MEETING REPORT

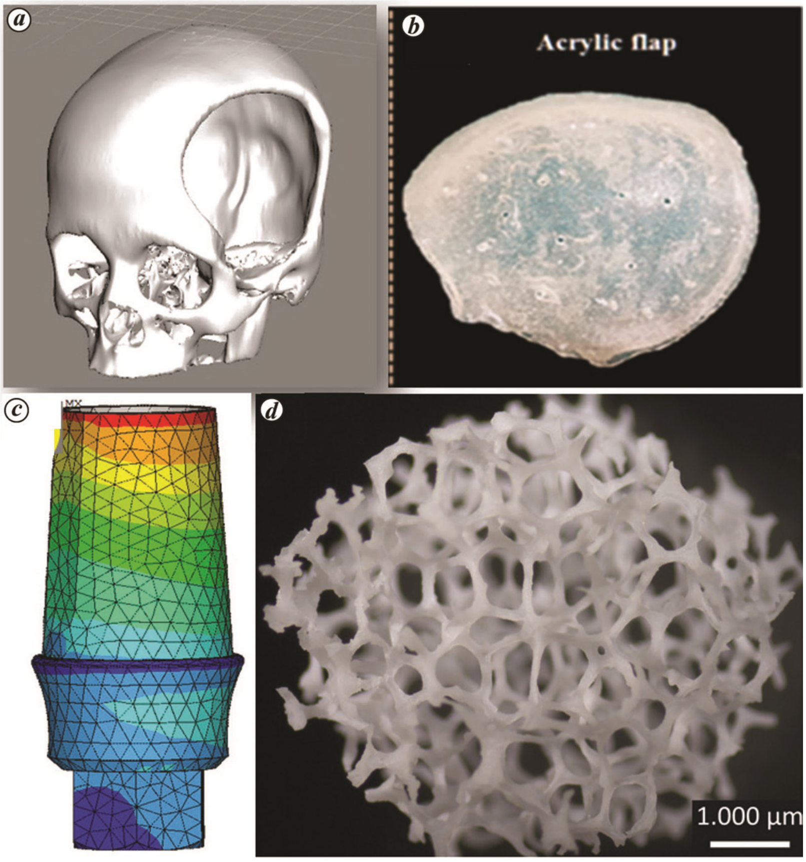
Biomaterials and implants for dental, cranio-maxillofacial reconstruction and bone regeneration*

As the life expectancy of humans is increasing, there is a growing need for medical support for the ageing population, which is more susceptible to accidental bone fractures and musculoskeletal disorders. But, providing solutions to bone-related clinical treatment are much more than an engineering challenge. Synthetic biomaterials (designed specifically for the anatomy of the patient) should not only match the properties of the natural bones but must also be accepted by the body. This requires scientists to discover the appropriate materials, biologists to understand biocompatibility, and medical doctors to validate through clinical trials, for effective translational research. Structurally, the bone substitute must mimic the natural bone (both geometrically and microstructurally), and integrate with the soft tissues around it for faster healing of bone defects, as required in autografts. Selecting a suitable biomaterial and fabricating the scaffolds pose a greater challenge.

Keeping the above perspectives in mind and building upon the learnings of the previous workshop, the discussions in recently conducted Indo-German symposium aimed to integrate state-of-the-art manufacturing technologies with the scientific understanding of biomaterials and implants and their transition to clinical trials. The symposium also incentivized Indo-German joint research venture and collaboration among the participants to scale up the production and commercialization of the undergoing innovations in the respective labs. In line with the objective of the symposium, the proceedings were distributed over 3 days and categorized under 11 technical sessions, each of which consisted of 3–4 speakers. Among the 35 presentations, 8 were made by participants from the Indian delegation, while the rest were from the German contingent, apart from one representation from Belgium. The Indian delegation had representatives from academia, medical schools, hospitals and industry: from IISc (Bengaluru), IIT Kanpur, IIT BHU, King George Medical University, Ramaiah University, Jaslok Hospital and Ceramat Pvt. Ltd (a Tata Steel Enterprise). The German contingent consisted of speakers from universities and hospitals spread over Germany, such as Dresden, Erlangen-Nuremberg, Frankfurt, Heidelberg, Cologne, Würzburg, Mainz, Potsdam, Bremen and Berlin.

The technical sessions of the symposium were categorized broadly into following four facets of orthopaedic research.

Additive manufacturing in orthopaedic applications: Additive manufacturing has been termed an integral part of Industry 4.0, where the focus is on manufacturing ‘on demand’ locally and to the specificity of requirements. With the advancement in 3D printing techniques, several biomaterials, metal, polymer, ceramics, composites and functionally graded materials could be designed and fabricated to match the patient-specific anatomy. Some unique applications are in treating malunions of the arm, zirconia dental implants and bridges, shape-changing 4D printed parts to replace surgical sutures, 3D printing of low-temperature phases of tricalcium phosphate as bioceramic implants and scaffolds, PMMA-based cranioplasty implants. Extending the idea of 3D printing to composites, a hybrid structure of calcium phosphate and collagen or silk



Illustrative examples of the research on biomaterials and implants for bone regeneration. ***a***, 3D rendered image of defective skull and cranial flap molded using PMMA; ***b***, Acrylic flap molded for a patient specific cranial defect; ***c***, Computational biomechanical analysis of dental implant abutment under virtual load; ***d***, 45S5 bioactive glass scaffold. (Credit: Marcela Ospina, FAU, Erlangen-Nuremberg.)

