Biomaterials for Bone Tissue Engineering Applications

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Lecture 1

Yeah! Welcome to the Popular Massive Open Online Courses Institute by NPTEL Government of India. The title of this course is Biomaterials for Bone Tissue Engineering Applications and I will be the instructor for this course. My name is Bikramjeet Basu. I am currently professor at Materials Research Centre of Indian Institute of Science, Bangalore and also Associate Faculty of Centre for Bio Systems, Science and Engineering that is an Interdisciplinary Research Program in the field of Bioengineering which I am one of the founding faculty and this particular program started in the year 2011 at ISC.

The subject of Biomaterials I have been pursuing for last more than last one decade. I started this research program at Indian Institute of Technology, Kanpur where as formerly a faculty member till May 2011, before I moved to Indian Institute of Science where I still pursue this subject to a significant extent. So this particular course some part of it or as a full course I have been teaching at various time points in both these premier Institutes of India that is IIT Kanpur and ISC Bangalore for both undergraduate students in Material Science and Engineering discipline as well as post graduate students at Indian Sub Science Bangalore.

So this (pa) this particular course over the years has attracted large number of students from multiple disciplines of Mechanical Engineering, Material Science and Engineering, Chemistry, Physics and a few Electrical Engineering students as well. Coming to the this specific course of NPTL this particular course is designed for the students who may not be having any formal background in Biological Science discipline and primarily from Engineering Sciences background.

Over next 20 hours of lectures I plan to combine the concepts drawn from Engineering Sciences and Biological Sciences discipline to show you how you can pursue research in the field of biomaterials which has emerged as one of the most socially relevant field of Science and Engineering discipline. Now I will I will just quickly go through that what would be the structure of this (co) structure of this h structure of this course and how I plan to progress through this next 20 hours of lecture.

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Couse content

Modules Duration	Module 1	Module 2	Module 3	Module 4	Module 5	Module 6
Week 1	Introduction	Biomaterial	Biocompatibility	Host response	Tissue engineering	scaffold
Week 2	Implant	Osseointegration	Proteins	Cell structure	Bacteria structure	Tissue structure
Week 3	Bone structure	Bone properties	Cell-material interaction	Cell-signaling	Cell fate processes	Cell division
Week 4	Cell differentiation	Stem cells	in vitro testing	in vivo testing	Prototype development	Biomechanical testing
Week 5	Clinical trials	Metallic implants	Bioceramics	Biopolymers	Biocomposites	Bioceramic coatings
Week 6	HA-Ti composites: processing	HA-Ti: Toughness	HA-Ti: Cell growth	HA-$BaTiO_3$ composites: Processing	HA-$BaTiO_3$: functional properties	HA-$BaTiO_3$ composites: Biocompatibility
Week 7	HA-ZnO composites: processing	HA-ZnO: antimicrobial properties	HA-ZnO: Cell proliferation	Dental glass ceramics: processing	Dental glass ceramics: in vitro results	Dental glass ceramics: Osseointegration
Week 8	Polymer-ceramic hybrid composites	Compression molding of acetabular socket	ZTA femoral ball head : fabrication	ZTA acetabular socket: fabrication	Summary : Biomaterials processing	Summary: Biocompatibility characterization

So as you can see in the first row that is I will there are five modules which I plan to give a series of lectures in the week one. I will first introduce that what is Biomaterial Science and how this field is different from conventional Engineering Sciences discipline. In the second module I will introduce that introduce the Biomaterials, I will define the Biomaterials, I will also make it a point to make distinction of this special material class from other structure materials.

In the third module will mostly deal with the biocompatibility which is a core concept in the field of Biomaterial Science and Engineering. This will be followed by host response meaning that when a material will be placed in an Osseous system how that (ma) implant will elicit a response in the host organism.

Fifth one is Tissue Engineering. Here again while defining the field of tissue engineering I will also try to make an effort to define the Scaffold and implant separately so that the students participating in this course would be able to distinguish the properties of Scaffold and how they are different from that of an implant. Often this scaffold and implant are used interchangeably in the field of biomaterials so therefore such distinction is extremely important as one who would try to pursue this particular field of research.

