Regenerative Implants
with 3D printed biomimetic microarchitecture

Osteopore International Pte Ltd
February 2018

INTRODUCTION
Our Mission

• Empower the body’s regenerative capability to heal tissues damaged through trauma, diseases and surgical procedures, so as to minimise or eliminate late complications.
Osteopore Technological Position
Pushing the Boundary of 3D printing technology

Osteopore pushes the technological boundary of 3D printing to develop & commercialise biomimetic microstructure that facilitates natural tissue regeneration.

Printed Organs: Distant Future
Bioprinted Tissue: Future
Regenerative Implants: Available
Permanent Implants: Available
Surgical Guide: Available
Model for Surgical Planning: Available

Biomimetic Microstructure
Stem Cells Propagation
Tissue Regeneration

Regenerative Implants
Choice of microstructure
Cancellous bone - the centre of regenerative activities

Macrostructure

Microstructure

Fresh autogenous cancellous, and to a lesser degree, cortical bone are the benchmark graft material that allograft and bone substitute attempt to match in *in vivo* performance.

### Key Technological Advantage
Facilitating the natural stages of bone healing

<table>
<thead>
<tr>
<th>3-D Printed Scaffold Cellular Matrix</th>
<th>Rapid Revascularisation</th>
<th>Conducive for Cell Proliferation &amp; Differentiation</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="3-D Printing" /></td>
<td><img src="image2" alt="Rapid Revascularisation" /></td>
<td><img src="image3" alt="Conducive Microstructure" /></td>
</tr>
</tbody>
</table>

- **With 3-D printing technology, a system of interconnected pores are constructed.**
- **The interconnectivity of the pores facilitate rapid revascularisation that delivers nutrients and gas exchanges in the microstructure.**
- **The microstructure is optimised to create a conducive environment for stem cells (such as mesenchymal cells) to proliferate and differentiate.**
Facilitating the stages of natural healing

Inflammatory Phase  Reparative Phase (~6 mth)  Remodeling Phase (2-3 yr)

1. Hematoma formation
2. Fibrocartilaginous callus formation
3. Bony callus formation
4. Bone remodeling

Images on stages of bone healing extracted from Pearson Education Inc.
Resolve Unmet Clinical Needs
Regenerative Implants expand treatment capability

As compared to Bone Graft Substitute, Osteopore’s products are:
- Easier to use
- Better guides tissue regeneration
- Better maintains height and width

As compared to Permanent Devices, Osteopore’s products:
- Prevents stress shielding
- Minimise/eliminate late morbidity
- Minimise revision surgery

As compared to Autologous Bone Graft, Osteopore’s products:
- No donor site morbidity
- Can be customised to fit
- Can combine with biologics

1. BCC Research 2015-2019
2. Transparency Market Research 2015-2023
Material Resorption in Tandem with Tissue Regeneration

- Biomimetic devices facilitate the body’s natural healing process. Once the healing is complete, no foreign materials should remain in the body to minimise or eliminate late complications such as infection, extrusion, dehiscence or fracture.

- Through a combination of 3-D printing and bioresorbable material, Osteopore International manufactures devices that biomimic the cancellous bone microarchitecture that facilitates the natural stages of bone healing.
# Present Solutions for Clinical Specialities

**10,000+ successful implants with more than 10 years follow up**

<table>
<thead>
<tr>
<th>Products</th>
<th>Neurosurgery</th>
<th>Plastic Surgery</th>
<th>Oculoplastic Surgery</th>
<th>Craniofacial Surgery</th>
</tr>
</thead>
</table>
| OsteoPlug                 | ▪ Burr Hole for Craniotomy  
▪ Evacuation of Chronic Subdural Hematoma  
▪ Cranial Spinal Fluid Shunt |                                                                               |                                       |                                            |
| OsteoStrip                | ▪ Cranioplasty gap filler to minimise bone edge necrosis                      |                                                                               |                                       | ▪ Cranioplasty gap filler to minimise bone edge necrosis |
| OsteoMesh                 | ▪ Craniosynotosis  
▪ Cranioplasty                                                                 | ▪ Facial Reconstruction  
▪ Orbital Reconstruction                                                                 | ▪ Orbital Reconstruction                                                                 |
| Patient Specific Implants | ▪ Coronal synotosis  
▪ Cranioplasty                                                                 | ▪ Facial Reconstruction  
▪ Orbital Reconstruction                                                                 | ▪ Orbital Reconstruction                                                                 |

