smartbone®

IBI designed SmartBone following a bottom-up approach: starting from its microstructure that, mimicking natural bone, allows to obtain a device that matches the macroscopic characteristics of a healthy human bone.

KEY FEATURES

A. BIOCOMPATIBILITY

Biocompatibility is a granted feature: all components used in the production of SmartBone are taken only from the market of materials already approved for human use (by both EMEA and US-FDA)!
Furthermore, all the steps of the production process of SmartBone are performed under strict GMP compliance.
All investigations performed under all ISO-10993 standards gave EXCELLENT results, confirming a **VERY HIGH BIOCOMPATIBILITY** of SmartBone.

All *in vivo* investigations and clinical trials gave excellent results, fully confirming the high biocompatibility of SmartBone and its impressive performances.

B. ADEQUATE-SIZED OPEN POROSITY & MICROSTRUCTURE

The first claim of IBI SmartBone is its human-like microstructure, which we evaluated via electron microscopy and microCT scanning.

- **Evaluation Technique and Instruments**

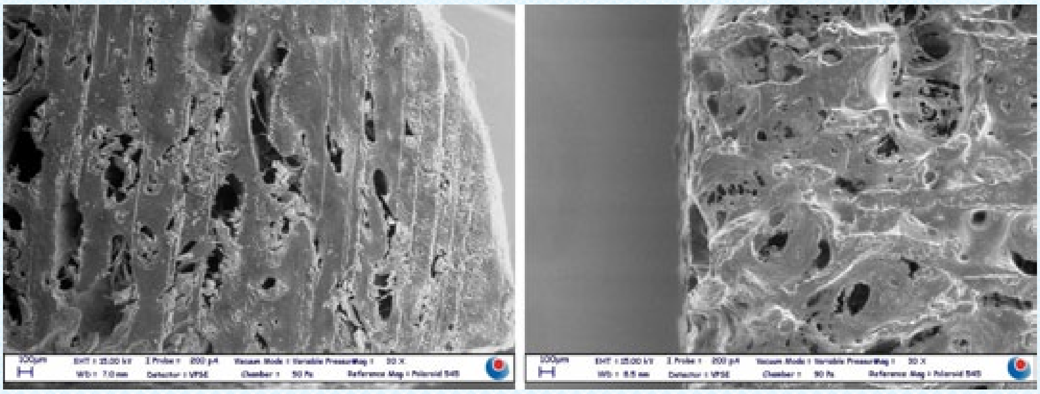
We chose Environmental Scanning Electron Microscopy (E/SEM) as main technique to evaluate SmartBone microstructure and morphology. A top level instrument was chosen to perform these investigations: a Evo 50 EP by Zeiss (Jena, Germany). Furthermore, thanks to the high investigative performances at extended pressure of the available instrument, no metallization nor any other preparatory treatment were needed on the samples prior to investigations.

Thanks to a cooperation with Phoenix|x-ray (a GE company), we performed microCT scans on our SmartBone (applying a VTomEx-s equipment) to investigate geometrical and volumetric properties.

ibi S/A
Via Cantonale 67, CH-6805 Mezzovico Switzerland
t. +41 91 228 01 75 | f. +41 91 220 72 00 | www.ibi-sa.com | info@ibi-sa.com

- **Results**

The application of our proprietary process produces a composite matrix with a microstructure that, evaluated by E/SEM, has a **strong resemblance with human bone** in terms of open mid-sized porosity.



E/SEM images taken at same magnitude of healthy human iliac crest bone sample (left) and IBI SmartBone (right).

Via microCT scanning, we were able to numerically evaluate the average geometrical characteristics of SmartBone: free volume (**ε, i.e. the degree of porosity**) and the surface/volume (s/v) ratio, resulting **ε=27%** and s/v = 4,46mm^{-1}, respectively.

Thanks to microCT scans, a 3D render of an IBI SmartBone was obtained via digital reconstruction (left) and IBI SmartBone open and interconnected porosity was easily confirmed: a typical microCT scan slide of an IBI SmartBone allows also evaluating volumetric parameters (right: a randomly taken scan from a 8x8x8 mm SmartBone block, used to fit the analytic chamber).

- **Regularilty of pieces**

Many bone substitutes available on the market show an inner variability due to their natural origin. Pieces from the same lot may, indeed, have different microstructure, higher/lower porosity, different density and highly variable physical and mechanical properties.
IBI's process was developed to obtain a smart biomaterial starting from a naturally derived mineral matrix and reinforcing it with biopolymers. Reducing this naturally occurring variability was one of IBI aims: **with SmartBone we now offer regular and homogeneous bone substitutes.**

C. HIGH MECHANICAL PERFORMANCES

Mechanical handling and performances of bone grafts during surgical maneuvering are tremendously essential features! Grafts are, indeed, expected to undergo heavy stresses and loads as far as they need to be shaped and cut before being placed. Furthermore they need to withstand drilling to allow the placement of osteosynthesis screws which must remain toughly in place, offering a solid mechanical bond to host tissue: the better the mechanical stability and the higher the surface contact with the host tissue, the higher and better the integration achieved. Hence, Smartbone mechanical characteristics can be summarised as follows:

- composite mechanical behaviour: both rigid and elastic
- adequately high elastic modulus
- extreme load bearing resistance
- dust and debris free shaping
- capability to withstand precise shaping
- tenacity to fixation screws
- hammering and heavy surgical manoeuvring resistance

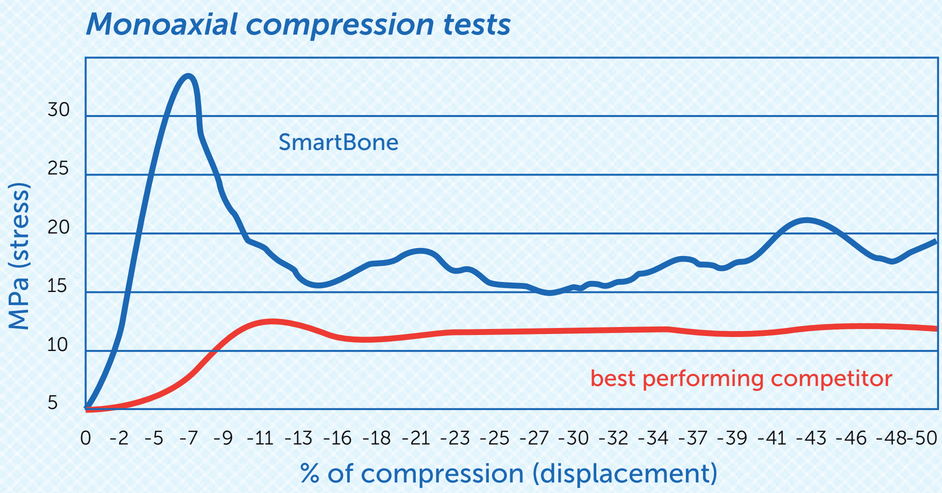
- **Mechanical testing and instrumentation**

A commonly used way to assess the mechanical behaviour of a bone substitute is the monoaxial compression test, which allows calculating maximum stress resistance (breaking stress) and Young's modulus (i.e. elastic module). Vertical compression tests on 10x10x10mm SmartBone blocks were performed using a calibrated MTS 858 MiniBionix.

To make this test more realistic, both dry and deeply wet SmartBone cubes were used, as far as the surgical field is bloody (hence wet) and almost all surgeons tend to dip bone grafts into hot patients' blood for some 20-30 minutes in order to have it absorb as much blood as possible (this widely used surgical practise is based on the evidence that blood starts coagulating inside the graft and thus several growth factors and biochemical signalling molecules are released, finally enhancing and speeding up graft integration once placed into target host site.

- **Results**

SmartBone showed the typical behaviour of an open porous structure where, under increasing load, a first pseudo-linear and pseudo-elastic behaviour, due to structural resistance, is followed by oscillating behaviour due to progressive breakage of structure and consequent compacting of matrix. Structural breakage is evidently and easily evaluated at maximum load bearing point and this allowed to compute the equivalent maximum stress (about **32MPa**), which was calculated on the full equivalent section (1 sq cm). This behavior is shared with all naturally derived bone grafts, being all of them porous, but with the highly relevant difference of the **tremendously higher performances owned by SmartBone, both at wet and dry state** (no differences were showed in any mechanical performance between dry and wet state)!



During comparative compression tests, IBI SmartBone (blue plot) showed off all its mechanical performances, being capable to withstand 3 times the maximum load borne by the best performing competitor (red plot) and being 4 times more rigid! (displacement [%] versus stress [MPa] is plotted according to compressive convention).

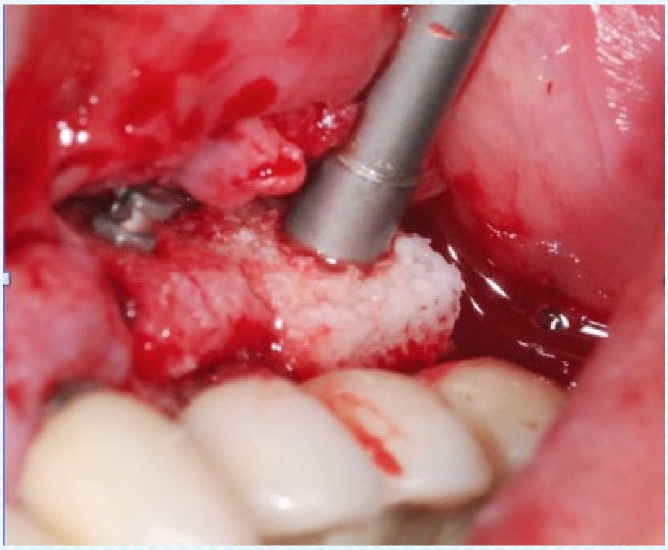
- **Shaping resistance**

Moreover, further qualitative mechanical investigations showed the capability of **very precisely shaping by common surgical instruments**, the absence of powder and debris formation during handling and a **very high resistance to screws** and fixation maneuvers.