Now while defining implants the Osseo integration or the integration of the implantable biomaterial in the in the host in the host Osseo structure will be introduced. Next few lectures will introduce the students to (())(6:06) tools of the Biologicals Sciences. I will start with the proteins. I will show that how proteins can be described as a biological polimer and what are the different level of the protein structures followed by structure of a biological cell that means Eukaryotic cells. Eukaryotic meaning truly nuclear type cell.

Then prokaryotic structures that is prokaryotic structure mostly that bacteria, bacteriosis will be introduced. This will be followed by (defi) definition of the tissue and also various classifications of the tissues will be introduced like four type of tissues: muscular tissue, epithelial tissue, nervous tissue those those tissue will be defined as well as another classification note like based on the elastics stiffness properties or mechanical properties in general hard tissue and soft tissue classification will be made.

Now most of the materials which have to be used for the biological applications many of them find place as a bone replacement materials. So therefore one would like to know how the natural bone structure is and also how this properties of the natural bone are different from many of the artificial synthetic materials. Now one of the core concepts in defining biocompatibility is the cell material introduction.

Now this cell material introduction is an very important is of significant scientific importance and these will be dealt in couple of lectures in this particular course. In particular I will touch up on the cell signaling process means (low) (li) like how two neighboring cells can frost up with each other and also how different kind of signaling mechanism lead to lead to a better cell material interaction.

And this will be followed by cell fate processes like different cell (pros) like cell proliferation, cell division, cell differentiation also will be introduced. One of the cells that have received worldwide attention in last few decades is the stem cells. Now stem cells are unspecialized cells which can differentiate to various specific lineages giving rise to a large number of different cell types with different functionality.

In few of its predominant importance in the Tissue Engineering Research and Regenerative medicine, the (ce) stem cells will be introduced at that time point. This will be followed by in vitro testing and in vivo testing. In vitro means like biological testing which is carried out using petri dishes or glass wares and in vivo testing means preclinical testings or biocompatibility testing in an animal model.

So what are the various in vitro testing that are used to analyze the cytocompatibility like cell level compatibility that will be discussed and this will be followed by in vivo testing that is essentially how a material when implanted in an animal model will have compatibility with the surrounding tissue structure.

Now once this in vitro testing and in vivo testing is done in vivo testing discussion is completed will discuss about that how this biomedical device prototype can be developed using a appropriate manufacturing technique and what are the different biomechanical testing that can be conducted on this device prototypes. And this biomechanical testing would include different joint stimulated testing in the context of bone tissue engineering applications like hip stimulator like knee stimulator etcetera.

Now once an implant or a device passes through all this series of series of testing it will go to finally the clinical trials. And one of the things that we will be discussing that how to take approval or ethical committee approval for the clinical trials and for that how one should design the clinical trial study.

So this is very important because this involves that voluntary human patient's participation to receive certain implants and see that how different outcome measures of such a clinical trial which can be either single centric or multi centric clinical trials can be properly analyzed. Next few lectures I will discuss different mechanic implants, bio ceramics, biopolymers and bio composites with some emphasize also on bio ceramic coatings.

Now specific examples that I am planned to deal in this course would include largely on the hydroxyapatite based materials development including hydro xyapatite titanium composites to demonstrate that how the fracture toughness of hydroxyapatite can be significantly enhanced or significantly improved using the addition of titanium at the same time how titanium addition would not cause any (compro) compromise as far as the cell growth or cell level compatibility is concerned.

Now natural bone has inherent piezoelectric properties and it has also certain conductivity properties. So this natural bone properties is very difficult to be mimicked in any artificial material. And for that many researchers are making attempts to develop bone mimicking properties with matching piezoelectric properties and conductivity properties. So to this to this end I will show you some research results on hydroxyapatite Barium Titanate composites.

Barium Titanate is a known ferroelectric materials which has been investigated over last few decades. As a functional ceramic materials it has a specific crystal structure which is known as perovskite structure. And because of this specific crystal structure when Barium Titanate is added to hydroxyapatite metrics it can potentially increase up to electric strain coefficient and so on.

