Introduction to Biomaterials

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Module No. # 01

Lecture No. # 01

Introduction to basic concepts of Biomaterials Sciences; Salient properties of important material classes; overview of body environment-1

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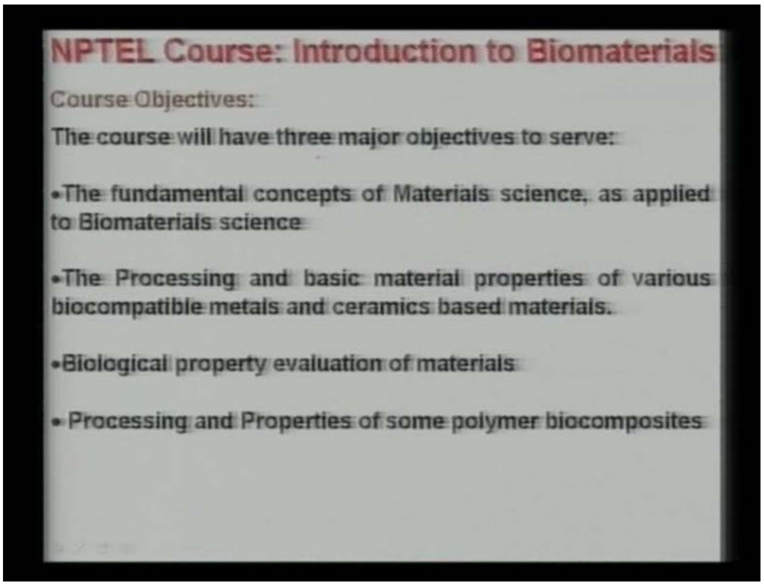

Good evening everybody. So, welcome to this NPTEL Course, introduction to biomaterials. Now, this course will have all together 42 lectures and this is the first lecture. So, first I will go through the, go through briefly the course objectives. The end of the course, it is expected that the students will be able to understand the fundamental concepts of material science and what is required to apply for biomaterials science.

Then second one is, the processing and basic material properties of various biocompatible metals ceramics and polymer based materials. Third one is, the biological property evaluation, like what are the typical biological properties that need to be evaluated to understand the potential or application of a given biomaterial and then finally, that processing and properties of some polymer bio-composites. So, these are like, most recent developments in the field of biomaterials, that also will be covered as part of this course.

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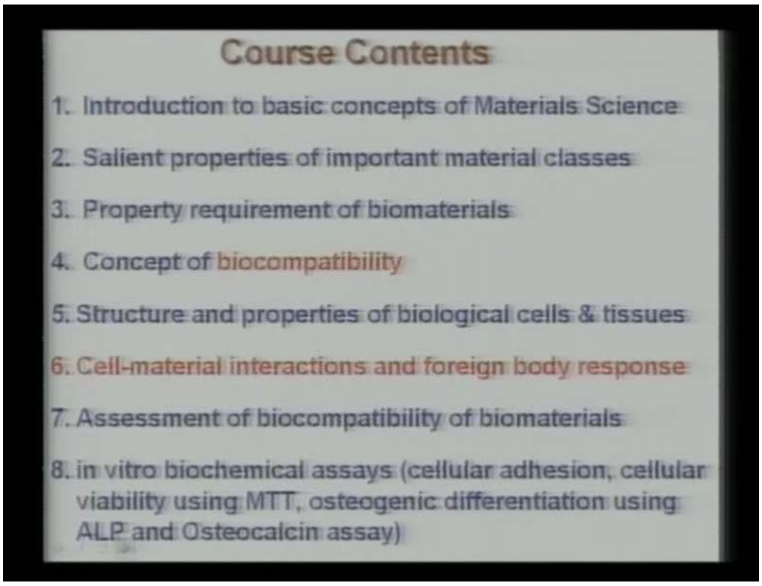

Now, this is briefly the course contents. So, first I will introduce you to the basic concepts of material science, because the biomaterials field, actually many people from a number of different disciplines like biology material science, mechanical engineering they all work together in this area. So, it is important first to have the basic concepts of material science. It will be then, followed by the salient properties of important material classes, namely, the material ceramics and polymers. Third one is the property requirement of biomaterials; the fourth one is the concept of biocompatibility.

So, biocompatibility is the core idea, with the core property requirement for the development of biomaterials. Therefore, an in depth understanding of what is meant broadly by the biocompatibility that, needs to be understood.

Now, essentially this biomaterials means, it is a it is an interface of the biology and material science. So, one is to have sufficient background of the biological cells and tissues, particularly what is the structure of biological cells. Then essentially, I will also be dealing with, at some stage, the structure of the protein molecules, polygons and hard tissues, soft tissues and so on. And then, what is the properties? Properties means, I am talking about mostly the physical properties and mechanical properties.

So, among these first five points, that biocompatibility is extremely important. So, I would like to put more stress on this biocompatibility. Then, comes, the cell-material interaction and foreign body response. I will try to deal mostly the theoretical aspects or theoretical understanding of a cell-material interaction; that means, how a biological cell interacts with a synthetic material and as well as the foreign body response. Like you know, when you implant material will be (( )) synthetic material will be implanted in the human body. What would be the response of the animal or what would be the response of the human being to this implanted material.

Then, seventh point is that assessment of biocompatibility of biomaterials; that means, what are the different ways, like what are the different testing procedures; how these biomaterials need to be evaluated. The next point is that in vitro biochemical assays, so here, I have mentioned, some specific in vitro biochemical assays that I will be dealing as part of this course. That is named the M T T osteogenic differentiation, using an L P and osteocalcin assay, so on.

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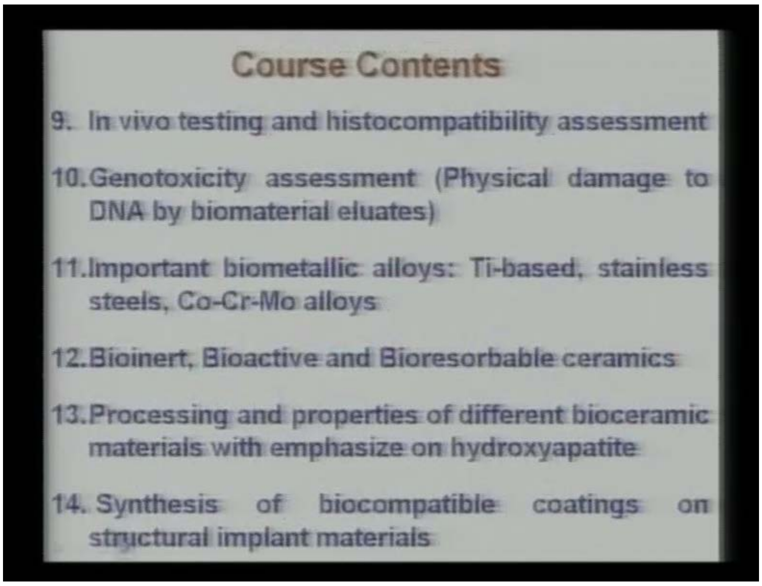

Now, after the in vitro testing, one needs to do in vivo testing and histocompatibility assessment. So, that will be also part of this course. Now Genotoxicity, Genotoxicity means when a biomaterial will be implanted inside the human body or any animal, then what would be the influence of the biomaterial elevates on the gene level toxicity. Like, whether this material will have any influence, so that, the D N A will be damaged and if D N A is damaged, then to what extent D N A will be damaged. What are the mechanisms of this D N A damage? Whether once this D N A is damaged, whether this D N A can be repaired by itself and how long it will take for this repair of that D N A.

So, all those things will be discussed in this course. Then, coming to the material part, one of my colleagues, Dr. Balani will be dealing with some important bimetallic alloys like, titanium based alloys, stainless steels cobalt chromium alloys. So, mostly these are like, these are used as the load bearing implant material.

Now, I will be dealing some part of the bioactive ceramics like hydroxyapatite base materials, bioresorbable ceramics like (( )) and so on. So, there will be lot of emphasize on the processing of hydroxyapatite base materials, because these are the materials which are widely researched in around different research labs in the world. Then, synthesis of the biocompatible coatings on structural implant materials, like hydroxyapatite coating on titanium or stainless steel. How they can be processed, what are the properties of this hydroxyapatite coatings and so on; that will also be discussed.

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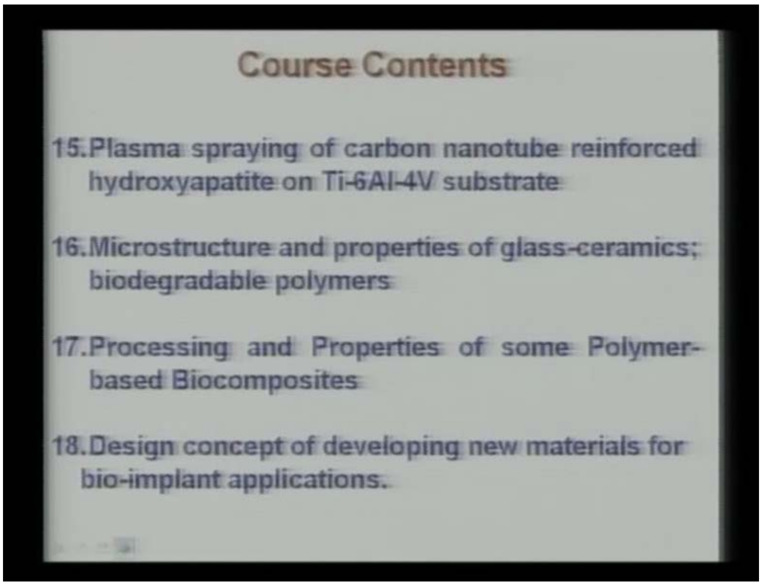

Now, plasma spraying of the carbon nanotube reinforced hydroxyapatite, that is the specialty of the other colleague Dr. Balani, who will be taking some lectures as part of this course. Now, microstructure and properties of glass ceramics. These glass ceramics are essentially used as a dental restorative materials.

So, these are researched in our group for quite some time now. So, I would like to spend some lectures on this glass ceramic based materials, mostly micro based dento glass ceramics. I will again focus there, on the, more the material aspects as well as the biological aspects. Mostly, material aspects means, how this glass ceramics are prepared by conventional heat treatment as well as (( )) and how their properties will differ, will vary depending on what is the content of the crystalline ceramic phase, in this glass material.

Now, coming to the next material class that would be dealt in this lectures, polymer based bio-composites like hydroxide polyethylene based ceramic composites. Lastly, we will be dealing with that, what are the design concepts for developing new materials for Bioimplant applications. Like, what are the different property requirements and how these properties can be optimized and how to process the different implant materials? The desired combination of both physical, as well as biological properties, those will be discussed towards the last few lectures.

