	9-10

Table 1 - Comparison of the mechanical characteristics of porous hydroxyapatite in relation to human bone

Post-operative fracture data reported in four multicenter clinical studies [Amelot 2021, Lindner 2016, Iaccarino 2015, Staffa 2012] for a total of 237 patients show an incidence ranging between 0 and 4.5%, with a surgical revision rate of **1.2%**. This was confirmed by a recent publication by [Mannella 2024] on 687 patients, showing an incidence of **2.5%** with a **1%** surgical revision rate.

It is important to note that none of the fractures — in either the clinical studies or the recent PMCF (Post Market Clinical Follow-up) publication, were attributed to device malfunction (incident), but rather to secondary trauma or malpositioning.

Bacteriostatic Properties

Infections represent the most common complications in cranioplasty. They can occur early, due to the patient's clinical condition or contamination during surgery, or later, typically due to the formation of a bacterial biofilm leading to infectious onset. Regardless of timing, infections often require surgical intervention with implant removal.

The most recent literature comparing different cranioplasty solutions reports lower postoperative infection rates with HA-based biomaterials (**4.9%**) compared with other synthetic materials (e.g., **titanium 14%, PEEK 7.2%**) [Morselli 2019]. Similarly, several clinical studies and case series have compared CustomBone with other cranioplasty materials (PHA vs Autologous Bone [Iaccarino 2015], PHA vs Titanium [Lindner 2016], PHA vs PMMA [Ganau 2020], PHA vs Acrylic [Millward 2012]). All confirmed lower explant rates due to infection in favor of CustomBone.

A recent study by [Mannella 2024], using a Kaplan-Meier statistical analysis, showed that in CBS patients, 2/3 of infections developed in the early months, with a stable behavior in later years, regardless of whether the population was pediatric or adult (Fig. 2).

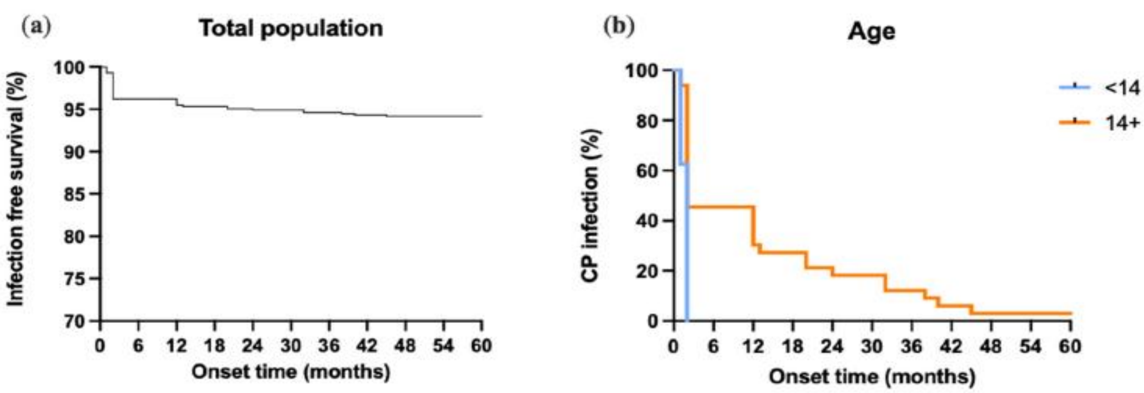

Figure 2 – Kaplan-Meier Statistical Analysis

This behavior is mainly due to the intrinsic chemical-physical properties of bioceramic hydroxyapatite which, through the formation of a "viscous mucopolysaccharide deposit," limits bacterial adhesion and biofilm formation [Piconi 2015], through a bacteriostatic mechanism Zaed 2022. This characteristic has been specifically demonstrated for CBS through recent laboratory tests conducted as part of a dedicated PhD program at the Department of Pharmacological and Biomolecular Sciences "Rodolfo Paoletti" (University of Milan) Zaed 2025.