So their processing and functional properties as well as biocompatibility properties will be lastly discussed in two lectures. Now prosthetic infection is one of the aspects that limit the implant life and therefore researchers use different type of antimicrobial agents like silver, zinc oxide etcetera. So in more than one lectures I will try to address that how zinc oxide addition can improve the antimicrobial properties with uncompromised cytocompatibility property in hydroxyapatite zinc oxide composites.

While titanium is used as an dental implant materials however this crown of the dental implant materials aa can be made up of this either glass ceramics or zinconia alone and there is a there is a recent technological advances in terms of fabricating all ceramic implants as far as the dental insulation is concerned.

So in discussing these issues I will be showing some of the research results from my own group on the dental glass ceramics particularly in the aspects of their processing, their in vitro results and also integration properties. Now one of the success story as far as the biomaterial application is concerned inverse were used as total hip joint replacement.

In the typical total hip joint replacement people use titanium stem and on the top of it you have a femoral head and in this femoral head will be in con formal contact with acetabular sockets. Now this (I'll) I will explain this particular aspect with more details in the coming slides. However at this point I would like to mention that this ultra (())(16:09) polyethylene based acetabular socket has been clinically used for quiet some time.

But this particular material has issues related to their wire resistance property and therefore the long durability of this kind of total hip joint replacement have often been an issue particularly when ultra (())(16:37) polyethylene is used. So we have made an attempt to address this issue in our research both at IIT Kanpur and Indian Subscience, so some results will be shown here to demonstrate how high density polyethylene, hydroxyapatite and alumina based composites can be a potential alternative to (())(17:06) polyethylene.

And to this extent I will show you that how compression molding of the acetabular socket can be h accomplished and to give a patient specific dimensions and so on. The next two lectures will mostly involved on the prototype development of the (())(17:29) and femoral polhead and acetabular socket and their some device related device performance (())(17:37) and properties also would be introduced.

This entire course will be summarized with respect to both biomaterials processing and biocompatibility correctization and with a take home message that that one has to carefully analyze in a very logical manner the biocompatibility property of a synthetic material and much emphasize should be given while designing this biocompatibility assessment on their targeted application.

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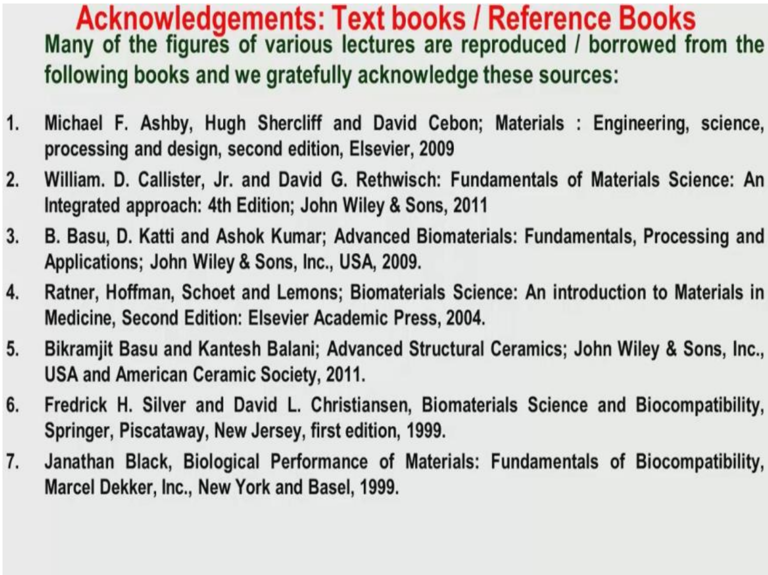

So now I will (sho) now I will ah I would like to acknowledge various textbooks and reference books which I will be I have taken h some notes some figures some tables from various books. I would like to mention one by one. First one is at by Michael Ashby's book Michael Ashby, Shercliff and Cebon that is Materials: Engineering, Science, Processing and Design published by Elsevier in 2009.

Second one by Callister that is Fundamentals of Materials Science An Integrated Approach by John Wiley. Third one is our own book that is myself with two of my colleagues from IIT Kanpur Dr. Dhirendra Katti and Mr. Ashok Kumar Advanced Biomaterials Fundamentals Procedure and Applications again from John Wiley and Sons. The first edition was published in 2009 and we are currently planning to publish the second edition.