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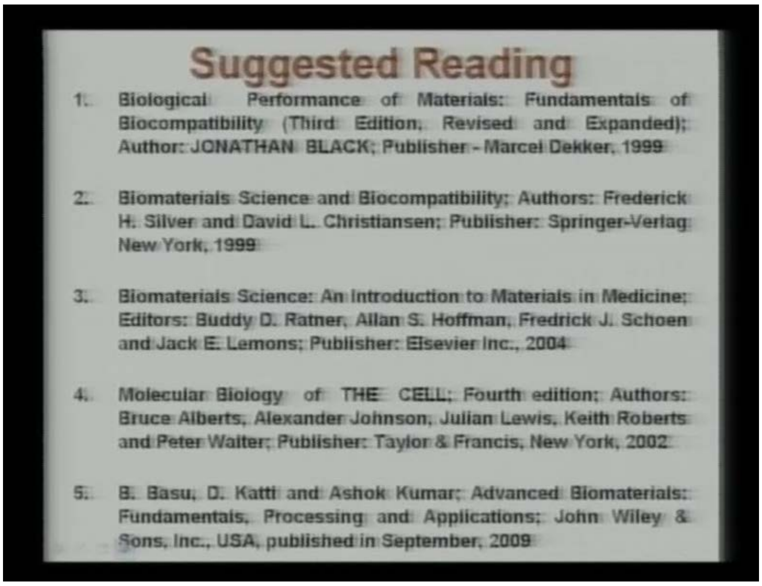

Some books that will be helpful in this a biomaterial course, the first one is that by Jonathan Black, who wrote this book in 1999, that is the biological performance of materials, fundamentals of biocompatibility. The second one is that Silver and Christiansen, that is biomaterials science and biocompatibility. Third one is that by Buddy Ratner from University Washington, Seattle. Actually he, along with his some of his colleagues wrote a book, who this "Biomaterials science: An introduction to materials in medicine". This book has been used as text book for this kind of course in many universities around the world.

Molecular biology of the cell. So, that is by Bruce Albert and again it is, this book is mostly devoted to the discussion on the molecular biology aspect of the cells structure, the different signaling processes, how this the extracellular matrix has been formed. All those things are discussed in details, from more from biological aspect in this book.

And then fifth one that is the book that we recently edited, that is the advanced biomaterials fundamentals processing and applications. So, this has been recently published by John Wiley.

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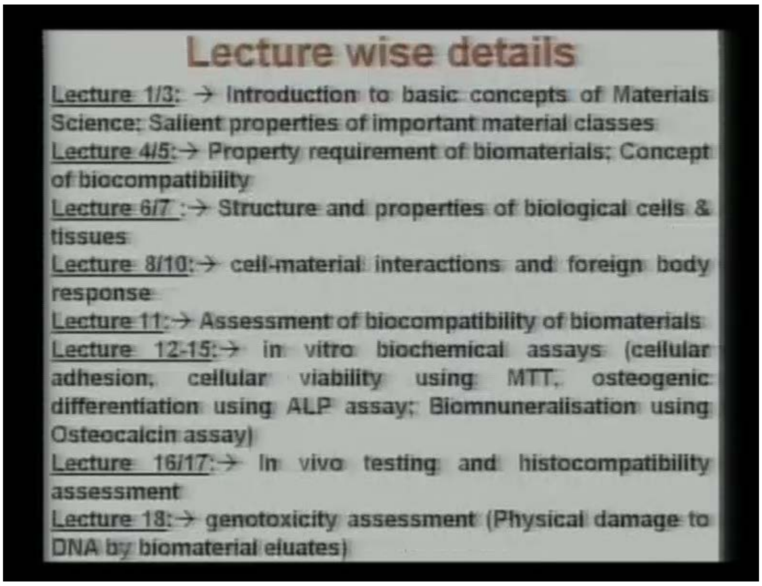

Now, these are the lecture wise details. So, first two or three lectures, I will be mostly dealing with the basic concepts of materials science, salient properties of important material classes. Then, next two lectures will be on property requirement of biomaterials concept of biocompatibility. Again, I would like to emphasize that concept of biocompatibility is important. So, one who needs to to research; one one who needs to really understand that how this biomaterials need to be developed in the laboratory or at the research lab or at the industrial scale production.

So, first we need to understand that what is meant by biocompatibility. Then, six and seven lectures will be on structure and properties of biological cells and tissues, and there I will also be dealing with the (( )) instructions and so on.

Then, lecture eight to ten will be cell material interactions and foreign body response. Lecture eleven, would be on assessment of biocompatibility of biomaterials, like what are the in vitro assays and in vivo assays, that will be covered in the following lectures. Lecture eighteen would be on genotoxicity assessment, that is, physical damage to D N A by biomaterial eluates. So, I will be mostly dealing with the comet assays and at the same time, I will be discussing our recent research results on the hydroxyapatite based materials genotoxicity affect.

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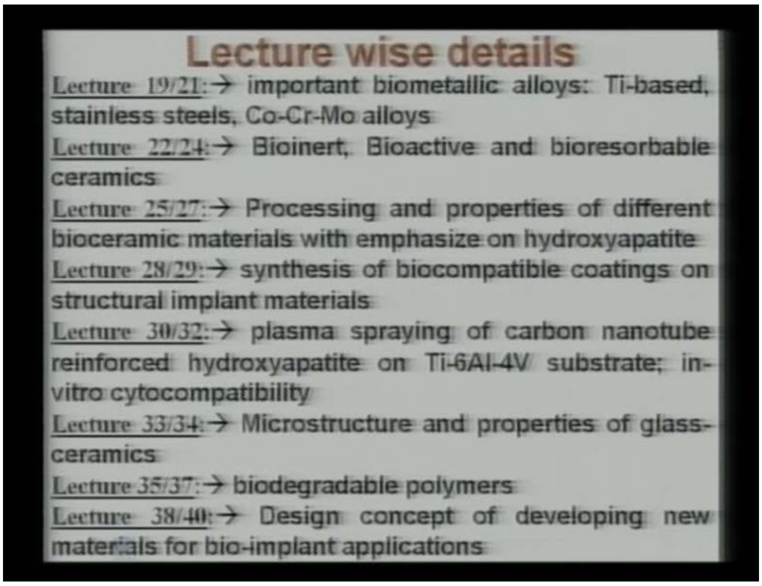

Lecture nineteen to twenty one, would be on the metallic materials. Similarly, other lectures, other subsequent lectures will be discussing the recent developments in bioinert, bioactive and bioresorbable ceramics as well as hydroxyapatite. There will be two lectures that will be on the biocompatible coatings, on the structural implant materials and then some lectures will be on the, specifically on the, carbon nanotube hydroxyapatite coatings on the titanium base substrate. Last few lectures will be on glass ceramics, biodegradable polymers, as well as design concept of developing new materials.

Now, the question is, what is material science? Material science, essentially deals with the structure property relationship for different materials. Like how, this, if the structure, that means, I, we are mostly dealing with the microstructure here. Like, if the structure at the micro scale, if they can be manipulated, how that will influence the properties. That is the core concept of the material science.

Now, this concept can be successfully applied, to understand the behavior or the properties of metals ceramics, polymers as well as the composites.

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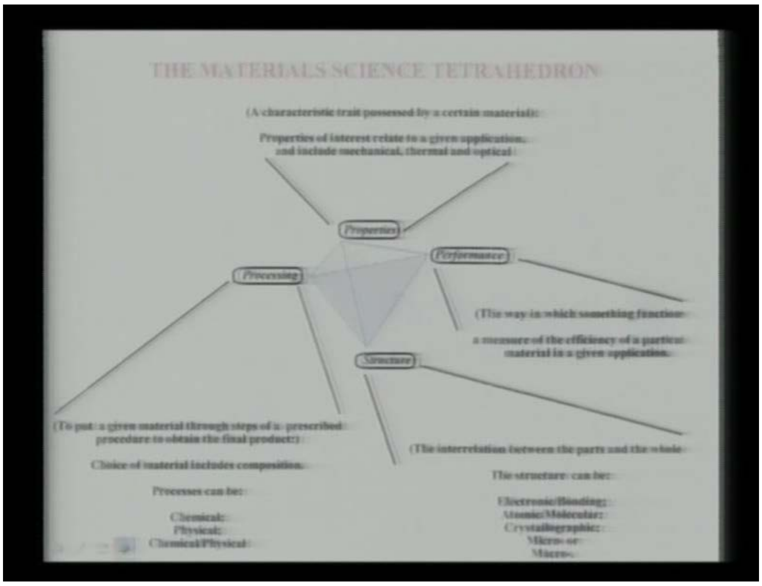

Now, this is the famous quadrilateral of the material science, about tetrahedron of materials science tetrahedron. So, this also appears in the one of the prestigious channel of materials science like (( )). And here, at the four corners of the tetrahedron, there are processing structure property, as well as performance. Like, now if I want to explain it little bit further, if I change the processing here, this processing will definitely change the structure of the materials, the way the processing is, the process parameter is baring.

For example, if I change the scene fringe temperature or if I change the scene fringe time, that will definitely will have a directly influence on the microstructure of this materials.

Now, if the structure is changed, then this structure will definitely influence the properties like hardness, fracture, toughness, spring properties. If the materials is compete tent, then it will have a better strength property. If materials is poorer, that will have poor elastic modulus poor spring property.

Now, if the material has inferior properties, they will definitely lead to a very poor performance, whether it is structural performance, whether it is a biological performance and so on.

So, what I am trying to see here, that all these properties processing structure, property performance, they are all four related with each other.

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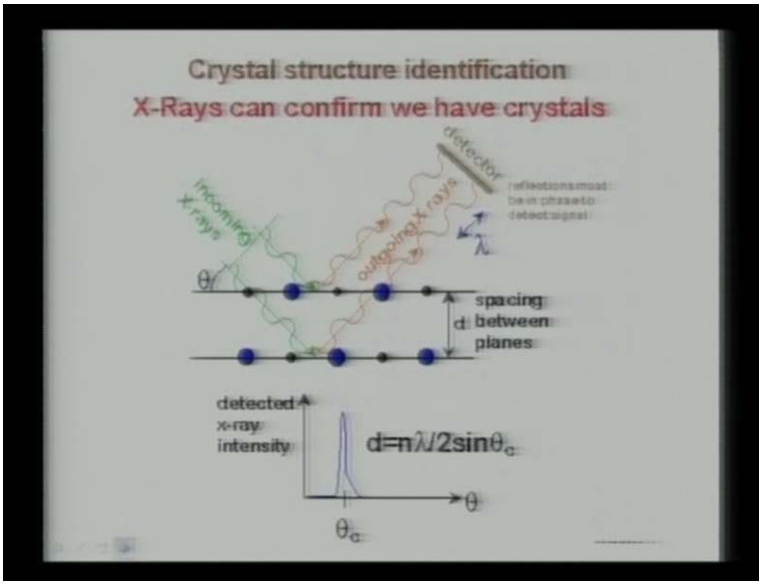

Now, how the structure can asses in a particular material. One of the simplistic way to use that extra diffraction. So, this extra diffraction means, like, if there are two parallel atomic planes, then if the incoming x rays are coming here, now they will be diffracted by the atomic planes. This diffraction based on this; what is angle of diffraction, then you can find out, there is bragg's law which is, n lambda is equal to 2 d sin theta.