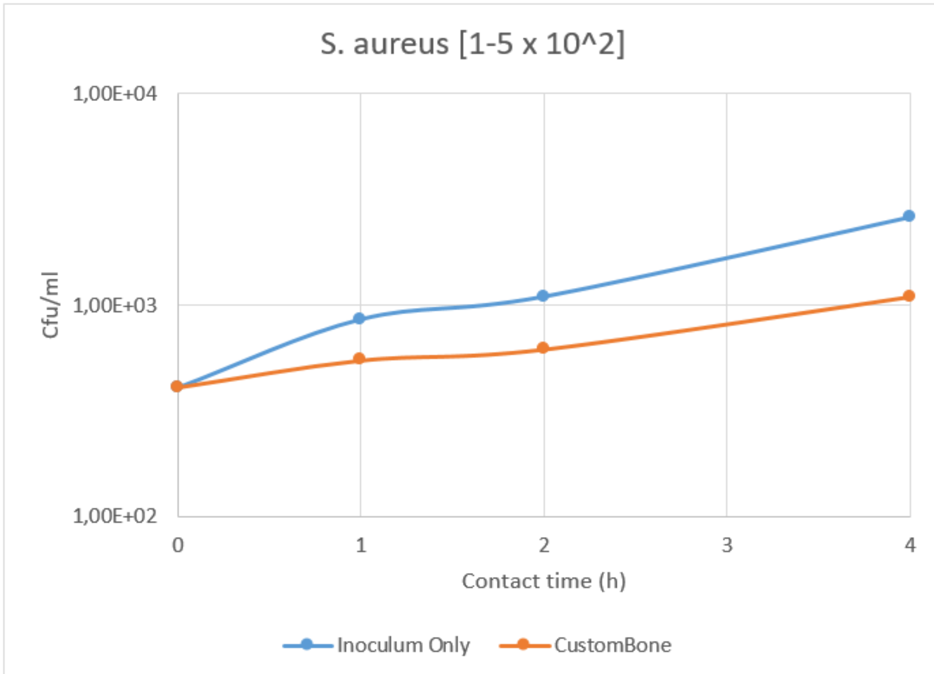

Figure 3

The inhibition of *Staphylococcus aureus* growth demonstrated in vitro when in contact with CBS appears to contribute to inhibiting biofilm formation (Fig. 3), thereby reducing late-onset infections.

Intraoperative and Postoperative Association with Antibiotics (Antibiotability)

Thanks to its high porosity and hydrophilic properties (Fig. 3), the device is capable of absorbing and releasing antibiotics.

Figure 4 – The interconnected micro/macro-porous structure of hydroxyapatite enables fluid absorption.

This characteristic allows CBS to be associated with antibiotics intraoperatively (Fig. 4). A clinical study *Amendola 2023* demonstrated that this intraoperative practice reduces the risk of early infections.

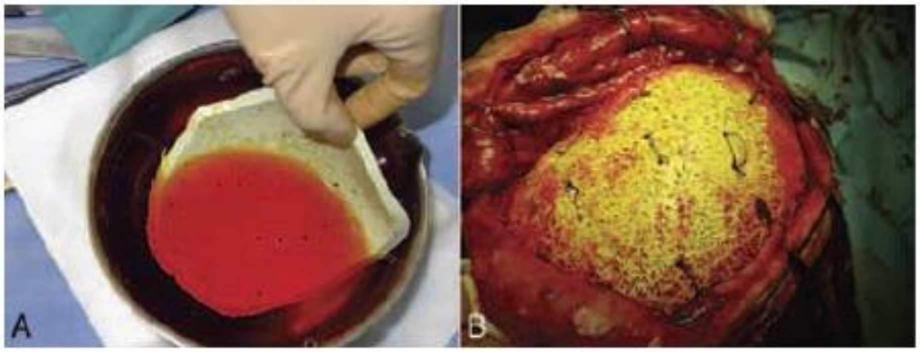

Figura 5 – A) Immersion of CBS in a sterile antibiotic solution (Rifampicin) diluted in solution for 20 minutes before final placement. B) CBS fixed in position; a yellowish discoloration can be observed after immersion in rifampicin.