Fourth one has been widely used as a textbook in the field of biomaterials and this book is written by Buddy Ratner from University of Washington, Seattle with three of his colleagues Hoffman, Schoen and Lemons. h the title of the book is Biomaterials Science: An Introduction to Materials in Medicine. And it is the second edition of this book is published in 2004.

Fifth one again is from my own book with one of my colleague Dr. Kantesh Balani from Indian Institute of Technology, Kanpur. The title of the book is Advance Structure Ceramics. The ceramic part of this course I will be last dealing from this our own book. It is again published by

John Wiley and Sons in 2011. Sixth one is Silver and Christiansen that is Biomaterials Science and Biocompatibility that is published by Springer, New Jersey.

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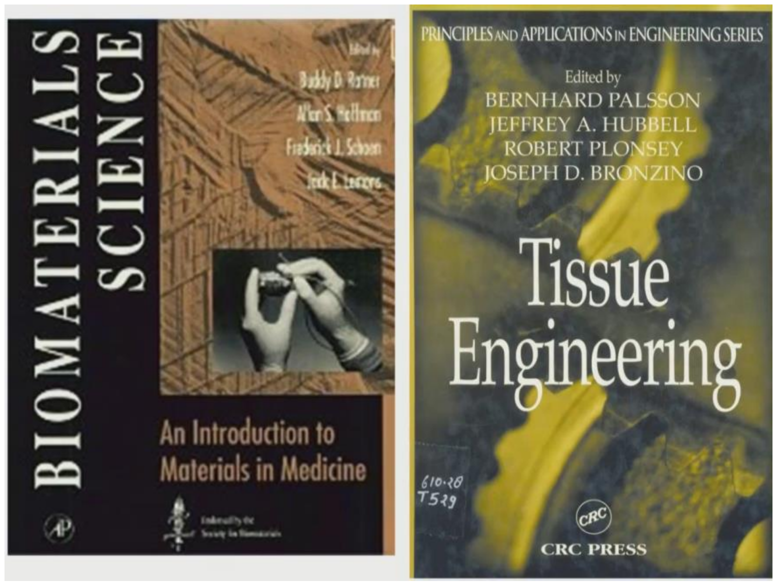

Seventh one is by Jonathan Black. Biological Performance of Materials: Fundamentals of Biocompatibility that is published by Marcel Dekkerh New York 1999. So some of this books the cover page is shown here. And the left one is this I was just mentioning few minutes ago that is An Introduction to Materials and Medicine that is by Buddy Ratner and his colleagues.

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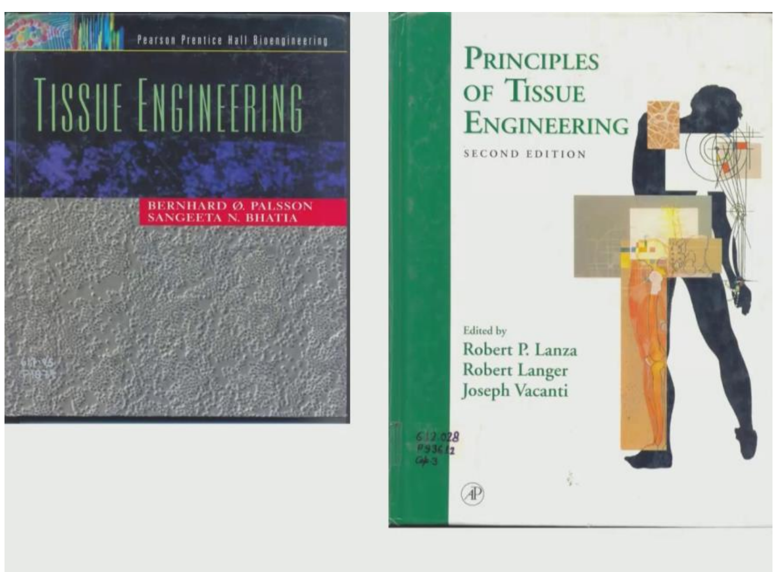

The right hand side this cover page is Tissue Engineering by Palsson, Hubbell, Plonsey and Bronzino and published by CRC Press.Sangeeta Bhatia from MIT has written one more book on Tissue Engineering with his colleague Palsson and Principles of Tissue Engineering that is again edited by Bob Langer from MIT with his two of his colleagues Dr.Lanza and Dr.Vacanti. The title of the book is Principles of Tissue Engineering.

