Just to describe our approach.

1. Bedside printing within 1 hour.
2. Immediate implantation without post processing (sterilization)
3. FDA approved materials

Scaffold material has FDA approved predicates in Orthopedics and Dental Bone grafting

Material to load the scaffold is an FDA approved Bone Allograft material that comes in a gel form.

Once FDA approved a surgeon will be able to use material of his choice to load the scaffold

4. The system is built specifically for bone grafting and fully integrated. System Consist of:

a) Proprietary software to convert a DICOM File into a printable G-code bypassing the STL format

Software Communicates directly with the proprietary aseptic printer and controls printer parameters including sterility tests

b) Proprietary 3D printer with an aseptic enclosure. The enclosure is similar to a laminar flow cabinet used by pharmaceutical companies to compound drugs that cannot be sterilized.

The printer is built specifically to print bone scaffolds out of our proprietary material.

5. The Scaffold is optimized to print with high speed and precision, and reflects the latest scientific understanding of optimal scaffold geometry for bone formation.
6. We are patent protected for the system and the proprietary printer. Latest patent was issued about 2 weeks ago and encapsulates a printer placed in a laminar flow enclosure.

Cerhum
Their collaboration is called True Bone 3D

This is a consortium-based collaboration involving Cerhum's 3D-printed scaffold technology and Bone Therapeutics' ALLOB, a cell-based bone regeneration platform. Based on the publicly available information, the specific scaffold material used by Cerhum is not clearly identified. From a development and regulatory perspective, this approach is likely to require an extended research timeline and a complex FDA approval process, potentially including human clinical studies. In addition, it is not suitable for chairside application.

This 28-months collaboration is called TrueBone3D and aims to develop biologically active, custom-made tissue engineered bone implants that could replace bone transplants harvested from patient's own bones (autografts). Autograft is the current standard treatment in bone reconstruction surgeries. However, harvestable autograft bone is only available in limited supply. This also requires an additional painful surgery. The current treatments are commonly associated with complications such as graft site infection and fracture, increased bleeding, nerve damage and reduced mobility. In addition, it is difficult to precisely shape autografts to fit the bone defect.

TrueBone3D's patient-specific, 3D printed scaffold of the new tissue engineered bone implant will be designed to accurately match the missing bone part. The use of bioresorbable material will allow the implant to integrate with the surrounding bone tissue and to be gradually replaced by newly formed, healthy bone. By combining the tailored scaffold with Bone Therapeutics' differentiated bone forming cells, ALLOB, the enhanced tissue engineered product is expected to exhibit strong bone-forming activities and stimulate bone regeneration. The aim of the resultant TrueBone3D's cell-enriched implant is to form a safe and structurally superior alternative to bone autografts. The final goal of the project is to evaluate the safety and efficacy of the new personalized, tissue engineered bone implants as treatment option for non-union fractures in a proof-of-concept clinical study.

The research partnership consortium has been specifically created to benefit from the complementary expertise of the specialized industry and academic partners for the development of the next generation of personalized, tissue engineered bone implants. 3D-Side, an expert in 3D software for patient specific medical devices, will develop the platform to plan the surgery and to determine the bone defect based on patient's CT scan images. Cerhum, specialized in bone 3D printing and coordinator of the TrueBone3D project, will use the 3D computer model of the bone defect to manufacture a patient-tailored resorbable implant. Bone Therapeutics' bone-forming cells will be added during the surgical procedure. The academic research centers, musculoSKeletal Innovative Research Lab (mSKIL) of University of Liège, Belgium, and IREC (Institute of Experimental and Clinical Research) of Université catholique de Louvain, Belgium, will investigate the biocompatibility and bioactivity of the newly developed tissue engineered bone implants in *in-vitro* and *in-vivo* models.

"*The TrueBone3D consortium will enable Bone Therapeutics to share its expertise in bone regeneration and, through collaborative activity, broaden the application of its allogeneic cell therapy platform, ALLOB, to other orthopedic conditions, including large bone defects, cranial and maxillo-facial reconstruction surgeries,*" said Miguel Forte, MD, PhD, Chief Executive Officer of Bone Therapeutics.

"*Currently, for these conditions, grafts from patients' own bone tissue are mostly used to repair the bone defects. This treatment is often associated with a range of serious complications. Bone Therapeutics, by joining forces with industry and academic experts, continues to pioneer the use of cell therapy in bone regeneration and develop potentially safer and effective treatment options that could be fully tailored to the need of the patient."*

About Bone Therapeutics

Bone Therapeutics is a leading biotech company focused on the development of innovative products to address high unmet needs in orthopedics and other diseases. The Company has a, diversified portfolio of cell and biologic therapies at different stages ranging from pre-clinical programs in immunomodulation to mid-to-late stage clinical development for orthopedic conditions, targeting markets with large unmet medical needs and limited innovation.

XILLOC CT Bone

The material used in this approach is calcium phosphate-based. From a practical perspective, it still requires post-processing and sterilization, which means it does not support a true chairside workflow. In addition, this solution is positioned as a patient-specific implant rather than a scaffold-based platform, placing greater emphasis on demonstrating reliable bone integration and remodeling. Calcium phosphate is a well-established material in this field, although its limitations are often discussed in the context of larger bone defects.

