

Advances in Additive Manufacturing of Materials: Current status and emerging opportunities

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Lecture41

Welcome back to this NPTEL course on additive manufacturing. In today's lecture, I will show you a clinical case study. a clinical case study on 3D printing of cranium models, cranium means human skull, skull models mediated bone flaps for patient specific cranioplasty surgery. I will show you a that how the design and additive manufacturing helps in personalized medicine. What is called personalized medicine? Personalized medicine is the form of clinical treatment which is based on patient specificity. I will give you sufficient clinical relevance and background so that you will be in a position to appreciate the importance of patient specific design and additive manufacturing technique to develop the bone flaps for cranioplasty surgery.

these are the topics that will be covered as I said first would be the clinical relevance. Second topic would be cranioplasty like what is the overview, key aspects, materials, designing the defect part and then there I will show you how different complex defects that cranio maxillofacial surgeon or neurosurgeons they normally experience while treating patients in many countries. And third one is a clinical studies conducted by Indian Institute of Science Bangalore and in particular my research group over last 5 years or so. clinical significance.

Traumatic brain injury is one form of injury which impairs the human patients particularly their neurological functionality and many other physiological activities. traumatic brain injury can be due to sudden falls like particularly for the older patients. This is the data from India. it is kind of 28% falls, 20% traffic accidents because of busy roads or citizens not following traffic rules at some instance while they are traveling on roads in many countries, 19% struck by or against or hitting at the traffic, 11% assaults and so on. if you look at this particular slide on the left hand side, healthy brain, you have the frontal lobe, they actually helps in concentrating human mind, problem solving, speech, parietal sense of touch, pain or temperature and then temporal like memory, organization, cerebellum balance and coordination of the activities, brain stem that is breathing, steady heart rate and so on.

what are these attributes or what are these aspects which will be compromised due to traumatic brain injury? These are mentioned on the right hand side as I am circling here. in the frontal part because of the traumatic brain injury, the patients will have lack of focus. they will get irritated very easily, they will have speech problem or language difficulty and if parietal part is injured then they will have difficulty with reading, spatial misperception , If there is brain stem there is some problem or it got hit then the patients will have problems in breathing and also swallowing. In the cerebellum part it is injured then patients will have difficulty in walking and slurred speech. it should be clear to you that when a undergoes traumatic brain injury, they will have not only neurological functionally related issues but also various other problems which will potentially impair the daily routine life or regular life of any human subject.

how this traumatic brain injury can happen as I mentioned and this is just a pictorial depiction of this traumatic brain injury. One can be stroke, another can be road traffic accident, injury due to road traffic accident, third

one can be brain tumor. if a human patient has brain tumour and the brain tumour is removed so that part of the skull is get depressed so that will experience more external pressure due to atmospheric pressure as a result neurological functionality will be impaired. treatment protocol that I will explain to you. first step is the decompressive craniotomy and then second step is to place a bone flap.

Now this bone flap since every human patients their skull structure their cranium structure is very different. the point is that one size does not fit all. what it means that this particular bone flaps will have different morphology in terms of the size, shape and contour. what I said size, shape and contour and that would be dependent on that what is the defect. morphology , because ultimately these bone flaps will be used to reconstruct this particular cranial defect.

if you remember the fundamental definitions I have given you a few lectures back on the biomaterials. these are the synthetic materials which are synthesized or fabricated or manufactured outside the human body and are placed inside the human body for the purpose of reconstruction, repair or regeneration of damaged tissues. this is just to recapitulate the definition that you learned a few lecture back on biomaterials. let me complete now first on the clinical perspective I need to mention here the decompressive craniectomy is the first step for the patients with stroke or traumatic brain injury. what is the purpose of decompressive craniectomy is to manage the intracranial pressure.

what I wanted to tell you that different parts of the human body for example, if you consider that eye, this eye inside the eye there is something called intraocular pressure. it is IOP. that IOP should fall within certain range so that optic nerves are not damaged and then optic nerves are damaged then visions will be impaired similarly intracranial pressure needs to be maintained within some physiological limit And for the patients with TBI, so the decompressive craniectomy, that is the first part. Anything called craniectomy means part of the human skull is being removed. Tomy means osteotomy, like some part of the bone needs to be cut, removal of the portion of the skull that is causing the pressure on the brain and then reduce the risk of severe brain damage and it can even be life saving.

the second stage, so this is stage 1. Second stage is cranioplasty. cranioplasty means that after the decompressive craniectomy, there will be some weeks of gap. the patient is brought back to the hospital. then the next stage is that you know to then the patient will undergo reconstructive craniofacial surgical procedure performed to restore a defect on the cranial wall after a previous decompressive craniectomy made by traumatic brain injury or even after removal of cranial tumours this one I have mentioned so, either the patient has a brain tumour that is removed or the patient has traumatic brain injury in both the cases you know that this particular cranioplasty surgery is followed which involves the use of the bone flaps.