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The left one is our own book that is this Advanced Biomaterials Fundamentals Processing and Applications. This is an edited book and the forward is written by Late Professor Larry Hench.

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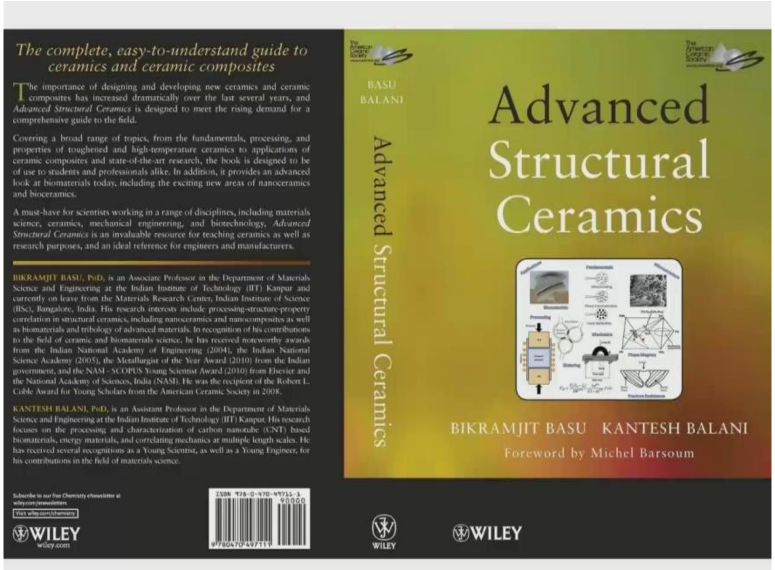

Structural of Ceramics again by our own group and with my colleague Dr.Balani from IIT Kanpur.

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Many research results that I will be showing you h during the course during this particular course are possible because of the financial support from multiple funding agencies in India and some of the International funding agencies. We have been receiving continuous financial support from Department of Science and Technology, Government of India, Council of Scientific Research Department of Biotechnology, again Government of India, DST UK India Education Research

Initiative Funding, Indo-US Science and Technology forum, Defence Research and Development Organization and Indian Space Research Organization.

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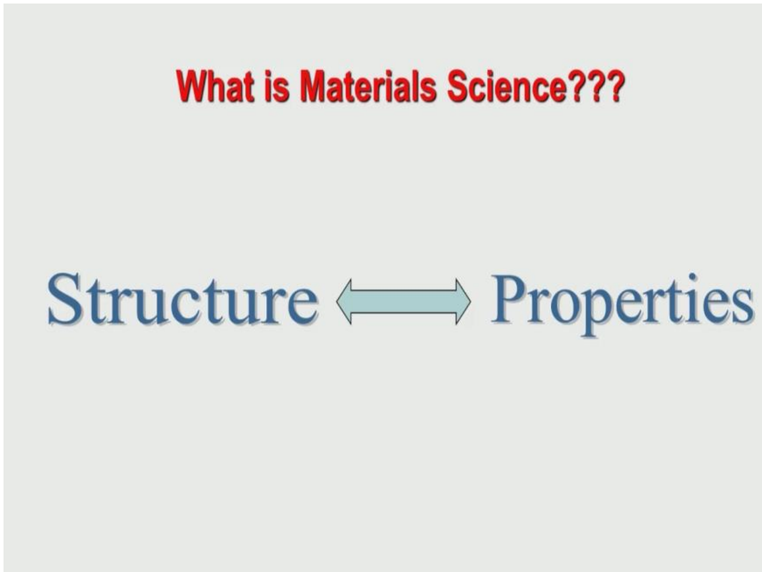

Now although many of you are from Engineering Sciences background however I thought that it is worthwhile to show you this very first slide that what is material science. So the core concept in Material Science is that it is a structure property correlations for variety of materials. So if you change the structure of a materials the properties h are going to are bound to vary.

