Cranioplasty treatment for human healthcare*

Decompressive craniectomy is one of the most challenging neurosurgical procedures to treat traumatic brain injury or stroke to release the intracranial pressure. Reconstruction of the skull vault defect is known as cranioplasty. Using the patient's own bone flap for reconstruction of the defect is considered the clinical gold standard practice, but this is plagued with a significant risk of infection and bone resorption. In the conventional clinical treatment approach, neurosurgeons use acrylic polymers and shape them into the skull defect before implanting them into the patient's cranium at the operation table. However, this approach increases the surgery time and often leads to a lack of restoration in cranium symmetry. Moreover, during curing, acrylic polymers release heat which may cause necrosis of brain cells. In recent years, the binderjet 3D-printed cranium mould-mediated fabrication of acrylic cranioplasts is shown to be safe with acceptable cosmetic and clinical outcomes in human subjects with decompressive craniectomy.

In the above backdrop, a National Conclave on 'Translational Research on Cranioplasty Treatment for Human Healthcare: Status and Challenges' was organized recently to discuss the current status of cranioplasty in India and brainstorm the challenges, together with the advances that can be pursued using artificial intelligence. It also paved the way to discuss the potential for future collaboration among academicians, clinicians and industrialists. The conclave was attended by 17 participants, including practicing neurosurgeons, biomaterials scientists, biomedical engineers/entrepreneur and research scholars.

The conclave was kickstarted in the morning of 12 December by Bikramjit Basu (Indian Institute of Science (IISc), Bengaluru) who welcomed the participants, and presented an overview of the clinical significance and market potential of cranioplasty. He also emphasized on 'Healthy India Mission', stressing upon the importance of high-quality, affordable, patient-specific implants for Indian patients admitted in Government hospitals. The emphasis on the need for cranioplasty set the right tone for Nitu Bhaskar (IISc) to touch upon some of the basic aspects associated with cranioplasty focused on the fabrication of patient-specific acrylic flap. This flap is designed by engineering design process and advanced imaging algorithms to achieve acceptable cosmetic and clinical outcomes in patients with decompressive craniectomy. The talk was based on a pilot clinical study using human subject-specific acrylic cranial prosthesis during 2017–20, a collaborative work between IISc researchers and neurosurgeons based in Ramaiah Memorial Hospital, Bengaluru. Bhaskar elaborated on the clinically acceptable structural and mechanical properties of implanted poly-methyl methacrylate (PMMA) with its safety profile and clinical efficacy in human subjects assessed using a simple and effective cranial index of symmetry (CIS) and clinically acceptable Glasgow outcome scores (GOS). Subsequently, Sandeep Iratwar (Datta Meghe Institute of Medical Sciences (DMIMS), Wardha) discussed the collaborative project initiated with Basu's laboratory for cranioplasty. Six patients had benefitted and were operated upon at Acharya Vinoba Bhave Rural Hospital (AVBRH), Wardha, by the flap design developed at IISc. Iratwar discussed post-operative clinical and surgical outcomes. He focused on the various difficulties that clinicians experience intraoperatively and identified the issue to be put forward for discussion. He also elaborated on the improved clinical outcomes evaluated by the Glasgow coma scale and the improvized cosmetic outcomes. Iratwar specified the quantification of bone remodelling during the time gap between decompressive craniectomy and cranioplasty.

Sulob Roy Chowdary (IISc) elucidated upon the calculation of CIS which is an essential tool to determine the post-operative outcome of cranioplasty. He also demonstrated how to process the CT scan data of patients to obtain the design of patient-specific 3D mould.

Manish Baldia (Jaslok Hospital and Research Centre, Mumbai) presented an overview of the clinical studies on cranioplasty. Starting from the timing of cranioplasty with regard to neurological outcomes, complications such as infections and seizures and hydrocephalus, he highlighted the outcomes of early and late cranioplasty. The importance of cosmesis outcome was highlighted with examples from his own published work on customized, cost-effective poly-methyl methacrylate cranioplasty and a cosmetic comparison with other low-cost methods. Some interesting aspects related to scoring of the flap were also highlighted together with examples from his work, and how 3D printed flaps would be a better option compared to hand-moulded or bone impression flap with respect to score was pointed out. Baldia also demonstrated the bone resorption process of autologous bone flap and the clinical significance of PMMA-based bone flaps. He concluded with the functional outcome and complications of cranioplasty, and its future aspects.