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fibroin biopolymers replicating the natural tissues and scaffolds are being studied. Such scaffolds, sometime in core-shell structure, can also be used to provide sustainable release of antibiotic drugs to control infections and aid tissue regeneration.

To obtain the scaffold of desired hierarchical morphologies, shape complexity and mechanical properties, a clear understanding of the parameters of 3D printing becomes indispensable. For instance, the hierarchical architecture of the lacunar–canalicular network determines the rate of bone regeneration during healing. Based on applications and choice of biomaterials, different 3D printing techniques are used, such as direct ink writing, extrusion-based 3D printing, fused deposition modelling, selective laser sintering (SLS), stereolithography, electron beam melting, 3DP technology and biological 3D printing. These processes have their unique processing parameters to be optimized, for example, to print alumina toughened zirconia by extrusion slurry solid loading and its rheological properties become important, whereas, for SLS of Ti-6Al-4V, the flowability and laser–matter interaction are the determining factors. Another important aspect of designing and developing the scaffolds is the simulation of their mechanical behaviour using finite element methods, followed by experimental validation and clinical study of the 3D printed parts. An emerging field of research is biomaterialomics, a data-driven systematic exploration of biomaterials and the development of machine learning algorithms to reveal predictive capabilities.

Biomaterials in bone regeneration and drug delivery: Even before we agree upon the suitable techniques for 3D printing, the biomaterials to be used in printing require scientific understanding of their mechanical properties, osseointegration, osteoconduction, osteoblast adhesion, tissue growth, antibacterial properties, soft-tissue integration, angiogenesis, biomineralization, drug release and biodegradability. These properties can be further tweaked by doping. For example, the incorporation of metallic ions, Zn, Sr, and B, into bioactive glasses is commonly adopted to enhance tissue growth and other biological functionalities such as antibacterial, angiogenic and osteogenic properties. Moreover, changes in the pH of the solution or surface tension can also help microtissue growth and mineralization. Nanostructured biomaterials, such as mesoporous bioactive glasses loaded with antibiotic drugs, are being developed for medical implants, interfaces of ceramic prosthetics, tissue regeneration, angiogenesis-vascularization and immunomodulation. Interestingly, even external fields such as electric fields can induce polarization in the synthetic bones, which improves their functional performance by promoting bone regeneration, protein synthesis, wound healing and antibacterial properties.

Translational challenges: With the development of new biomaterials and designs, it is equally important to validate their adaptability with clinical trials, following the standard regulations. This requires a holistic approach to soft tissue restoration as well as vascularization near the bone restoration area during rehabilitation. Platelet-rich fibrin around bone substitute materials provides the biologically active component that accelerates wound healing and regeneration. From a surgeon's perspective, the implant design must be built patient-specific, using 3D scanning for applications such as cranioplasty and oral-maxillofacial surgery. The clinician's responsibility is to restore the large bone defects and promote the healing process. This requires, for example, collaboration with plastic surgeons to grow fibroblast keratinocytes for skin regeneration. The development of biomaterials in dentistry for regions with low volumes of bone and exposed nerves is also an open challenge for treating cleft alveolar bone. It is especially relevant for developing nations like India, where 80% of the biomaterials and implants are imported from North America and Europe, which is usually forbiddingly expensive and sometimes anatomically ill-suited for the Indian population.

Commercial production of biomaterials and implants: Industry, businesses and start-ups are essential to proliferate the biomedical discoveries made through collaborations between scientists and clinicians. This has tremendous potentials in the transition of innovations from discovery to medical practices. Industrial representatives shared their experiences in commercializing orthopaedic biomaterials and functionally graded materials mimicking trabecular bone structure with excellent osseointegration of cortical and trabecular bones. The journey of developing biomaterials, from idea to large-scale production, is challenging and rewarding, inviting more players and researchers to participate. 3D printing is becoming a prevalent technique for biomedical applications. Special attention is also needed to synthesize powders of the desired biomaterials.

During the brainstorming session, there was an emphasis on strengthening the interdisciplinary collaboration with national labs, academicians, clinicians, and industries, as was the mandate of this workshop. Scientists and medical doctors play crucial roles in public health, and communication among them is necessary for success in translational research. As summarized beautifully by Singh, one of the Indian clinician delegates, 'To make a real contribution to the society, we, as scientists, clinicians, and manufacturers, will have to come together and speak with each other in a simplified language that could be mutually understood.'

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