And then structure meaning that structure can be at different length scales. Like you know that atomic scale structure, can be at the grain level structure micro structure as well as the macro structure. And the moment you change certain length scale morphology of certain microstructure elements for example grain size is a typical example that is being given in various classroom lectures to Material Science undergraduate students.

Now if you change the grain size the strength property will definitely be influenced and according to Hall-Petch relationship there course of the grains inferior the strength property. If somebody wants to increase the strength of a material then one has to go down in the microstructure length scale in terms of the grain size. So finer the grain size better is the strength property.

However this kind of direct correlation between the structure, microstructure and biocompatibility property which is a central theme of that biomaterial science is difficult is is not possible simply because of the fact that the biocompatibility property is more dependent on the surface properties rather than more on the bulk properties. And any biological response like be it protein hydration, be it cell adhesion, cell proliferation and differentiation is more driven by the cellular microenvironment.

Now this cellular microenvironment in the context of Biomaterial Science also involve the surface properties but at the same time there is other factors also would influence this biocompatibility property. You will get to know more about it as we go along with this particular course.

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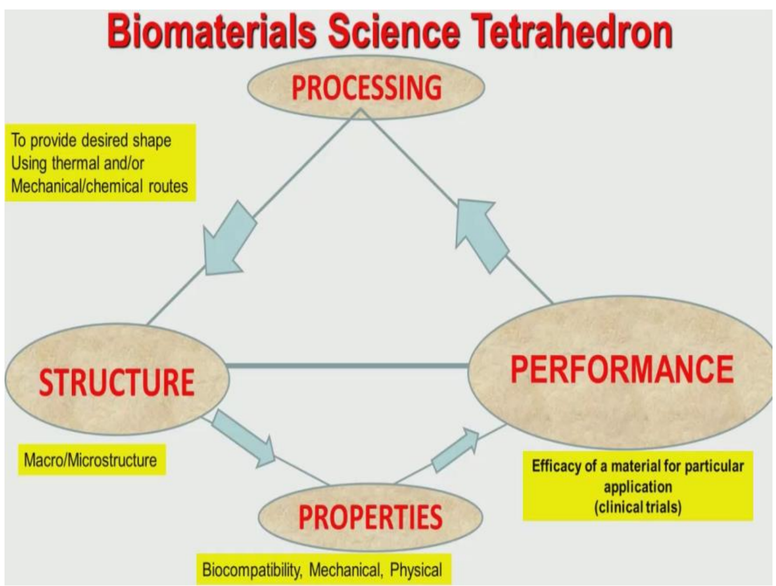

At this time point I thought it may be instructive to show you that Biomaterial Science Tetrahedon. So this is been adopted from one of the tetrahedron image that always appear on one of the famous Material Science journal that is ActaMaterialia journal. And this ActaMaterialia front cover always keeps this kind of processing structure properties performance this kind of tetrahedron and again this is a kind of core concept in the Material Science. I have tried to adopt same tetrahedon to make you understand that what are the different aspects of this Biomaterial Science tetrahedon.

Like as far as the processing is concerned one has to provide desired shape and (devic) desired shape and size using thermal or mechanical or chemical routes. These are like different processing routes. In terms of the structure both microstructure and macrostructure is important. Now properties the first and foremost properties are important that is the biocompatibility property.

And as you can see the biocompatibility property is more important h biocompatibility property is more important than any other property be it physical property like strength and so on. So just to substantiate this my statement if you consider the two materials A and B, the material B may have higher strength properties, material B may have higher fracture toughness properties than material A.

However if the material B has inferior biocompatibility properties compared to material A then material B cannot be chosen for a given biomaterial applications. So I hope you understand that biocompatibility property is of prime importance as far as the application of this biomaterials course and their mechanical and other physical property will be given lower priority than biocompatibility property.

Now finally the performance of this materials need to be assessed that how this materials can be finally useful to treat certain human diseases. And therefore this human disease model needs to be needs to be considered by developing this biomaterials. Now some of the common human diseases maybe orthopedic applications like osteoarthritis or osteoporosis treatment, there can be cardiovascular applications like stents and so on.