Manish Amin (Avay Biosciences, Bengaluru) spoke about the opportunities of direct 3D printing of PMMA and polyether ether ketone (PEEK) based bone flaps using the fused deposition modeling (FDM) approach. The primary challenges faced were to procure PEEK and PMMA in the form of filament. He also mentioned the technical parameters to print PMMA without any hassles. In conclusion, Amin mentioned that the printing of PMMA and PEEK will make the process easier, considering that there is a specific FDM printer manufactured by Avay Biosciences, which can print PEEK and PMMA filaments directly into patient-specific customized bone flap.

Ashutosh Bagde (DMIMS, DU) elaborated on the ecosystem for translator research at DMIMS (DU) along with the collaborative institution, and demonstrated the data-collection mobile ODK app developed by DMIMS (DU) for the cranioplasty project. This app can store collective information of all patients undergoing cranioplasty surgery. The proposed app includes 85+ questionnaires which need to be answered during pre-operative, intraoperative, post-operative and discharge of patients. The

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regular follow-up at intervals of 1, 6 and 12 months will be collected in the same app. This type of patient-specific information can provide an overall understanding about the successful outcome of cranioplasty throughout India.

The next focus was on machine learning. N. H. Gowtham (IISc) introduced the fundamentals of machine learning and different types of algorithms. The applications of machine learning in the field of clinical translational research were discussed briefly as well as the possibility of deep learning to generate cranial implants. Gowtham mentioned that deep learning algorithms/statistical methods can be used to reconstruct the full skull from defective skull. These algorithms can also directly generate patient-specific cranial plate with exact thickness that can minimize problems of post processing/misfit of implant during surgery. This will be particularly helpful when the defect crosses the midline and symmetry can no longer be used to generate the implant. The recent Grand Challenge – AutoImplant and online resources were also briefly discussed by the speaker.

G. K. Anil Vishnu (IISc) talked about micro-engineered implantable devices and related technologies for neural recording and brain tissue analysis. His work presents multi-pronged neural recording and stimulation strategy for diagnostic and therapeutic applications using multichannel, silicon-based, microneedle electrode arrays and flexible electrode arrays fabricated on a biocompatible polyimide substrate. Details on developing a hand-held steerable probe integrated with micro-engineered devices (interdigitated electrodes and piezoelectric micromachined ultrasound transducers) for brain tumour delineation were also discussed.

In the brainstorming session, the participants revisited the clinical significance for cranioplasty surgery. The participating neurosurgeons mentioned that in a given month, 11 patients in Ramaiah hospital, Bengaluru; 7–8 patients in DMIMS, Wardha; 35 patients in Christian Medical College, Vellore and 2–3 patients in Jaslok hospital, Mumbai; on an average are treated for cranioplasty surgery. Similar statistics for other hospitals in India was however not available to the participants. During the brainstorming session, challenges in the existing approach for treating cranial defects, as well as the different implants used and their advantages and disadvantages were discussed. In addition, clinical outcome analysis using patients' pre- and post-operative CT-scan data and benefits of cranioplasty for patient care, future perspectives of cranioplasty research and its implementation in Indian hospitals were discussed.

As part of the concluding session, the participants also discussed about implant manufacturing protocols comprising design of bone flap, materials analysis, choice of 3D printer, post-printing treatment, sterilization and packaging techniques, quality control of 3D-printed bone flaps, cost estimation and business plan for future implementations. Basu and his team is excited to work together to take the 'FlapIn' implant for the cranioplasty surgery of patients in city-based, district-level and rural hospitals, with the manufacturing plan to be implemented in Good Manufacturing Practice – compliant facility in India.

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