This n means, that is, order of reflection, lambda is the wave length of the X ray, d is the inter-planer spacings here, what is meant by d here and theta is the angle that I have explained just now.

Now, depending on what is the material, what is the composition all the materials will diffract the x rays that characteristics wave length and at a characteristic angle theta. Once, we have a intensity first as 2 theta, that is the plot, then you can find out that depending on which is copper nickel or iron, it will have the characteristic. We can, that is the way you can actually find out the presence of different materials or different phases in a microstructure.

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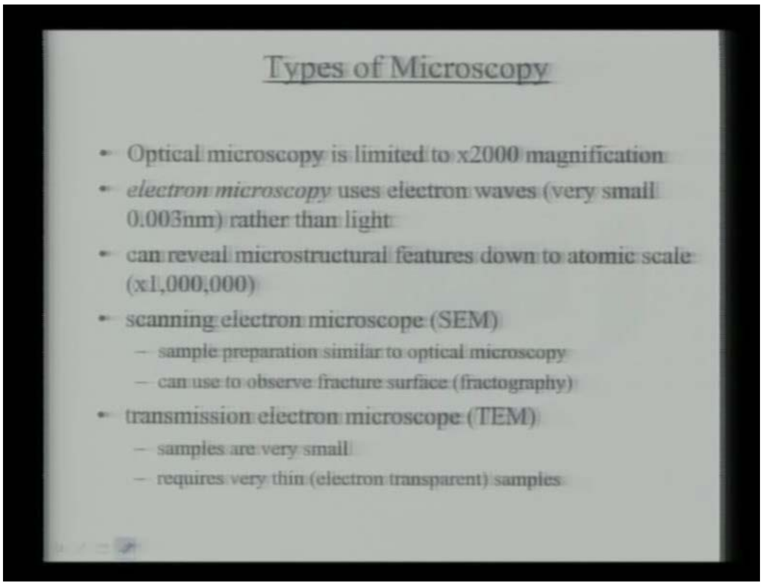

What are the different microscopy one would be use in this material science? First one is the optical microscopy, which essentially uses the simple optical rays or simple light. This light, in because of the large wave length of this light, the magnification is also limited. Like, you cannot really go through the very high magnification here.

Then comes the electron microscopy, which essentially uses the electron waves and it has a very small wave length, which is of the order of 0.003 nanometer, depending on what is the accelerating voltage. Then, these electron microscopy like scanning electron microscope or transmission electron microscope, the way I have mentioned here, they can be conveniently use to reveal the structure at a much more details, like up to 1,000, 000 or more than 1,000,000 magnification.

Now, scanning electron microscopy is very easy to make the samples, because sample preparation is very similar like ball samples can be used; what transmission at the microscope, the samples need to be essentially very thin. These thin samples, essentially require because this should be electron transparent. That is, one of the important criteria for the samples to be used in the transmission electron microscope.

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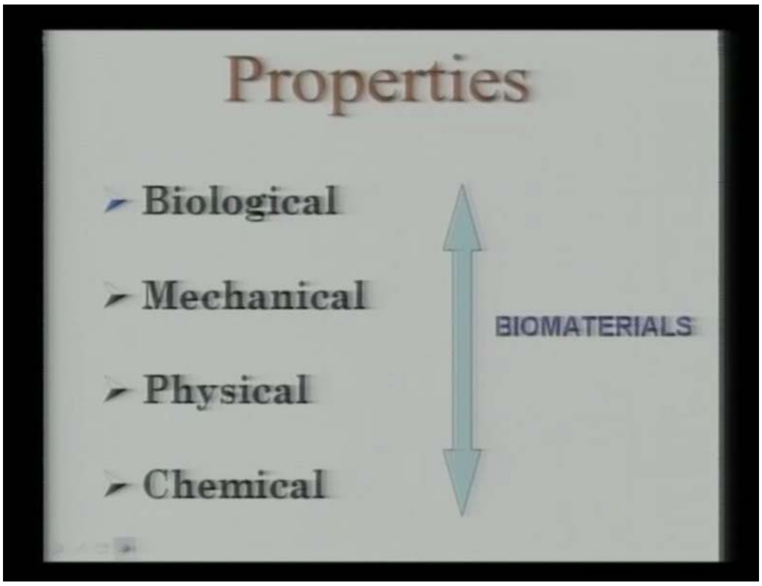

Now, what are the properties that should be required for biomaterials? The first one is the biological properties. This biological properties mostly means, like you know, what are the, whether the material is bioactive, bioinert or biodegradable in the in vitro in vivo environment. Then comes mechanical properties like, you know what is the strain. So, biological properties is the most important parameter here, as far as the biomaterials application is concerned.

Now, next comes mechanical properties. Here, I would like to draw your attention to the fact, that mostly in the material science, where the materials had to be used for structural applications, it is the mechanical properties many times which you are required to be optimized. Mechanical properties need to be optimized or beta mechanical properties has the criteria that is set for various applications. Like you know, you should have very high hardness or high strength, but, when it comes to the biomaterials applications, it is not the mechanical properties, but, the biological properties must be first evaluated to a satisfactory level.

Now, if the biological properties, they meet the criteria for the material to be used in the biological applications or in vitro or in vivo environment, then only the other properties will be of relevance, like mechanical properties, chemical properties or physical properties.

So, therefore, biological properties as opposed to mechanical properties, that need to be evaluated and that need to be given more importance while evaluating the biomaterials, while evaluating or while developing the biomaterials.

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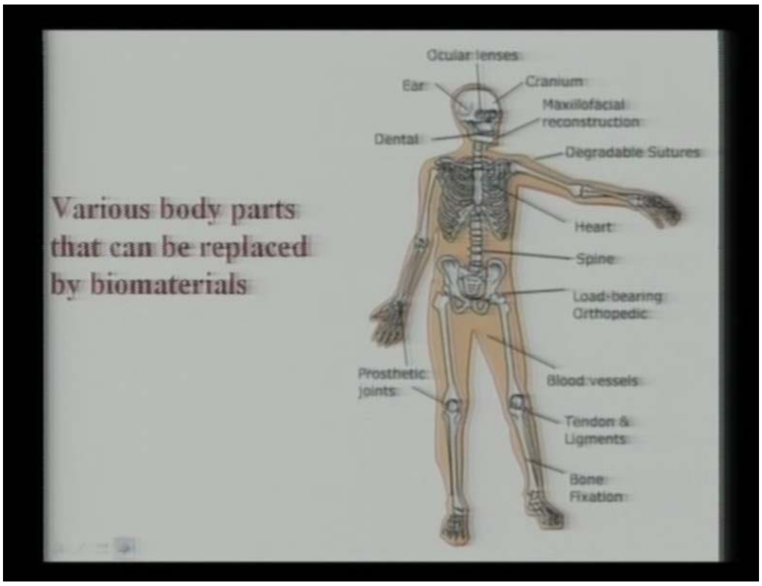

Now, this view graph essentially shows, that you know that different body parts of human being, which can be potentially replace by synthetic materials or biomaterials. So, essentially, this synthetic materials, this can be either metals or synthetic metals or ceramics or polymers or their composites. These materials, they can essentially replace either dental, for example, dental restorative like glass ceramics I was talking about, so this dental applications. Many of the ear implants, like you know, in the ear they use this hydroxyapatite base materials. Now cranium or the brain surgery, people use some materials which are radio transparent like some of the polymeric base materials, they can be used in cranial applications.

Maxillofacial reconstruction also, people use some synthetic materials; heart valve like carbon Polytetrafluoroethylene, in that they can be used as the artificial heart valve. So, then spine also, some load bearing implants can be used. This orthopedic implants like hip joint or knee joint, here a combination of materials need to be used like metals, ceramic, polymer. Like typical in the heap joint, the stem had to be made by titanium, the femoral ball can be ceramic like alumina and then, there is a articulating surface which can be made of a ultra high molecular polyethylene or high-density polyethylene.

So, these kind of materials is not a single material that can be used at all parts of the total hip replacement, but, a combination of materials that needs to be used. Similarly, for knee joints also, people use the cobalt chromium alloys or ultra molecular polyethylene. These are like typically used in this knee joints also.

So, these I must here mention that, both these knee joint as well as these hip joint, their mechanical properties are also important. But again, here I would emphasize, that again biological properties first, then mechanical properties, the second mostly important property in this kind of applications.

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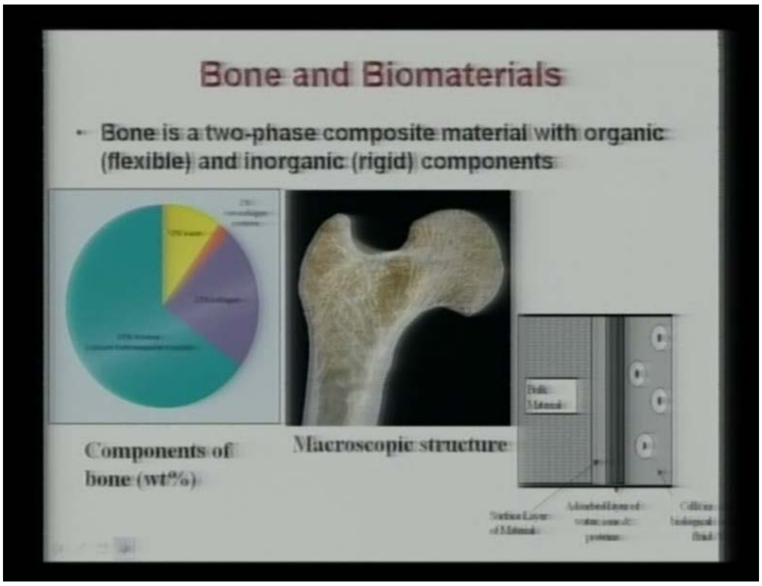

Bone and biomaterials. Like, what are the typical compositions of a bone? So, this one actually shows the microscopic structure of a typical human bone. Now, you can see it has a very irregular kind of a fracture, right. It is a part of femur and this left hand side, this shows actually the part of the different components, which have contained in this bones structure. And, what you see here, the 65 percent of the calcium phosphate, that is, calcium hydroxyapatite mineral, these are present along with 23 percent of collagen.

Now, this collagen is actually polymeric based materials, mostly protein based materials, then, you have 2 percent non-collagen type protein, then 10 percent water. So, essentially what you can say here, from this structural point of view, that bone is nothing but, bone is equivalent to polymer ceramic composites. This ceramic composite, it has essentially natural hydroxyapatite and this hydroxyapatite content is 65 percent and then rest of this third half is that 23 percent collagen. So, accordingly, some amount of research is also being carried out by various research groups on the developing the polymer ceramic composites to mimic the natural bone composition, natural bone structure.

Now, this shows, that you know, when we implant the biological material or biomaterial, then how this cell material implant takes place. But, this will be discussed in more detail in some of the future slides.