So where shape memory alloys like nickel titanium alloys are used. There can be neurodegenerative diseases and neurodegenerative diseases may require nerve replacement and so on by some compliant materials, elastically compliant materials. So these are some of the applications where biomaterials play an important role.

And anytime the if the (de)device design concept is changed or at any given point of time if the material composition is changed to any significant extent then this material is to be tested all through the way from physical property measurements to the biocompatibility assessment both in vitro, in vivo or preclinical study and then subsequent it to clinical trials before this material can be considered as biologically safe to be used in biomedical applications.

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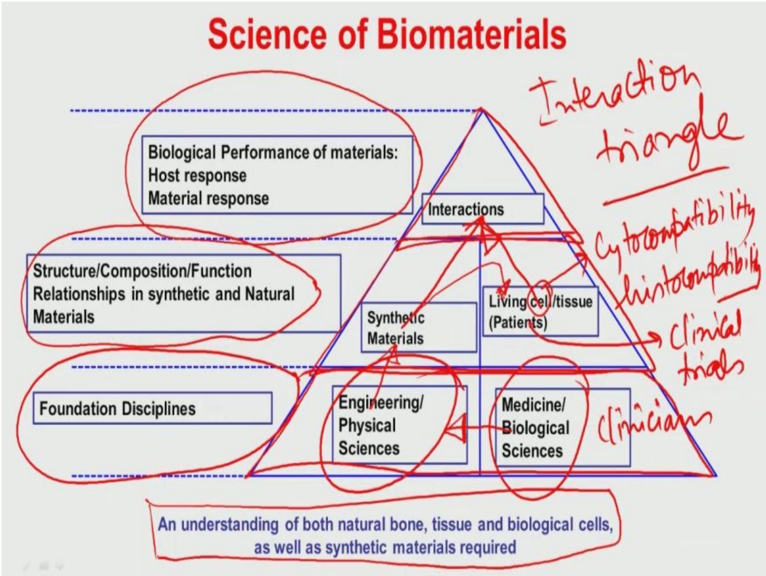

Now the above (th) ff the preceding discussion can be sarized h to some extent with this interaction triangle so what we call this introduction triangle. And that this base h in the base of this interaction triangle as you can see that there is two remotely linked disciplines. One is the Engineering and Physical Sciences and one one is that Biological Sciences and Medicine h these are mentioned.

So essentially that first thing that one has to understand that the biomaterials development should be driven by the clinical net or biomaterials development should be inspired by the fact that the (ma) that materials that we are going to develop should ultimately be used to treat human diseases. So this arrow therefore indicates that one needs to interface with clinicians at hourly stage of research on biomaterials.

And clinicians would need to define that what are the relevant clinical problems and how the new biomaterial concept can potentially help h this particular clinical need. Now one of need certainly the Fundamentals of the Engineering Sciences discipline to develop synthetic biomaterials. And this synthetic materials necessarily to the synthetic materials have to interface or interact with the living cells or tissues.

And this living cells essentially you need to establish the cytocompatibility property like compatibility at the cell level and also histocompatibility property means compatibility at the tissue level before it can be passed for clinical trials or before (eu) one can even consider to go for the clinical trials in patients. So essentially the patients means this is a clinical trials. And the earlier two assessments these are like at the preclinical level.

Now this interaction essentially are very important and these interactions h will define that how a synthetic material can interface with biological systems. Meaning like what is this living cells or protein interaction with the materials and when implanted in an animal model how this synthetic material would interface with a tissue of particular animal model.

So while describing this three levels of this interaction triangle, the first base level is actually the foundation disciplines that is the Engineering and Physical Sciences. The next level h here we have to define what is the structure, composition or functional relationship in synthetic and natural materials. And the highest level or the top of this interaction triangle would define that what is the biological performance of the materials with respect to host response and material response.

So the comment that I have made at the end of this slide is very relevant that all the discussion we had so far would clearly place an importance for you to understand h both natural bone tissue and biological properties in terms of their structure and properties as well as how the structural materials can be manufactured and processed in laboratory.

And how this synthetic materials their properties will vary from that of the natural bone therefore the Material Science approaches need to be adopted to develop bone mimicking materials. I think I would stop now and then I will come back for the next lectures.