D. HIGH HYDROPHILICITY

Thanks to its microcomposition, SmartBone shows an extremely high hydrophilicity, being capable to quickly (less then 60 mins) reach a **38% $^{w}/_{w}$ swelling ratio** (mass test performed in PBS and dynamic assessed using a Mettler-Toledo 4 decimals calibrated scale).

This extremely good feature was evidently confirmed also during clinical studies where a **very high capability to absorb and retain blood once in situ** was observed.



Hydrophilicity is a clinical essential feature: indeed, as said, it is a scientific and clinical evidence that, if the blood is soken up by the graft coagulating inside of it, several growth factors and biochemical signalling molecules are released, hence enhancing and speeding up graft integration once placed into target host site.

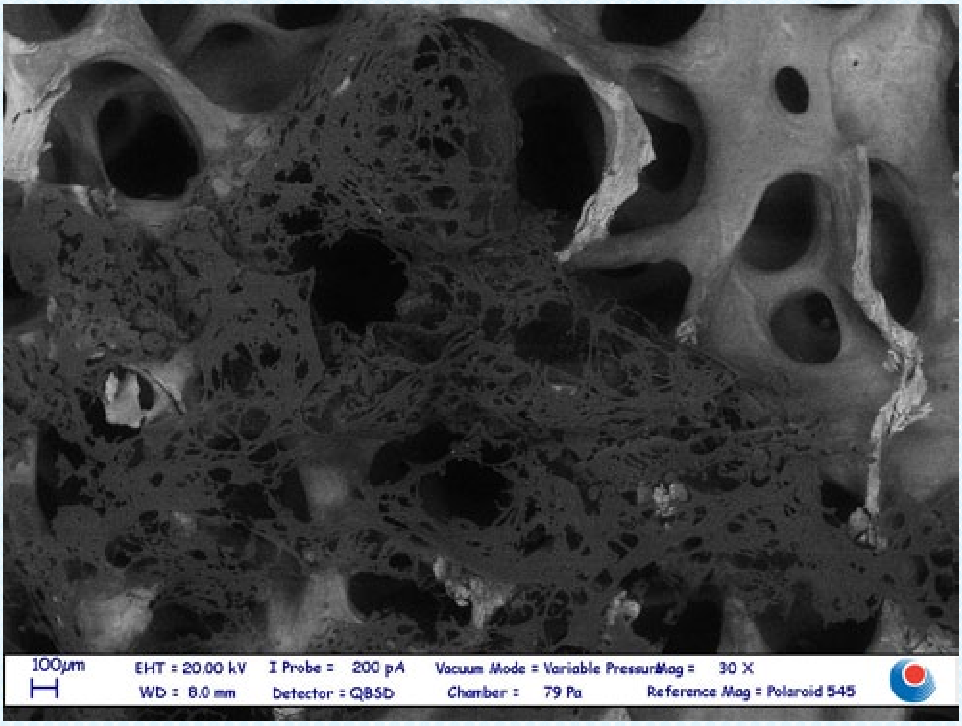
A hand-shaped SmartBone block quickly absorbs patients blood once placed in situ in direct contact with a bloody substrate (the graft was, on purpose, placed without having being previously soaked into patients blood).

ibi S/A

Via Cantonale 67, CH-6805 Mezzovico Switzerland
t. +41 91 228 01 75 | f. +41 91 220 72 00 | www.ibi-sa.com | info@ibi-sa.com

E. HIGH TISSUE INTEGRATION

A robust physiological integration into host tissues is an essential feature for a bone substitute. In addition to all ISO10993 compulsory investigations, we assessed *in vitro* citocompatibility and cell viability using both standard line cells and human adipose tissue derived mesenchymal stem cells (HatMSCs). Biological and histological investigations showed how **SmartBone is a very supportive substrate for cell adhesion and growth**; HatMSCs showed *in vitro* capability to properly colonize the scaffold and, once induced, to differentiate!



Electronic microscopy image of a "slice" of SmartBone during cell colonization *in vitro* tests.
The analysis evidenced the presence of wide and well structured cell formations ins SmartBone,
whose micro-structure and composition favor cell colonization already after only 7 days.

In vivo studies were performed to assess osteointegration on a 4 months observation timeframe. Histological analysis proved confirmation of **SmartBone integration, with natural bone formation** and cells and vessels colonizing pores within it during time.

Summarizing, SmartBone main biological features are:

- high cell viability and proliferation support,
- high osteoinduction, conduction and integration.

F. CLINICAL PERFORMANCES

SmartBone is a **bone substituted intended and specifically developed for bone regeneration applications.** SmartBone has been used by surgeons in oral and maxillofacial surgery, allowing **impressive performances** and giving **great results**.

ibi S/A

Via Cantonale 67, CH-6805 Mezzovico Switzerland
t. +41 91 228 01 75 | f. +41 91 220 72 00 | www.ibi-sa.com | info@ibi-sa.com