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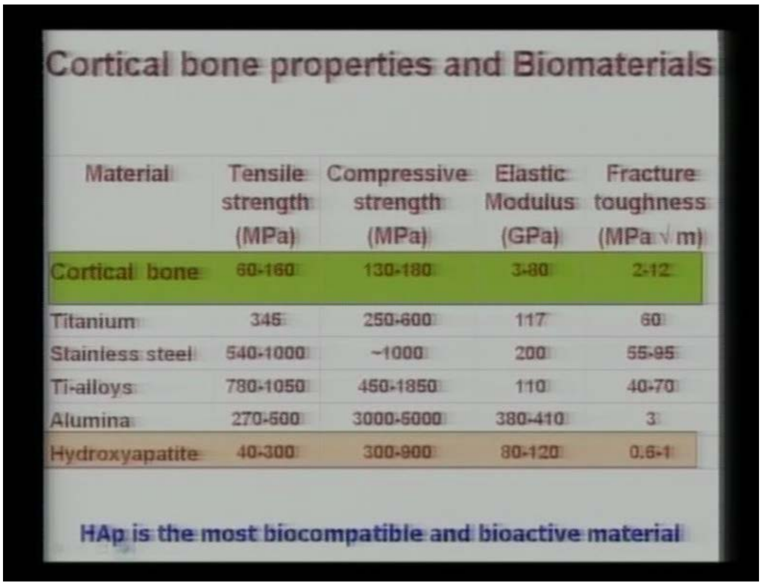

Material	Tensile strength (MPa)	Compressive strength (MPa)	Elastic Modulus (GPa)	Fracture toughness (MPa √m)
Cortical bone	60-160	130-180	3-80	2-12
Titanium	345	250-600	117	60
Stainless steel	540-1000	~1000	200	55-95
Ti-alloys	780-1050	450-1850	110	40-70
Alumina	270-500	3000-5000	380-410	3
Hydroxyapatite	40-300	300-900	80-120	0.6-1

Now, coming to the cortical bone properties and different materials, this particular table tells you, that you know, what are the different properties or combination of properties that one can create with a natural bone.

So, first let us focus on the cortical bone, which is the compact bone or compact part of the bone, if it is not a cancellous porous bone. So, cortical bone is that most the outer cell of any femur or outer cell of a mostly mature bone. Now, this mature bone, depending on the anatomical location, now if you see that there is a large variation in the tensile strength, like tensile strength varies from 60 to 160 M P A. Now, this large variation tensile strength essentially, is due to the anatomical location. That is, depending on the anatomical location of this cortical bone in the human body, like whether it can be shoulder or whether it can be thigh or whether it can be hand, depending on what part of the anatomical location that bone you are taking from. So, depending on that anatomical location, your cortical bone property also vary. This variation essentially depends on the anatomical location, but, largely what you can see, compressive strength property is around 130 to 180 M P A, elastic modulus is around 3 to 80 G P A and fracture toughness, depending on again anatomical location is around 2 to 12 M P A square root meter. Now, I have put a star on this fracture toughness because, I want to highlight here that hydroxyapatite, pure 100 percent hydroxyapatite, which is the most biocompatible and bioactive material and all the materials being investigated or developed till today, they match most of the properties of the cortical bone. Like you know, it has also equally high tensile strength, much better compressive strength property than natural bone.

Elastic modulus also can be tuned to some extent by 80 to 120 gigapascal. But, however, if you look at this fracture toughness property, this fracture toughness is around .6 to 1 M P A square root meter. This does not even meet the lower bound of the fracture toughness of the cortical bone, which is around 2 M P A square root meter. So, therefore, you need to improve the fracture toughness of the hydroxyapatite by some means, so that, it needs this particular requirement of the cortical bone property of the fracture toughness. The second point; so, first point as you can mention or you can note down, the fracture toughness is important and fracture toughness needs to be improved for this hydroxyapatite, in order to meet the lower bound of the cortical bone property.

The second point is the elastic modulus. Now, this elastic modulus also needs to be tuned for all the synthetic materials. This needs to be tuned between this level, 3 to 80 gigapascal. Now, if the elastic modulus is very high, then what will happen? The materials will carry most of the load, instead of the natural tissue, which is around the synthetic material. For example, if you look at the titanium, the elastic modulus is 117 stainless steel it is 200, titanium alloys is around again 110 and alumina is very high around 400 gigapascal.

Now, this magnitude of this elastic modulus here, clearly shows that, pure titanium, pure alumina, if they are used, they really over shoot the cortical bone property. However, hydroxyapatite, they are kind of at the higher level or higher, near the higher bound of the elastic cortical bone. So, therefore, this elastic modulus also needs to be studiously controlled. So that, each actually meets the, it is somewhere in between the two bounds of the elastic modulus of the cortical bone, like lower bound as well as in the upper bound of the cortical bone property.

So, this is important; otherwise, this mismatch in elastic modulus, this elastic modulus mismatch can lead to what we call in biological Biological science, that is called aseptic loosening. Aseptic loosening means, that material will take most of the load and as a result, after sometime, material will be loosened and will will break their biological contact with the neighboring tissues and then there will be stress shielding effect. Once this aseptic loosening takes place, then the implant will be failed and the implant failure leads to revision surgery and there is extreme pain on the patient.

So, we do not want the aseptic loosening to take place. In case of the synthetic material, and that is the reason, I am emphasizing on the fact, that aseptic, that elastic modulus mismatch needs to be avoided to the maximum extent, as much as possible to get a better biomaterial with acceptable property.

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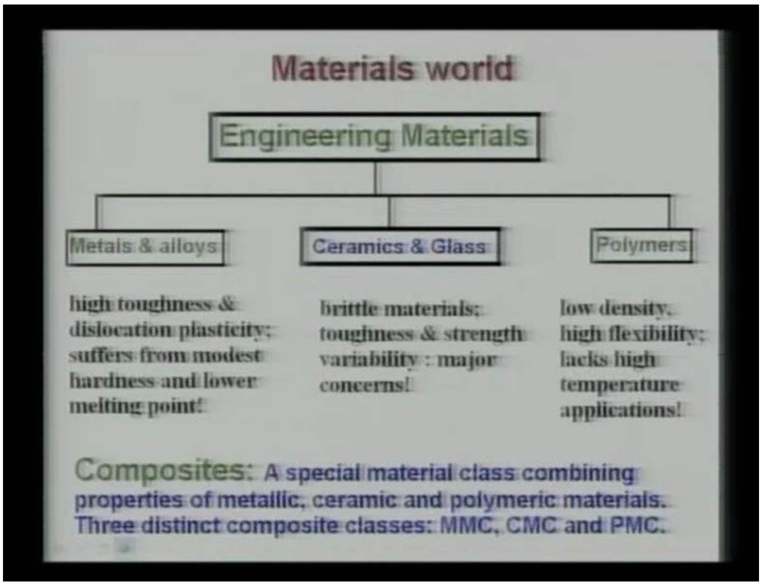

Now, coming to the different materials as I said, that you know, I will be dealing also with that. You know different excess of materials. So, essentially all the engineering materials, they can be classified. So, these metals, ceramics and polymers, what I call them, these are like primary material classes. Primary material classes means, these are the major materials, but, they are different in properties and they have certain advantages properties and they also lack in some properties. For example, metals and alloys, they have very high toughness. This toughness property is very good, but, they have a very modest hardness, like hardness is not very good when compared to ceramic based material.

Now ceramics, they have toughness and strength variability. These are major concerns, in case of the ceramics and they are essentially brittle. So, these these things needs to be also taken care of, that you know, while developing ceramic based composites. Now, when in the case of the polymers, polymers have a low density, it has a high flexibility, but, it really lack the high temperature applications.

However, this high temperature application is not really went for biomaterials applications. Now, when it comes to composite, so essentially, you can make metals with ceramics. So, which you call, if the metal volume percent is more than 50 percent, we call it M M C; that is meta matrix composites. Now, you can call also ceramic matrix composites like ceramic, if the ceramic volume fraction is much more, then it is called ceramic matrix composites.

Now, if the polymer volume fraction is much more than ceramic, then we can call them PMC; that is the polymer matrix composites. Now essentially, all this composites are developed to take advantages or to take essentially, to optimize the good properties of the metals with the good properties of the ceramics. Or, essentially to combine the advantages properties of the two materials to develop a better material with better combination of properties. That was the major motivation of developing the composite materials.

And I repeat here, that metal matrix composites, ceramic matrix composites and polymer matrix composites, these are like three different classes of composite materials which are developed and started.

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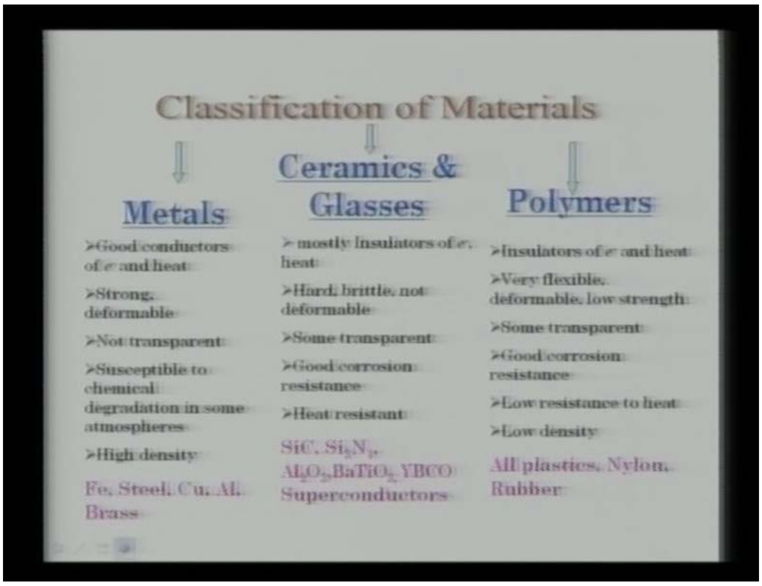

This is like; you know little bit more about these three different materials, like metals, ceramics and polymers. Some of the examples are given here like iron, steel, copper, aluminum, brass; like steel is an essential alloy of iron and carbon.

So, this carbon, as an instead industrial element in the iron and that alloy is called steel. Similarly, copper zinc is crossed. So, these different alloys, different metals, they are traditionally used for various conventional applications.

Now, some of the ceramics which are bio compactable like alumina. They are also developed for different applications. Polymers, like you know, high density polyethylene or essentially polyethylene based or P, that is the poly ethylene ether ketone, these are like different bio comfortable polymer.

Now metals, they are strong and they are deformable, but, not transparent. These are, essentially high density, for they are much heavier. Now, ceramics, they have good properties like very high hardness, but, this is a concern, like they are very brittle and they have a good corrosion resistance. Polymers, they are very, some are transparent; however, they are very flexible, deformable and they have a low strain.

So, these are like, those highlighted parts or those underlined properties, these are somehow relevant to biomaterial applications.