Based on the same principle, in cases of late infections, the device can be treated with systemic antibiotics, attempting to avoid prosthesis explantation, as reported in literature [Iaccarino 2016, Zanotti 2018, Mannella 2025] (Fig. 5).

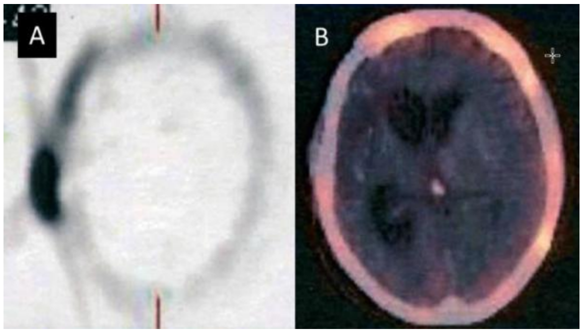

Figure 6 - A) A SPECT scan with Tc-99m-labeled anti-granulocyte monoclonal antibodies shows pathological tracer accumulation at the cranioplasty site, indicating active infection B) A 2-year follow-up using the same methodology rules out any residual infectious foci.

Cranioplasty remains a high-infection-risk procedure, due to heterogeneous prognostic factors related to surgical techniques and patient conditions.

Although it cannot be stated that CustomBone is the ideal device for cranioplasty, **the literature has documented that porous hydroxyapatite, due to its hydrophilic properties, demonstrates lower infection and explantation risk compared with other materials.**

In critically ill patients or in late infections, this favorable outcome is due to two main factors: the possibility of intraoperative antibiotic association thanks to the interconnected porosity; the ability to respond to systemic antibiotic therapy postoperatively due to revascularization enabled by biomimetic properties.

Osteointegration

Although osteointegration does not significantly improve device efficacy or safety, it represents clinical and biological evidence of a biomimetic material.

As described above, biomimicry provides CBS with bacteriostatic properties that help reduce infection risk.

The interconnected (micro and macro) porosity of CBS supports the formation of biochemical continuity with host bone, playing an important role in bone regeneration and facilitating cellular colonization.

Osteointegration processes, however, depend heavily on surgical technique.
A complete edge coaptation is necessary, with positioning as close as possible to vascularized tissues [Carbonaro 2024] (Fig. 6) and absence of micromovement.

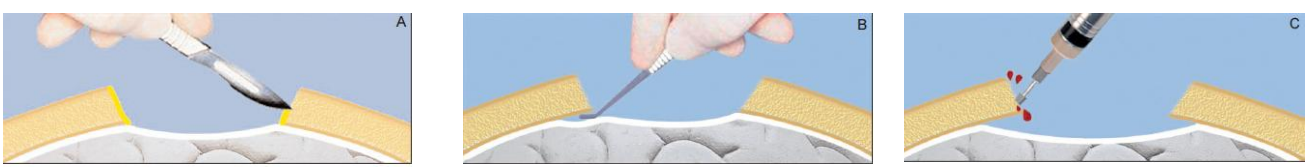

Figure 7 - (A) Debridement of the entire bone-defect perimeter from fibrous tissue - (B) Dural-plane dissection from bone edge to facilitate implant placement - (C) Bone-edge drilling through gentle perforation until bleeding trabecular bone is reached.

A correct surgical technique ensures optimal biological and aesthetic results [Wherli 2012] (Fig. 7).
Conversely, a device lacking interaction with vital bone tissue will never undergo osteointegration, leaving a bone gap [Frassanito 2012] (Fig. 8).

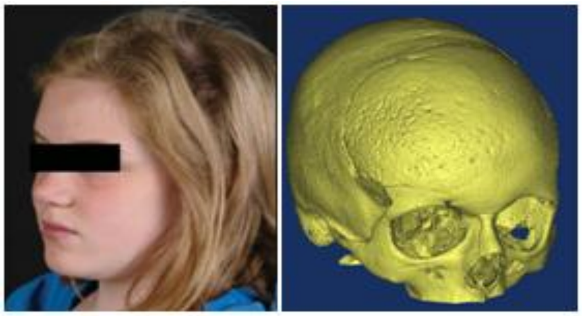

Figure 8 – Clinical appearance at 10 months post-surgery. Right: CT at 40 months showing excellent osteointegration and aesthetic results.