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Advantages for Healthcare Stakeholders

• **Payors** (Government, Insurance, Patient):
  – Minimise / eliminate future payments for re-surgery and associated long term care, reducing overall treatment expenses

• **Hospital resource utilisation**:
  – Focus consumption of hospital resources for new patients, instead of re-admission and revision surgery

• **Surgeons**:
  – Providing a surgical solution with sustainable clinical outcome to patients and their families.
Platform Technology Overview
Both standard and customised products are 3D printed

Integration of Medical Imaging + Computational Mechanics + Biomaterials Technology

CT Scan → Digitized 3D Image → Scaffold Design → 3D Porous Scaffold → Scaffold Fabrication
Choice of Material
Resorption in tandem with bone healing

Polycaprolactone (PCL) Highlights

- The natural stages of bone healing starts with the inflammatory response, followed by revascularisation and mesenchymal cells proliferation. Cancellous bone will completely form in about 6 months, followed by the remodelling phase to cortical bones over 2-3 years.
- Polycaprolactone (PCL) is the material of choice in our devices. This material has been approved for use in implants for over 30-years. It fully resorb in 18-24 months and the by-products are carbon dioxide and water. The gradual resorption profile makes it a predictable material for matching to the natural stage of bone healing.
- The rate of resorption of PCL is very much in tandem with the natural stages of bone healing. Eventually the neobone will assume the final stages of the remodelling, evolving to the strength of its intended function.

Key Comparisons with Titanium

<table>
<thead>
<tr>
<th></th>
<th>Osteopore</th>
<th>Titanium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bioresorbable</td>
<td>Yes 18 – 24 months</td>
<td>No</td>
</tr>
<tr>
<td>Potential infection or extrusion</td>
<td>Unlikely</td>
<td>Likely</td>
</tr>
<tr>
<td>Trimming to Shape</td>
<td>Easy</td>
<td>Results in sharp edges</td>
</tr>
</tbody>
</table>
Publications that Lead the Science
Highly referenced publications

4 technical publications
23 in-vitro & 20 in-vivo publications
6+ clinical publications
Product Registered for Global Market Access
US FDA 510(k) and CE Mark Approved
# Clinical Performance

## Neurosurgery Application

<table>
<thead>
<tr>
<th></th>
<th>Pre- &amp; post-operatively</th>
<th>CT images over time</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Osteoplug</strong></td>
<td><img src="image1" alt="Image" /></td>
<td><img src="image2" alt="Image" /></td>
</tr>
<tr>
<td>• Burr hole</td>
<td><img src="image3" alt="Image" /></td>
<td><img src="image4" alt="Image" /></td>
</tr>
</tbody>
</table>

| **Osteomesh**        | ![Image](image5)         | ![Image](image6)    |
| • Craniosynostosis   | ![Image](image7)         | ![Image](image8)    |

| **Patient Specific** | ![Image](image9)         | ![Image](image10)   |
| • Coronal craniosynostosis (Germany) | ![Image](image11) | ![Image](image12)   |
## Clinical Performance
### Neuro & Plastic Reconstruction

<table>
<thead>
<tr>
<th>Patient Specific (Adult)</th>
<th>Pre- &amp; post-operatively</th>
<th>CT images over time</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Cranioplasty</td>
<td>![Image A]</td>
<td>![Image F]</td>
</tr>
<tr>
<td>(Germany)</td>
<td>![Image B]</td>
<td>![Image H]</td>
</tr>
</tbody>
</table>

**Osteomesh**

- Orbital floor reconstruction

<table>
<thead>
<tr>
<th>Pre-op</th>
<th>Post-op 2 ½ yrs</th>
<th>Normal architecture restored</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolapse of the left orbital contents into sinus</td>
<td>Normal architecture restored</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pre- &amp; post-operatively</td>
<td>CT images over time</td>
</tr>
<tr>
<td>--------------------------</td>
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<td>---------------------</td>
</tr>
<tr>
<td><strong>Osteomesh</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rhinoplasty (Korea)</td>
<td><img src="image1" alt="Pre-op image" /></td>
<td><img src="image2" alt="Post-op image" /></td>
</tr>
<tr>
<td>Nasal Tip Augmentation (Korea)</td>
<td><img src="image3" alt="Pre-op image" /></td>
<td><img src="image4" alt="Post-op image" /></td>
</tr>
</tbody>
</table>
### Clinical First-in-Human
Oral Maxillofacial, Dental and Orthopaedic applications