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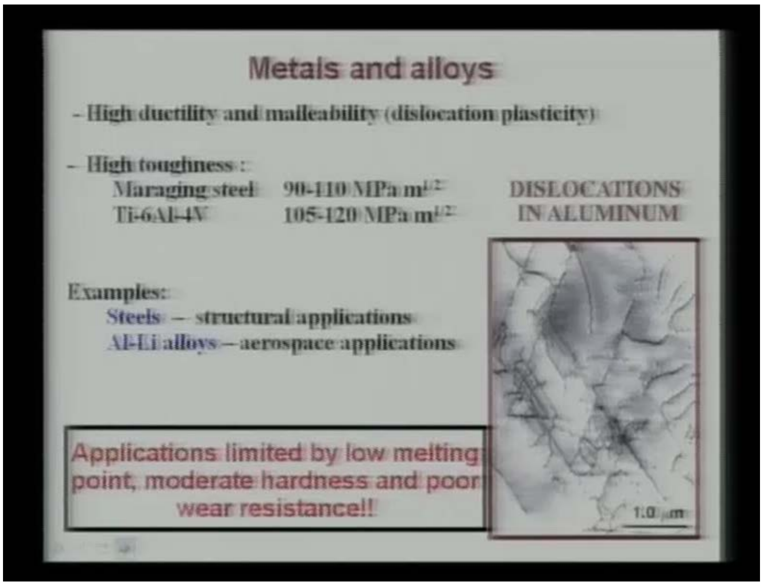

Now, some of the alloys, like biomaterials, like titanium 6, aluminum 4 V, these are the extremely high toughness by 105 to 120 mega pascal square root meter. Most of the ceramics, they have a toughness of place than K (( )) square root meter. So, some of the metals, which are used in biological applications, they can have one order of magnitude higher fracture toughness, than their competing ceramic base materials. And, however, these applications are essentially limited by the moderate moderate hardness and poor wear resistance properties of the metals.

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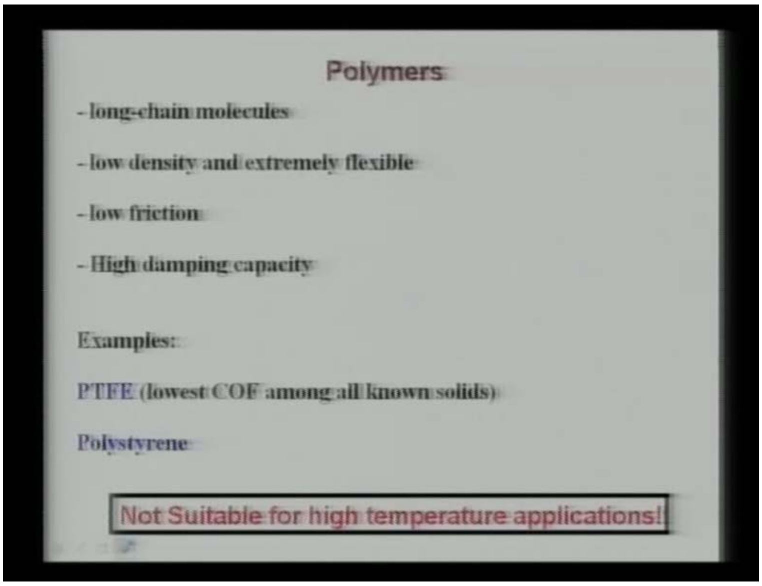

Now polymers, now they are essentially are composed of meuniers or monomers and they are essentially long chain molecules. They have a very low density and extremely flexible. There will be low friction and typical polymers, which are used in hot fall, for example, polytetrafluoroethylene or polystyrene. These materials are certainly not suitable for very applications, which are essentially for very high temperature.

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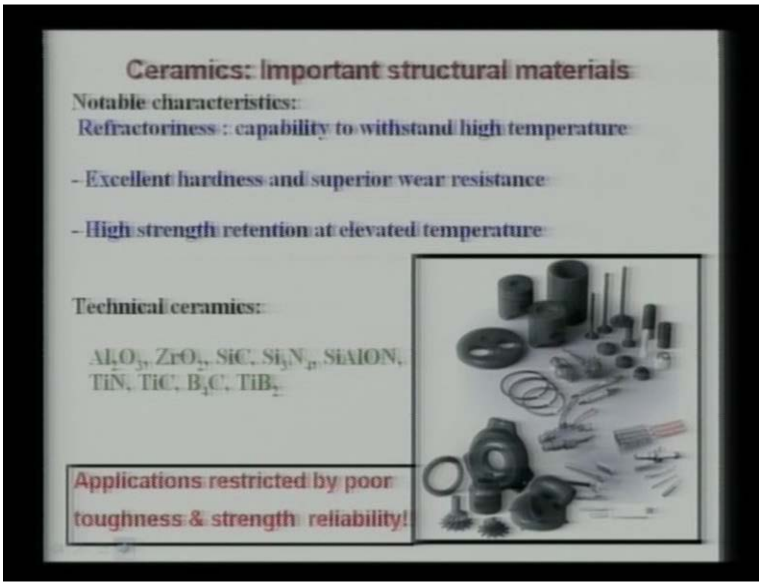

Now, third important primary class of material, that is ceramic. It has excellent hardness, much higher hardness than metals. Some of the ceramics are alumina, zirconia; these are like materials which are extremely good for biomaterial applications.

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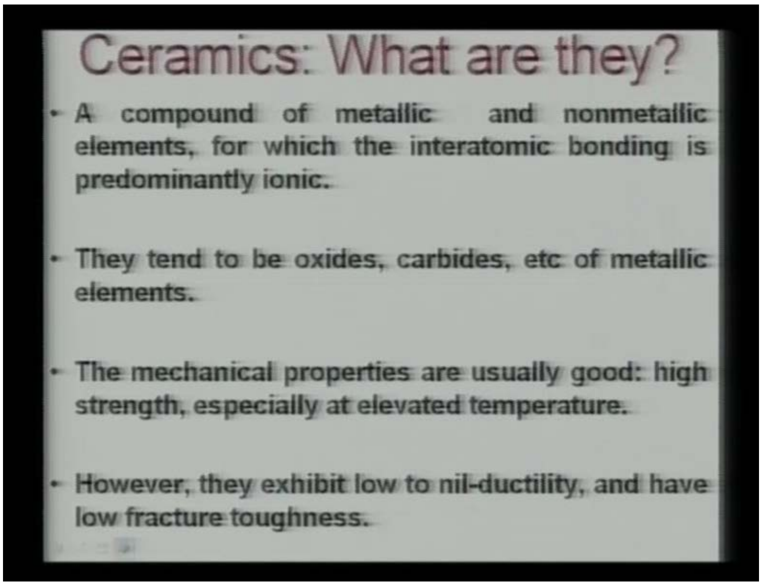

Now question is that, what are Ceramics? Ceramics, is essentially a compound of metallic and nonmetallic materials nonmetallic elements and for interatomic bonding is primal predominantly ionic.

They can be oxides, carbides of metallic elements. Like you know, oxides means like zirconium or alumina, these are like different oxides. And mechanical properties are usually good, high strength; however, they exhibit very nil-ductility or very low ductility and this is a concern for the ceramic based materials.

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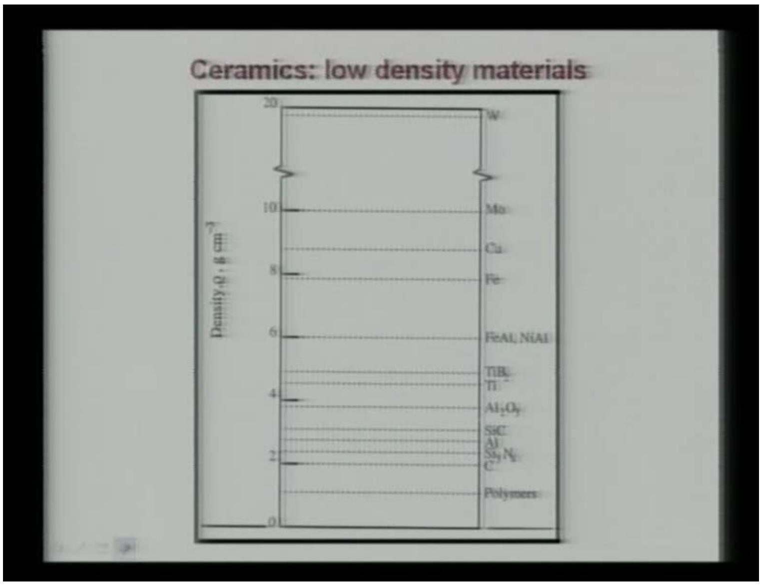

Now, to give an example that you know, how the different properties of the ceramics are, in respect to different other materials. For example, alumina, these are the density of around close to 4 gram per cc; however, iron, these are the density of 8 gram per cc. That means, equal volume of alumina and equal volume of iron, they have almost like half of the way, right, this this is important. For many times, implant applications, because, if you want to replace the steel material with equal volume of alumina, the patient also will feel much light at this implant, because alumina is a much lower density compare to that of the steel.

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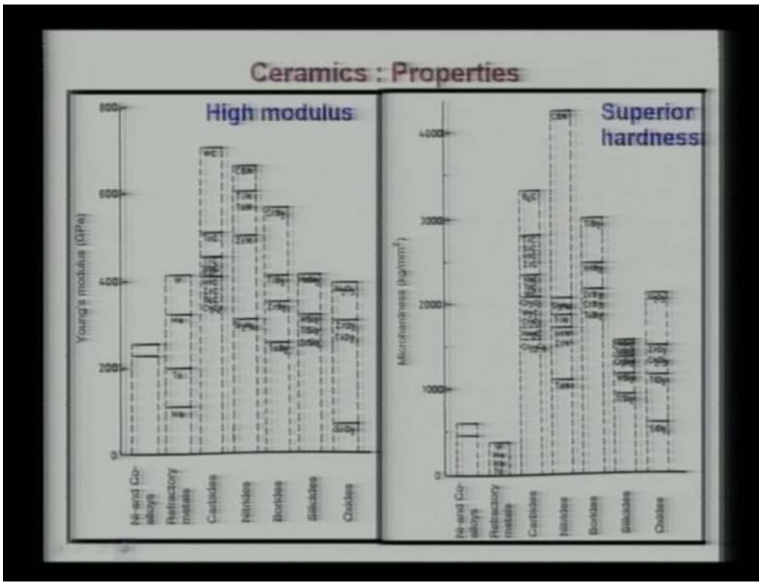

So, that way density also plays an important role, in case of the selection of implant. Now, coming to the modulus, now as I said that, modules is important, because elastic modulus, there should not be much miss match and the alumina zirconia have relatively much higher elastic modulus compared to even steel.

So, this elastic modulus needs to be tuned, before any potential applications can be realized. Now, coming to the hardness. This ceramics, traditionally, you can see that they are very high hardness, more than 10 gigapascal and above. That is one of the important properties of the ceramics, which are largely exploited in different applications.