Early next year we will start 3D printing personalized ceramic implants to augment the skeleton, called CT-Bone. CT-Bone is made from calcium phosphate and has a strength comparable to trabecular bone. It is therefore indicated to use for non-load-bearing augmentation implants (e.g. to augment the zygoma, the mandible angle, the skull, etc.). It has been demonstrated to be converted into real bone by the patient's bone cells. The main advantage of CT-Bone is that it requires no heat treatment (sintering) after 3D printing. Such a heat treatment causes significant shrinkage and reduces the resorbability. Unlike hydroxyapatite, which is non-resorbable, CT-Bone is invaded by bone tissue, bone marrow and bone resorbing osteoclasts. Without the need for sintering, CT-Bone can be designed to perfectly match the patient's anatomy and can be accurately 3D printed to fit perfectly, thereby optimizing the bone-implant interface.

CT-Bone®: real bone from the 3D Printer

Patients requiring skeletal augmentation, for example those with facial asymmetry resulting from either trauma or congenital defects, would be helped best with a bony implant made to match their anatomy. Typical bone augmentation implants are made from alloplastic materials (like PEEK or titanium) or the patient's own bone is cut and repositioned. CT-Bone® is a bone-like customized implant that can be 3D printed and is converted to real bone by the patient.

3D printed CT-Bone implant for mandible augmentation

3D printed CT-Bone implant for zygoma augmentation

After taking a CT-scan of the patient, a patient-specific implant is designed by our biomedical engineers in collaboration with the surgeon. This design perfectly fits on the anatomy of the patient, ensuring good bone-to-implant contact and facilitating bony ingrowth. The design is 3D printed in calcium phosphate, the main constituent of natural bone. The 3D printing process has a very high accuracy, resulting in implants that fit perfectly onto the bone of the patient, as designed. Even very complex shapes and designs can be 3D printed; for example, 3D printing enables the production of implants with engineered (controlled) porosity, similar to natural bone. When implanted, CT-Bone® unifies with the patient's own bone in the next months.

From CT-scan to 3D model to patient-specific implant design

Unlike other 3D printed ceramics (like Hydroxyapatite or Beta-TCP), CT-Bone® does not require a thermal process (sintering) to increase mechanical strength and therefore also displays better bony fusion (sintering increases crystallinity which adversely affects biodegradability). Sintering also causes shrinkage of ceramics which results in a non-optimal fit. Since CT-Bone® does not require sintering it displays better bony fusion and is dimensionally stable, so it keeps a perfect fit.

Other manufacturing methods typically produce random porosity, whereas the process of 3D printing allows complex shapes and 100% interconnected porosity.

CT-Bone® is brought to you by Xilloc in collaboration with Next21 (Tokyo, Japan) and is awaiting regulatory approval under the new MDR in Europe.

Particle3D

This approach is also based on tricalcium phosphate and presents limitations similar to those of XILLOC. It does not appear to include an integrated proprietary printing system and is not designed for chairside use.

P3D Bone

Particle3D is developing P3D Bone PSI; a Patient Specific Implant that remodels into real living bone. Made from 3D printed tricalcium phosphate, the individualized implant will deliver a clinically relevant bone porosity and tailored morphology to match patient needs. The result is a more natural implant in terms of both material, shape, and structure that enables a full restoration of the functionality and appearance of facial bones.

Mimetis

Biomimetic hydroxyapatite compound deficient in calcium and β-TCP. This is why the body recognizes it as the patient's own bone, so the use of the graft presents no risk of rejection or infection. Same problems as Particle 3D and Xilloc. Cannot be printed chairside and immediately implanted. Material itself is not very good for large bone defects.
Above all, Mimetis Biomaterials is undeniably the first and only to print patient-specific biomimetic synthetic bone graft in 3D. It is important to realize that Mimetis engineers use the patient's bone defect's medical images to design and print a perfectly customized bone gra ft.

Most important, the biomimetic synthetic bone graft is not sintered. In other words, we do not subject it to any extreme temperatures hardening process. With this purpose in mind, its structure and composition are similar to the bone mineral phase, exhibiting a high specific surface and multi-scale porosity.

This is why MimetikOss 3D is perfect for vertical bone augmentations and complex geometries.

This represents a fundamentally different material and manufacturing approach and is not suitable for bedside scaffold fabrication. The process involves mixing the material with a lipid phase, printing the structure, burning out the lipid, and then sintering the remaining material. As a result, the workflow is too lengthy and complex for practical chairside use. Based on the available process description, the scaffold appears to be primarily hydroxyapatite-based. Similar scaffold technologies

are also being developed by TRS Systems, a University of Michigan spinout in the United States, and by Osteopore in Singapore, which uses PCL as its main component. However, none of these approaches currently offers a viable chairside solution.

Ossiform is founded on a widely applicable and worldwide IP protected technology invented while investigating the possibility of 3D printing bone implants for human use.

Our solution is a bio-ink composed of powder particles suspended in a solid but meltable fatty acid matrix. The bio-ink enables a new 3D additive manufacturing process where objects are constructed directly from a computer-aided design (CAD) file.

The bio-ink is loaded into a syringe, heated to its melting point and extruded as a thin line onto a cooler stage on which it re-solidifies. The fatty acid is then removed through burning and the powders are sintered together.

The technology is patented worldwide, and can be used with many materials and in many industries beyond the medical field.