Figure 9 – Evidence of failed osteointegration due to incorrect coaptation.

Osteointegration can be demonstrated through diagnostic exams such as densitometry [Messina 2024, Maenhoudt 2018] (Fig. 9) and PET [Sprio 2016] (Fig. 10).

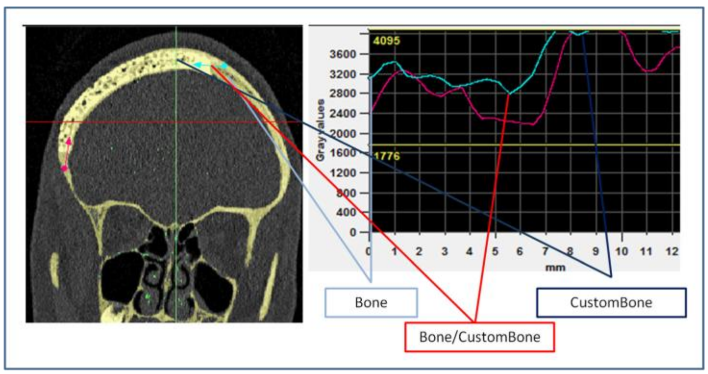

Figure 10 – Bone density is measured using the Hounsfield Unit (HU), a quantitative scale describing radiodensity, supported by the use of Mimics software (Mimics Innovation Suite v17.0 Medical, Materialise, Leuven, Belgium), designed for the processing of 3D medical images derived from CT. Normally, bone density is greater than 1600 HU (yellow line in the graph). CBS has a density higher than natural bone (as shown in the right part of the graph). If the bone density at the host bone/custom bone interface is similar to natural bone, osteointegration is considered optimal.

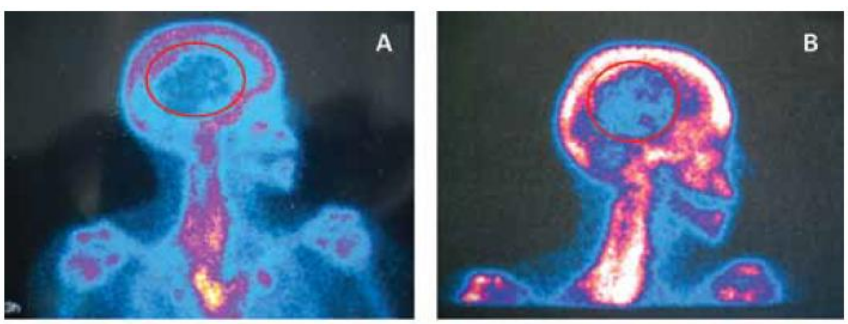

Figure 11 – Scintigraphic analysis.
(A) Patient after 7 months
(B) Patient after 36 months
The red circles highlight the area affected by new bone formation.

But osteointegration has also been shown through histological investigations both in animal clinical studies [Martini 2012] (Fig. 11) and in humans thanks to explants not determined by device-related adverse events [Fricia 2015] (Fig. 12), [Zanotti 2020] (Fig. 13A, 13B, 13C).

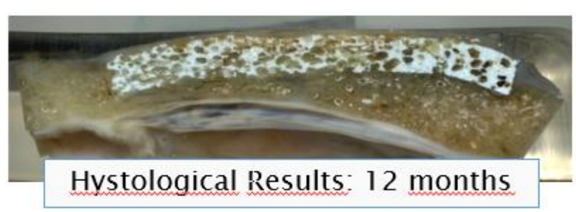

Figure 12 – Evidence of bone regeneration at 6 and 12 months in a sheep animal model undergoing cranioplasty.