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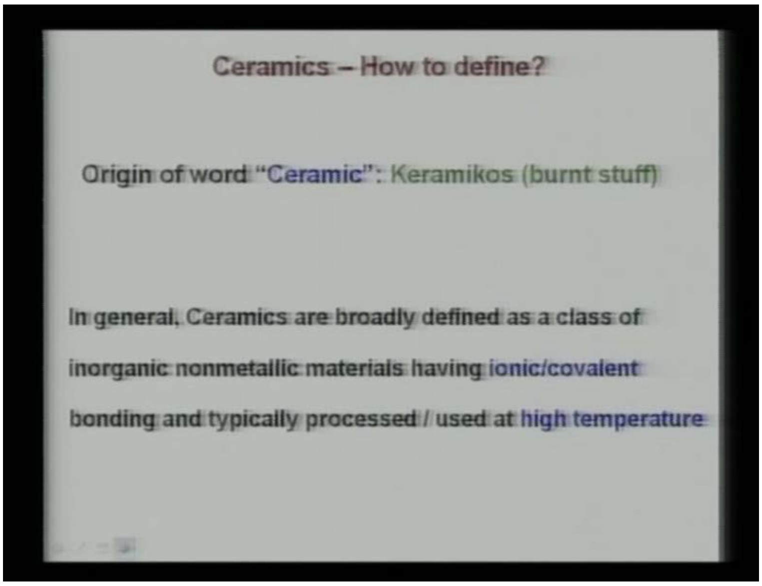

Now, the origin of the word ceramic is derived from the Greek word keramikos. That is, burnt stuff and this ceramics are broadly defined as a class of inorganic nonmetallic materials having ionic and coherent bounds and typically processed or used at high temperature. This is like very formal definition of ceramic base materials.

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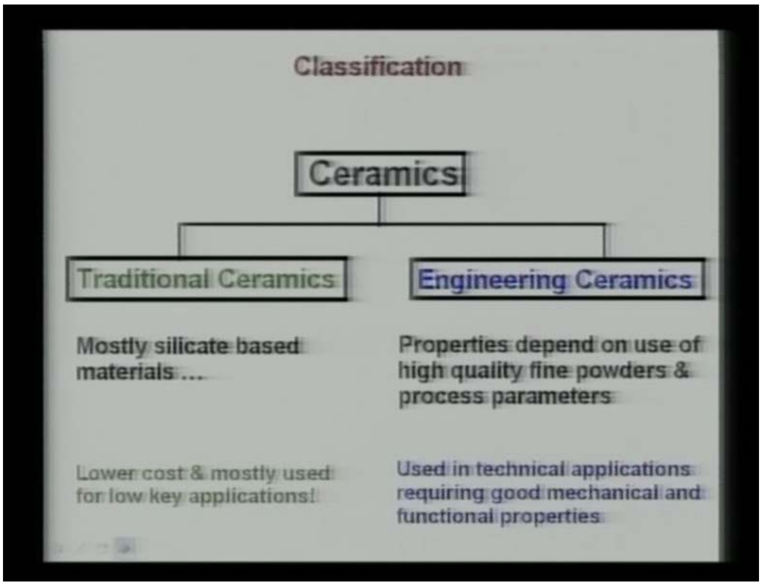

So, that means, that it has a pure inorganic material and it has ionic or coherent bonding. They are typically used or processed at high temperature. Now, ceramics can be broadly classified into traditional ceramics and engineering ceramics. But, as per biomedical applications are concerned, we will be mostly dealing with engineering ceramics like alumina and zirconia, where that properties are also depend on high quality fine powders and process parameters.

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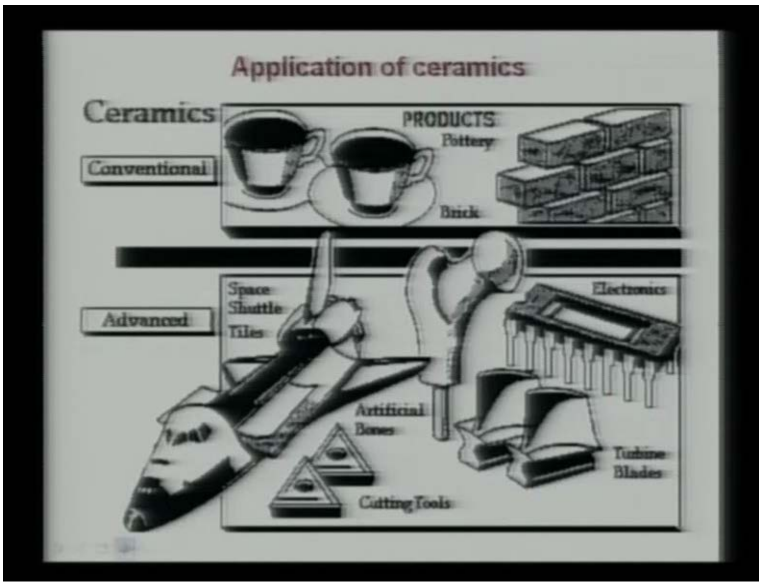

Now, as I said that, we are mostly dealing with advanced applications and one of the advance applications is this artificial bones. These artificial bones, here essentially are shown here, that is for hip joint applications and as I explained that, this is a combination of materials which are used for hip joints.

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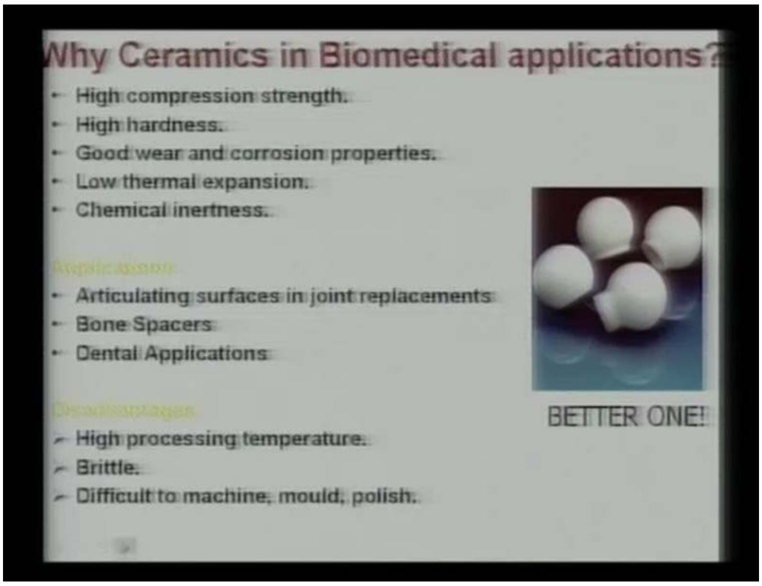

What are the important properties which are of relevance for ceramics and biomedical applications? That includes high compression strength and high hardness of these materials. It also is a good wear and corrosion properties. Applications, it can be used articulating surfaces in joint replacements, bone spacers, as well as the dental applications.

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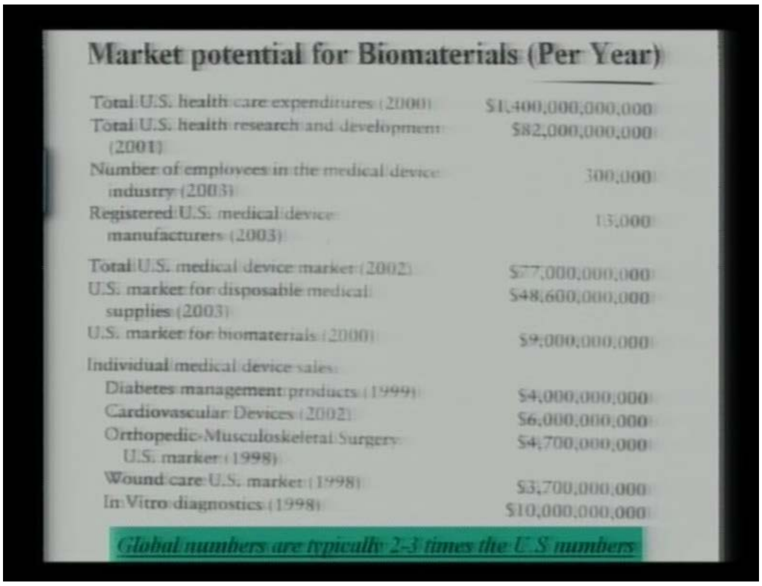

These advantages are that, it has a very high processing temperature and they have mechanical brittle behavior. In next few slides, I would like to highlight the importance of biomaterials. Now, in this view graph, actually I am showing you that market potential for biomaterials per year. This market potential shows that in the year 2000, the total us health care expenditure was around this much, several thousand US dollars.

And out of this total US health care, the expenditure I mean in 2001, it was estimated, that you know, a quite had double fractions of the expenditure was for the R and D development. That is, for the research and development work for developing biomaterials, that was also spent. If you see that US market, that was in 2002 for medical device, it was quite a good fraction of the total US health care expenditure, right.

And if you see that U S market for biomaterials, for say in 2000, it was again, some you know one tenth or one eighth part of the total US medical device. So, what I am trying to emphasize here, that if, you see the total US health care expenditure, that is and if you see, the total US health care expenditure for biomaterials, that is quite a good fraction of that total US health care expenditure in the year 2000. The global numbers, like if you talk about that similar expenditure in Asia as well as Africa, and so, many other and as well as the Europe, so these numbers are typically 250 times the U S numbers, because these total health care expenditure also depends on the living condition, as well as the economy of individual nations.

Therefore, these total global health care expenditure, as well as that the ratio of the total market for the biomaterials, that will be quite a good fraction of the large amount of expenditure that is required for the health care. So, from that part, the development or the R and D activity of the biomaterials are also equally important.

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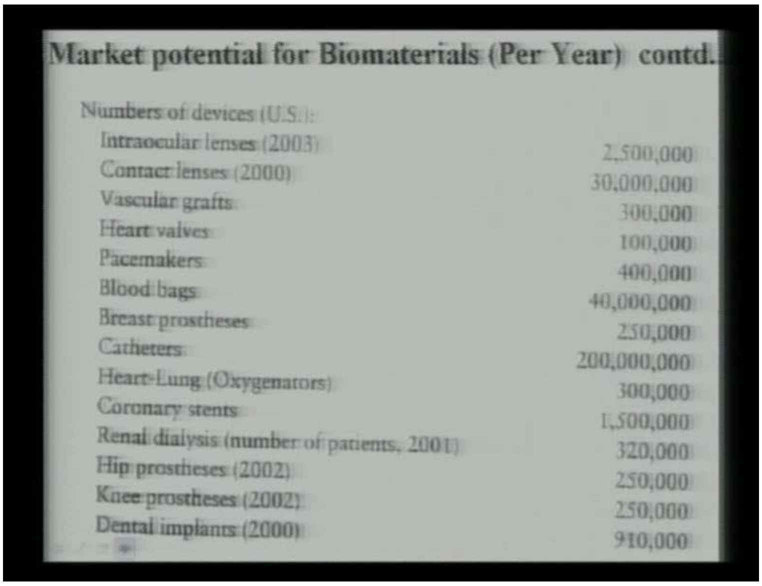

Now, this slide shows you, that you know, what is the market potential of biomaterials per year. Now, if you see that, you know the number of devices in US for intraocular lenses, is like several thousands. As well as, if you see the knee prostheses and hip processes, these are numbers in 2002 that was like 250000 in each and then dental implants is much more in 2000 that is 900 to 10000 dental implants was required.