And what are the materials that are typically used in cranioplasty surgery it is either titanium mesh. hydroxyapatite, polyetheretherketone and poly methyl methacrylate. polyetheretherketone PEK and poly methyl methacrylate. essentially square box around polymethyl methacrylate because clinically it is time tested for many decades. And if you look at the clinical evidences of the safety and efficacy of the poly methyl methacrylate that comes at the top position at the top level.

this is the material which has been used time and again. Titanium mesh and hydroxyapatite or polyether ether ketone those are also used but much less in numbers. the clinical evidences for these materials are relatively new and not to that extent that we have PMMA. what are the selection criteria for the materials to be used as

bone flaps for cranioplasty surgery? These are like first in is that fitting cranial defect to achieve complete closure. Then second one is a radiolucency, third one is a resistance to infections and fourth one is the heat resistant and it should be biomechanically strong.

these are the different attributes that a biomaterial implant must have. what I am going to show you is that how the design is to be conceived and completed for the patient specific design, then manufacturing, implant quality validation, affordability this also one of the points that needs to be considered in many developing nations or third world nations while choosing the materials which they have to do for cranioplasty surgery. let me also go back to that these are like one of the factors and this particular clinical relevance and other things as you can also find in one of the review papers which our group has written and which was published in Acta Biomaterialia in the year 2022. what are the factors which will determine the clinical outcome? when you consider the bone flaps for cranioplasty, first one is that you get the CT or MRI scan data of the patients and based on that you define the cranial defect morphology. it is like DICOM image to stereo lithography file .

stl then that you give it to a 3D printer. 3D model that will be generated and engineering design and 3D printing. this 3D model will be generated and this 3D model essentially will be generated by considering different views of the cranium. And then after that you do 3D printing and 3D printing of this cranium model will allow you to cast the bone flap materials into particular shape as you can see that is the manufactured implant. Then that will be placed during the cranial plastic surgery which I will show you in also a few minutes and then during the surgical intervention the bone flap will be implanted and then after that clinical outcome analysis will be recorded for over longer period of time and this clinical outcome analysis will be assessed.

And in today's world, people are trying to use also different data science approaches and these data science approaches are also useful for accelerating the cranial defect design aspect. Now, what are the computer software? web platforms that we use like materialise software, then you can use Autodesk MeshMixer, Solidworks and so on. these are some of the common platforms we always use in designing the cranial defect. what are the different type of defects? you can see that what is the process that has been used. you have the defect , Now what you can see as I trace this defect, I can show you this is the size.

But you do notice that there is a certain thickness of this defect and this thickness may not be uniform at different locations of this cranial defect part. There is a variation, so I repeat there is a thickness variation at different defect location and also you consider the shape and contour of the defect. therefore, the perfect design of this particular brain defect, cranial defect is very important. here what you see that how to do this? you have a defective skull. here defect is even much thicker.

and you actually consider the complete skull. by considering the complete skull minus defective skull that subtraction will give you what is the defect, morphology, shape and thickness. The same way you can see that you know that in the top part A, B, C so in the C part it is your bone flap ,it is in yellow color as you can see when it is placed here in the cranial defect it should be able to perfectly fit into the cranial defects that is the one of the key criteria for better clinical outcome in this cranioplasty surgery. I will show you that what are the different types of defects are possible, different defect size, morphology of defects. this is a kind of a very deep defect but it is more or less like rectangular shaped defect, now you can have a kind of a spherical defects, you can have a triangular like defects, so you can have you know square type of defects, so there is a different type of defects these are possible .

These are like different type of defects these are possible. essentially what you notice from this particular set of CT scan images that depending on the patients one has to design the different shaped bone flaps with various morphology and those designs has to be translated to the manufactured bone flaps right. this is just to show that how to reconstruct the skull. For example, you can see this is the input CT scan image and this is the complete brain image, complete cranium image. In different parts during the reconstruction process, they use the different combination of software, some of their open source software.

and some of the softwares that one has to have licensed and all some of the license softwares are to be used while reconstructing the human skull. This is that how these different cranial implants are kind of generated. You can see that implant model design, many times premorbid anatomy not known in many clinical cases, premorbid anatomy. And mirroring of this image is of the limited use because skulls are really perfectly symmetric. you have to remember that skulls are really perfectly symmetric and defect is over the midline.