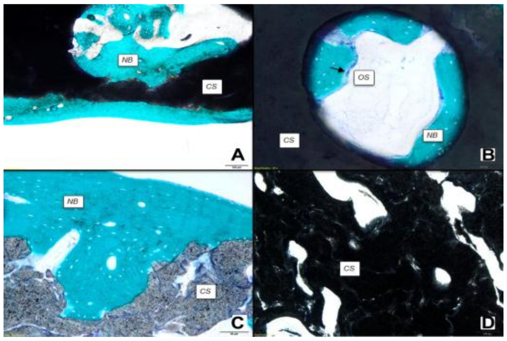

Figure 13 – (A) explanted 24 months after primary HA cranioplasty: trabeculae of newly formed bone in the external (A and B) and lateral (C) surfaces of the cranial prosthesis. Calcified tissue is stained green (NB), while osteoid is blue (arrow, OS). Various magnifications: (A) 8x and (B), (C) 20x. (D) Case no. 1B same patient explanted 6 months after backup HA implant cranioplasty: absence of newly formed bone in the cranial prosthesis. 8x magnification. Toluidine blue-fast green staining. CS, cranial substitute; NB, newly formed bone; OS, osteoid.

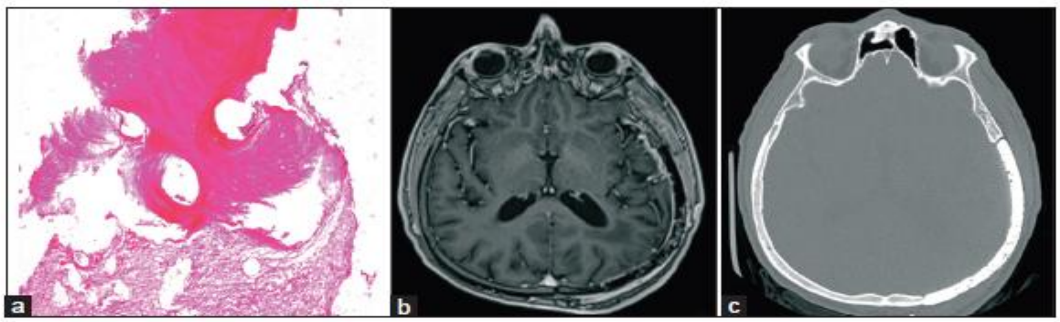

Figure 14 A – Image of the histological exam, after decalcification of the sample, showing the presence of bone tissue integrated within the prosthesis.

Figure 14 B – Preoperative contrast-enhanced MRI showing progression of meningioma with bone invasion.

Figure 14 C – Preoperative CT scan with bone window showing peripheral osteointegration.

Osteointegration is therefore the expression of a biomimetic behavior that derives from chemical, physical, and geometric characteristics that are unique within the landscape of current cranioplasty materials, and that impact the device's medium- to long-term effectiveness.

Conclusions

In conclusion, CustomBone Service is a cranioplasty implant that is safe from both a biomechanical and biochemical perspective [Carbonaro 2025]: the porous structure of synthetic hydroxyapatite plays a key role in the osteointegration process, making the material suitable for cell housing and enabling the immune system to identify the prosthesis as "self." Furthermore, the device is also characterized by bacteriostatic properties capable of limiting the formation of bacterial biofilm, resulting in a reduced infection risk. In the scenario of postoperative infections, the porous structure also allows the device to be treated locally with antibiotics, avoiding removal (in some cases).
All these characteristics, summarized in Table 2, together with 25 years of collected and published clinical data, make CustomBone Service a highly reliable device with unique properties in the field of modern cranioplasty.

CHARACTERISTICS	ADVANTAGES	BENEFITS
SAFETY	*Structure similar to human cancellous bone. Biomimetic behavior also in biomechanical safety.*	*Identified as "self" by our immune system.*
BACTERIOSTATICITY	*Resistant to infections. Limits formation of bacterial biofilm on the implant surface.*	*Lower infection rate compared with other materials in long-term follow-up.*
ANTIBIOTABILITY	*Possibility of association with antibiotics in intra-op and responsiveness to systemic treatment in post-op.*	*Reduced early infection risk and possible treatment without explantation in late infections.*
OSTEOINTEGRATION	*Implant revascularization and biomimetic behavior.*	*Bone regeneration reduces adverse events compared with other materials.*

Table 2 – General characteristics of CustomBone Service

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