Now, these are like, you know materials which are used for the load bearing applications and these are like different metals and ceramics or polymers, they are lastly used for these kind of applications, like, which includes the hip knee process and dental implants.

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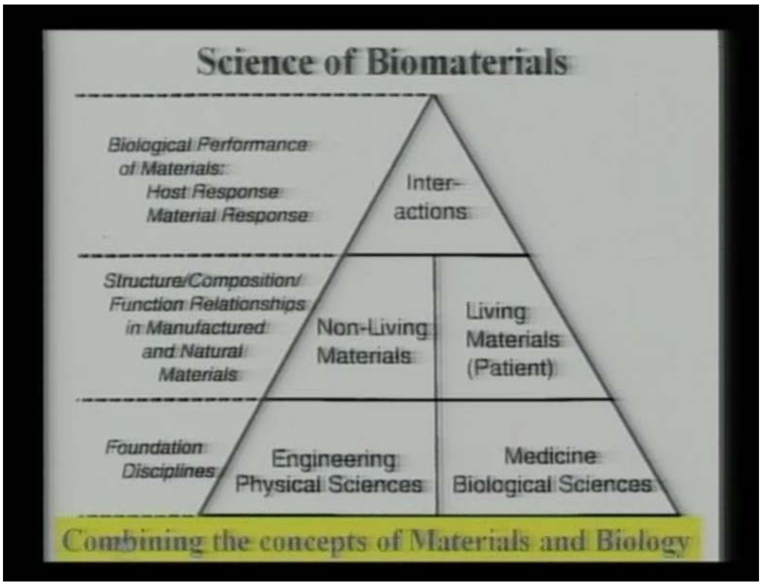

Now, this slide is important and I would like to spend some time on this slide. Now, if you see this triangle, this triangle tells you that at the lower level, it is important to have collaborations for the engineering as well as the medicine. Engineering means, this is like material science, like MSC material sciences engineering and also mechanical engineering, chemical engineering.

Now, these are like major engineering branches, which are under the physical sciences. They are actively involved in this biometric researches around the globe and there should be (( )) reversible kind of, there should be reversible dialogue or there should be reversible exchange of information or research expertise, that should be there to ensure good progress for the science of biomaterials.

Now, once this collaboration is developed, now this material science people, they will be developing nonliving materials. Nonliving materials means, like synthetic materials, like metals, ceramics, polymers. The medicine people, they have quite good understanding that how different materials can possibly take part in the wound healing process or in the health care of the living materials; living materials means like patients.

Now, if this two understanding, again they are like fuse together, then their interactions actually is important. Like how, nonliving materials when implanted in the patient, how they will interact and what is the scale of this interactions? What is the material response? Like you know, how this material will be developing the neo born or new born in the implanted region and what is the host response. Like you know, at the implanted region, in the animal or in the human being, whether there is a inflammation are not, that is also equally important.

Now, when the materials will be developed by this material science people or mechanical engineering, certain aspects need to be understood properly. That is, structure composition function relationship. As I told you earlier, that is is the structure property relationship, in manufacturer natural materials, these are like important. From biological aspect like force response and the material response, these interactions, like when material is implanted in the human body that is also important.

So, if I repeat this particular slide because this slide is important. So, at the basic level, researchers from engineering disciplines like material science engineering, mechanical engineering, chemical engineering, they should interact and they should collaborate with biological sciences people as well as the medicine people. Like clinical for clinical priors, like with that medical practitioners or the active researchers in the field of medicine like doctors and so on.

So, they should be collaborating with each other and there will two way exchange of information. Two way exchange of expertise that is required to totally understand the interaction, that I have talked a few minutes ago. Interactions means, how a material, nonliving material or synthetic material will interact with a living material, that is the human patient.

So, that is why I have mentioned here at the bottom of the slide. So biomaterials, this particular sign, essentially combines the concepts of materials and biology

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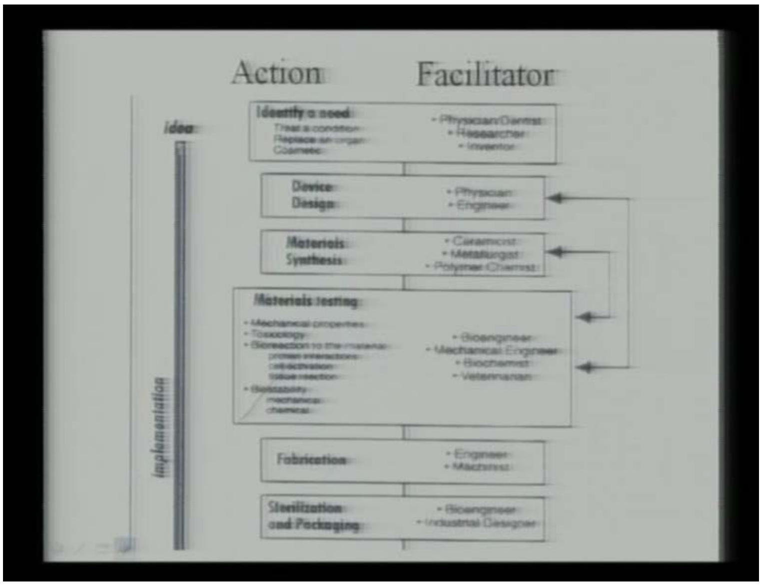

Now, how this entire biomaterial science has been developed. Now, this starts with that fabrication of the materials and here it requires the engineer, machine people, as well as metallurgies and also ceramics people and polymer scientist, for developing the ceramic based and polymers based materials. Then, you require a device, to design a device, you require a physician or engineer to collaborate and initially, you have to identify need. Like you know, what for this material is to be involved and for that you require dentist or physician or researcher, to answer certain questions. Typically, different material testing will facilitate biomaterials researcher that include mechanical property toxicology, like you know, like genotoxicity, cytotoxicity and so on.

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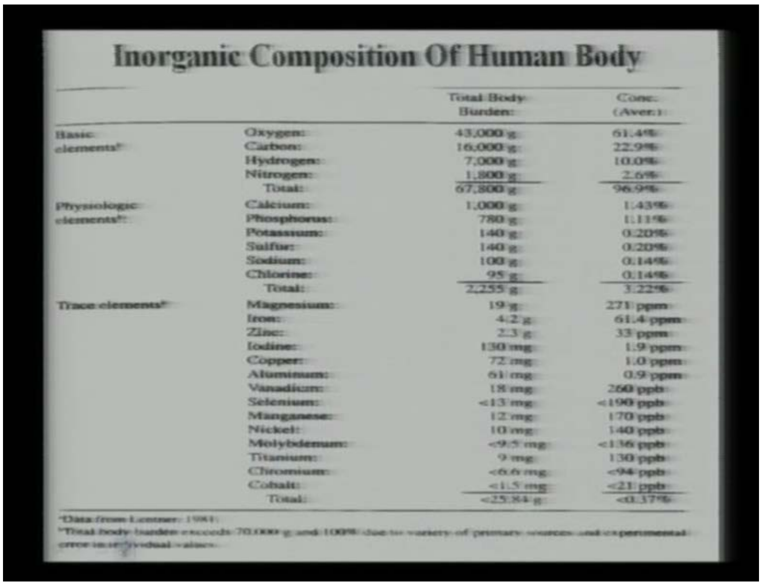

Inorganic Composition Of Human Body

		Total Body Burden:	Conc. (Aver.):
Basic elements*	Oxygen:	43,000 g	61.4%
	Carbon:	16,000 g	22.9%
	Hydrogen:	7,000 g	10.0%
	Nitrogen:	1,800 g	2.6%
	Total:	67,800 g	96.9%
Physiologic elements*:	Calcium:	1,000 g	1.43%
	Phosphorus:	780 g	1.11%
	Potassium:	140 g	0.20%
	Sulfur:	140 g	0.20%
	Sodium:	100 g	0.14%
	Chlorine:	95 g	0.14%
	Total:	2,255 g	3.22%
Trace elements*	Magnesium:	19 g	271 ppm
	Iron:	4.2 g	61.4 ppm
	Zinc:	2.3 g	33 ppm
	Iodine:	130 mg	1.9 ppm
	Copper:	72 mg	1.0 ppm
	Aluminum:	61 mg	0.9 ppm
	Vanadium:	18 mg	260 ppb
	Selenium:	<13 mg	<190 ppb
	Manganese:	12 mg	170 ppb
	Nickel:	10 mg	140 ppb
	Molybdenum:	<9.5 mg	<136 ppb
	Titanium:	9 mg	130 ppb
	Chromium:	<6.6 mg	<94 ppb
	Cobalt:	<1.5 mg	<21 ppb
	Total:	<25.84 g	<0.37%

*Data from Lentner 1981.
**Total body burden exceeds 70,000 g and 100% due to variety of primary sources and experimental error in individual values.

Bio stability, like you know, in viewer environment, how this material is stable. We, in biological environment, that will also needs to be investigated. Now, before understanding biological response of material, it is important to know, what is the inorganic composition of the human body? For example, if you take the basic elements like oxygen, carbon, hydrogen, nitrogen; oxygen is around 61.4 percent, carbon is 22.9 percent.

Now, coming to the physiologic elements like calcium and phosphorus, now calcium is around 1.43 percent and phosphorous is around 1.11 percent. You have also potassium, which is, potassium as well as sulphur. So, these are like very small amount, like 0.2 percent. Some phase elements are there like magnesium and iron, so on. So, these are like PPM level. You can see that the amount actually is quite small, when it comes to magnesium iron and zinc because; it is in the PPM level.