What is the desirable approach? Desirable approach is the first automatic implant design using deep learning algorithms. deep learning is one of the subset of this overall data science approaches that researchers have been consistently using and then I will be explaining that deep learning things also when I will discuss about the data science approaches. On a large structured database of segmented skull CT scans. implant manufacturing what is called subtractive like either milling like titanium peak or PMMA implants or generative like you know 3D printing like SLA for polymers, SLM or EBM for titanium or titanium mesh that I have shown, next few slides I will show you that how this particular clinical study has been conducted in two different hospitals in India and these hospitals are essentially located one in Datta meghe Institute of Medical Sciences in Wardha and one in the Ramaiah Memorial Hospital in Bangalore. And before doing this clinical study, what we have to I have to emphasize that we have essentially designed a clinical study involving the neurosurgeons in these two hospitals.

And this the inclusion criteria is the patients aged over 18 to 70 years who have undergone decompressive craniotomy for trauma, traumatic brain injury or stroke. And patients, what is the exclusion criteria? Exclusion criteria is a patient with previous allergy to acrylic, patients with previous infection at the operative sites and pregnant women and children they were not recruited during this pilot clinical study. There is informed concerns that every patient has to fill up before they went for surgery and we have to take ethical committee approval from the hospital. This is just to show what we ethical committee approval that we have done.

first is the clinical study design. Then is that institutional human ethics committees approval. And then comes that hospitals ethics committee approval. Then one has to get the CTRI approval, this is the Indian Institute of Science Ethical Institutional Human Ethics Committee approval. Then we have essentially applied for approval on the Clinical Trial Registry of India and that is essentially managed and maintained by Indian Council of Medical Research, National Institute of Medical Statistics. And then we have got registration number CTRI /2018 /09/05680 for Ramaiah Medical College.

And we have done, we have essentially validated this clinical study outcome what we have done at Ramaiah Medical College in Datta meghe Institute of Higher Educational Research in Wardha that is in the state of Maharashtra and then we got CTRI approval in 2021. you can see that how the CTRI approval essentially looks like. this is an interventional procedure. here is a single arm trial and this is the title of this our scientific title of the study. and then who are the clinicians who are involved, who is the lead PI clinicians who are involved and CTRI number that is also mentioned.

once the clinical study is over, we have to again report the clinical study outcomes in the clinical trial registry of India. and then this entire study is completed. these are the ethical approaches that one must follow while conducting clinical trial clinical study in India. this is the inclusion exclusion criteria that I have mentioned. what are the approaches that we followed in our clinical study? we have taken this is just for a single patients I am showing that what are the steps that we have taken.

We have taken the front view, back view, lateral view and superior view. these are the four views for every CT scan image that we have considered to essentially formulate this digital image data that DICOM data to printable design code that is STL file using 3D slicer. that is the first step. step 1, the way I have just described that many times this is the key step because that if you do anything wrong, then the exact precise fitting of the bone flaps into the cranium defects will not be accomplished. this step often takes the most time consuming and their most intellectual input is also necessary and then second thing is that normally once you prepare the DICOM image and patient's STL file, normally we send it back to the clinician for their approval.

and if they approve the design then only we do this further 3D printing to make the cranium model to the bone flap and so on and so forth. The second thing is that one of the major thing I repeat and I reiterate the thickness of the bone flap and as has been mentioned in few slides back that human skull in many patients is not perfectly symmetric, that causes or that adds additional challenges in the design aspect. And then when you give this 3D printer, then you give this 3D printed cranium model, then you get this PMMA bone flap. After you get the PMMA bone flap, you make intentionally several holes randomly at different locations that clinicians they do. and that actually allows that exchange of cerebral spinal fluid and other neurophysiological fluid components in that when it is placed in the implants.

if you look at this one of the patient specific cranioplasty surgery and this is a little long video and what you notice that this patient specific cranioplasty surgery. now the cranio maxillofacial surgeons and neurosurgeons they are preparing the bone flaps at the side of the operation table in the preparation they are putting the titanium screws also there or they are making some holes there intentionally as I am saying. through these holes they will be placing the titanium mini plates and screws. to place the implants perfectly at the site of the cranial defect. Like you can see, this is the titanium screws that they are putting, the titanium screws of specific size that they are putting.

And then I am just fast forwarding this particular video. at different locations they are putting. once that is done, they have made the patients under full anesthesia. I apologize to those viewers and then students who have difficulty in seeing this clinical images with lot of blood stains and that is the disclaimer that have been also used at the beginning of this course. Now these particular bone flaps this is the polymethyl methacrylate bone flaps those are now put into the cranial defect place and this is sutured and they are sutured and they are essentially placed in the patients and you can see they are kind of perfectly fitting into the cranial defects .

And after the cranial defects they are placed in this titanium bone plates and titanium screws and then you can see that it is perfectly placed at the cranial defects. at the end of the cranioplasty surgery and after everything is over then clinical outcome analysis will be assessed at different time points. I will come back to continue this particular lecture in the next class. Thank you.