<table>
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<tr>
<th>Pre- &amp; post-operatively</th>
<th>CT images over time</th>
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<tbody>
<tr>
<td><strong>Patient Specific:</strong> Mandible Reconstruction (Germany)</td>
<td><img src="image1.png" alt="Image" /></td>
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<td></td>
<td><img src="image2.png" alt="Image" /></td>
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<tr>
<td></td>
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<tr>
<td></td>
<td><img src="image4.png" alt="Image" /></td>
</tr>
</tbody>
</table>

| Osteoplug: Alveolar Ridge Preservation (Singapore) | ![Image](image5.png) |
|                                                 | ![Image](image6.png) |
|                                                 | ![Image](image7.png) |

| **Patient Specific:** Segmental Tibial Reconstruction (Germany) | ![Image](image8.png) |
|                                                               | ![Image](image9.png) |
|                                                               | ![Image](image10.png) |
Competition
Biomimetic bioresorbable space

**Biomimetic microstructure**
- MedPor (Stryker)
- Anatomics
- AccuShape (MedCad)
- TiMesh (Medtronic)
- KLS Martin
- Depuy Synthes

**Solid Structure**
- Permanent Implant

**Bioresorbable**
- Rapidsorb (Synthes)
- Lactosorb (Biomet)
- Macropore (Medtronic)
- Osteotrans (Takiron)
- Inion CPS

**Competitive Advantage**
- Ability to integrate with surrounding bone and/or tissue
- Bioresorbability with no documented long term regenerative problems
- 3D printed to specific patients needs when required to achieve clinical advantage
**Awards & Analyst Quote**

**OSTEOPORE INTERNATIONAL PTE LTD**

**2016 FROST & SULLIVAN SINGAPORE 3D SCAFFOLD ENTREPRENEURIAL COMPANY OF THE YEAR**

**Analyst Quote**

“Osteopore’s 3D scaffold tissue engineering technology platform is uniquely poised above its competitors as it facilitates natural tissue healing and regenerative functions. The technology comprises novel biomimetic and bioresorbable 3D printed microstructure implants that can be efficiently used across neurological, craniofacial, maxillofacial, orthopedic spinal and dental applications. The company’s innovative 3D scaffold technology has the potential to address the rising incidence of bone-related injuries and may transform the global bone graft market that is currently valued at around $5 billion USD.”

Vandana Iyer
Research Analyst
Frost & Sullivan

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**Cyberdyne**

2015 – Japan’s Ministry of Health, Labour and Welfare approved first medical device: CYBERDYNE’s cyborg-type robot, HAL (Hybrid Assistive Limb) that regenerates and improves patients’ brain-neuro-physical functions

**Sino Medical Sciences Technology Inc. (SINOMED), based in Tianjin, China, has developed a next-generation stent that is based on two different functional layers grown on the surface, eG® coating base layer and biodegradable PLGA drug carrier in combination with Sirolimus**

**Osteopore**

Developed 3D scaffold tissue engineering technology that uses bioresorbable implants for natural tissue healing and regenerative functions

**SymbioMed**

2017 – CFDA approved first ever TAVR (transcatheter aortic valve replacement) device in the country, with trials to begin at the end of 2017

**Biosfield**

Designed a lightweight air-powered endoscopic robot with three movable arms to give surgeons hands-free control and better visualization

With technology advancing in leaps and bounds, several cutting-edge innovations have emerged in the region in recent years.
News through the years

2004

*This plastic can heal that hole in the head*

*New Procedure Helps Regenerate Injured Bones*

2008

*2008 Channel New Asia*

*Dental Implant First-in-Man*

2016

*Health Minister asks to cure girl with giant tumor*

*2016 VietNamNet Newspaper*

*Girl La Thị Lusa with giant tumor on the body (Photo: SGGP)*

*Replacing teeth? 3D scaffold may ease pain*

*The Straits Times Monday October 3, 2016*

*Osteoporosis Offers Islam-Friendly 3D Printed Bioresorbable Medical Implants*

*2017 The Straits Times*

*Gold Coast man receives 3D-printed shinbone in world-first surgery*

*2017 Channel News Asia*

2017

*Operating on my brain? Carry on, I’ll play my guitar*

*The Straits Times, September 9, 2017*

*Founders’ Valley: Horizons of Health (2017 Deutsche Welle)*

*2017 The Sydney Morning Herald*

*Tibia Reconstruction First-in-Man*
Empowering Natural Tissue Regeneration