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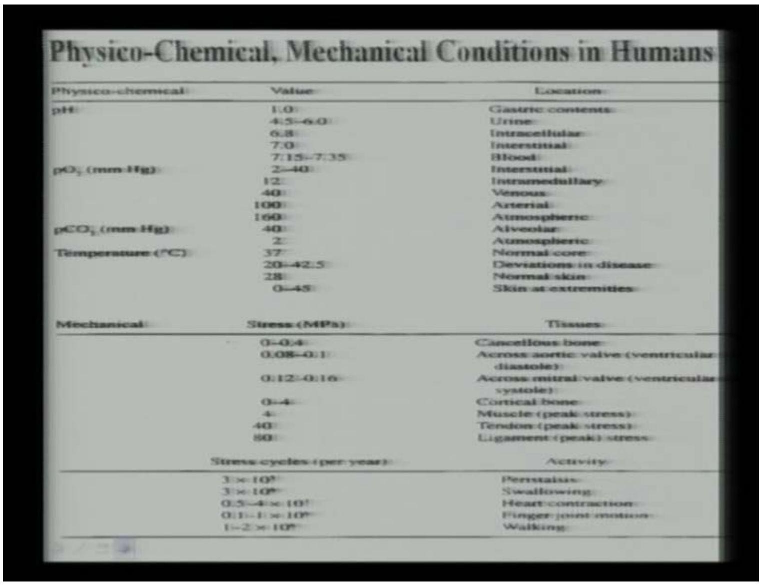

Physico-Chemical, Mechanical Conditions in Humans

Physico-chemical	Value	Location
pH	1.0	Gastric contents
	4.5–6.0	Urine
	6.8	Intracellular
	7.0	Interstitial
	7.15–7.35	Blood
pO_2 (mm Hg)	2–40	Interstitial
	12	Intramedullary
	40	Venous
	100	Arterial
	160	Atmospheric
pCO_2 (mm Hg)	40	Alveolar
	2	Atmospheric
Temperature (°C)	37	Normal core
	20–42.5	Deviations in disease
	28	Normal skin
	0–45	Skin at extremities

Mechanical	Stress (MPa)	Tissues
	0–0.4	Cancellous bone
	0.08–0.1	Across aortic valve (ventricular diastole)
	0.12–0.16	Across mitral valve (ventricular systole)
	0–4	Cortical bone
	4	Muscle (peak stress)
	40	Tendon (peak stress)
	80	Ligament (peak) stress

Stress cycles (per year)	Activity
3 × 10[illegible]	Peristalsis
3 × 10[illegible]	Swallowing
0.5–4 × 10[illegible]	Heart contraction
0.1–1 × 10[illegible]	Finger joint motion
1–2 × 10[illegible]	Walking

Now, coming to the physicochemical and mechanical conditions in human beings. Physicochemical means like PH value. Now, what you see normally here, at PH; this PH value also differs depending on the anatomical location of the human body. Like PH is equal to 1 for the gastric content, PH is 4.5 per CC in the urine and 7.15 to 3.5 in blood. So all, since the blood, actually blood PH is 7.15 for 7.35 and that is a PH level that is typically maintained in all in vicro experiments. That is why, it is suggested the P H value of 7.4 is to be maintained.

However, you have to note that this PH value, that changes, it is not constant throughout the entire human body and this constant is not true. This PH value changes depending on what is the anatomical location in the human body that you are considering. Now, coming to the PO 2 level, like in the phineas and the RTL region, so, you have the very high PO 2 level and temperature also, it is 30.7 degree celsius because that is the normal core temperature of a human body.

But, there is a fluctuation in this temperature, like skin at the extremities can go 0 to 45 degrees Celsius. Normal skin, it has 28 degrees Celsius. Coming to the mechanical stress conditions in different tissues, like cancer less tissues, which are like very porous is just like stresses, can be a maximum of 0 to 0.4 M P A. So, which is extremely low load, because of the porous nature it cannot take very high load. Now, ligament and tendon, like some of the hard tissues, they can bear the load up stress up to 40 to 80 M P A, which is relatively high.

Stress cycles, which is important for the fatigue property. So, number of stress cycles, if it is more, then fatigue properties are also much better. Now, typically for walking, if you see, 1 to 2 into 10 to the power 6 phase cycles are required for the walking. That, when human being walks; that means, this human being actually, moving parts of the human body, they experience 1 to 2 into 10 to the power 6 number of cycles.

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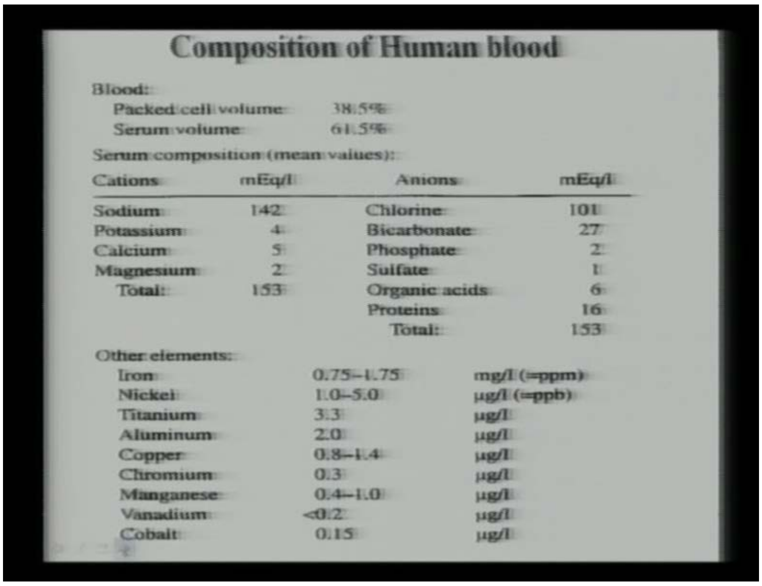

Now, composition of the human blood. Now, blood contains different cells as well as different other elements. Now, different other elements means, iron, it is around 0.75 to 1.75 milligram per liter, it has different sodium, potassium and so on. These are like different Cations, which is sodium is there for 142 level, chlorine is around 101 molecule equivalent per liter and it has also serum, which his around 61.5 percent.

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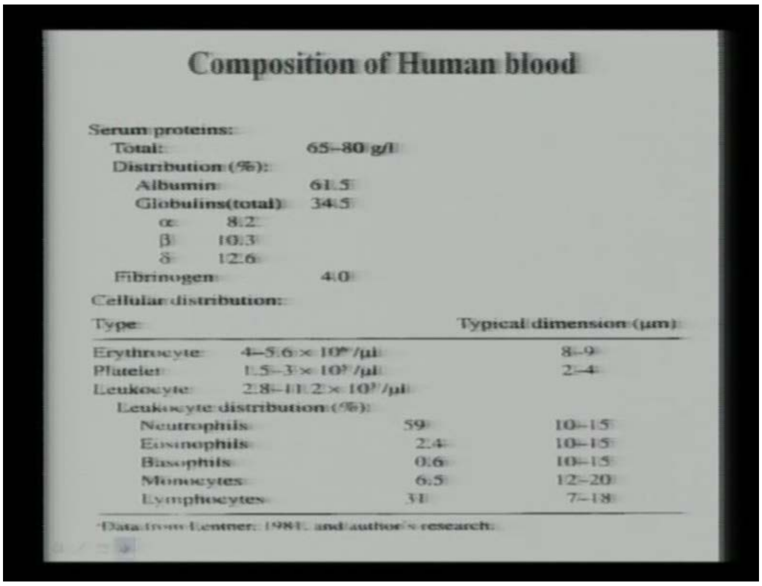

Total protein in the serum blood serum is around 65 to 80 gram per liter and it has albumin, is 61.5 percent and globulins is 34.5 percent. So, these are like different proteins which are available in the blood and fibrinogen is also 4 percent. Now, blood also contains different cells, as I just mentioned, it is erythrocyte. It is like, typically 8 to 9 micron dimensions and it is like large number of erythrocytes are available up to 10 to the power 6. So, this number is 10 to the power 6.

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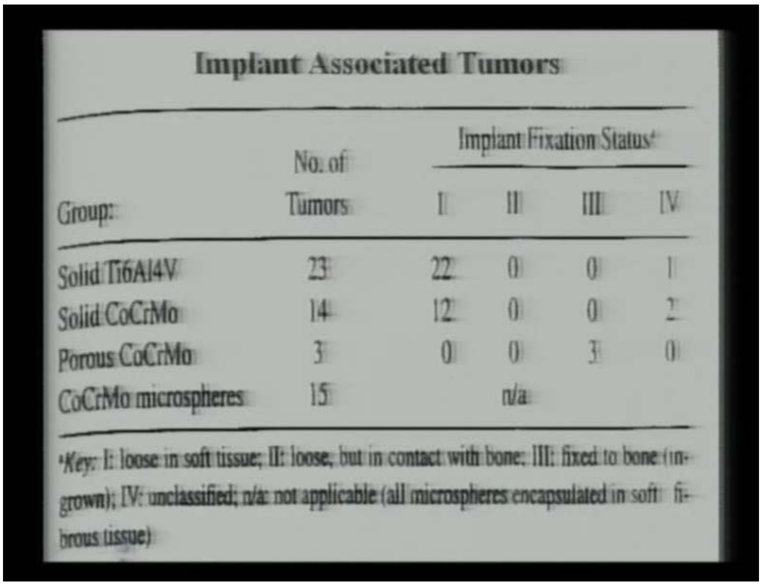

Now, you have the blood platelet, which is there for 10 to the power 5 per micro liter and lymphocytes is also 10 to the power 3 per micro liter. Now, other things which are important in that; now, now implant associated tumors, like if you talk about the different metallic solids like titanium 6 aluminum 4 (( )), number of tumors certain patients were investigated. Now, it has the largest tendency of causing tumor and these tumors, if they are malignant, then they can pass cancer in the patients.

Now, solid cobalt chrome also, it has large number of tumors, that it has experience, it has cost is 14 for number of tumors, they have experience is 14. Cobalt chrome microspheres is also, number of tumors is 15. Now, these tumors, essentially, if they are genotoxic in level, like if they cause the D N A damage, then it cannot be used in a particular implant application. They are again, I must emphasize that these t I 6 a l 4 v cobalt chrome molescous, have a very good combination of mechanical properties.

However, when they are implanted inside the human body, they are wear particles like cobalt or chromium containing or mole containing wear particles. They can potentially cause this genotoxic effect when implanted for the longer duration. Therefore, they have also tendency to form large number of tumors and that is the reason that they need to be replaced with better materials.

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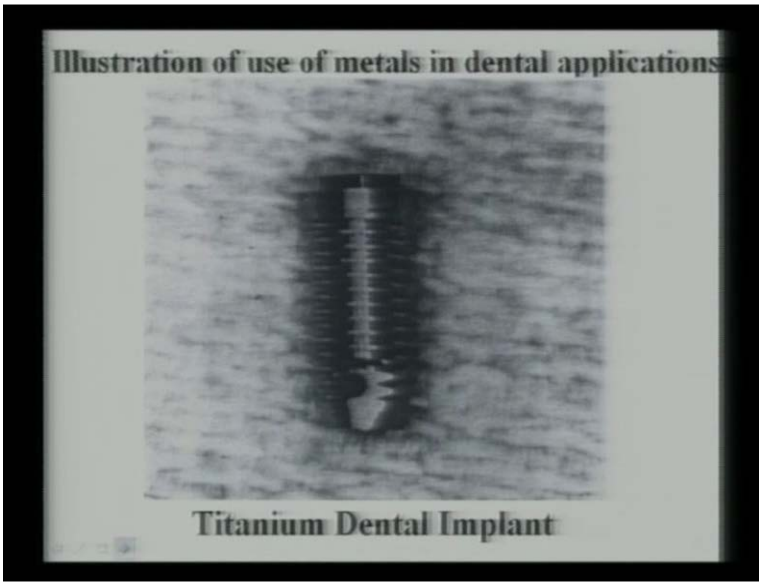

So, although they have better mechanical properties, that does not mean they should be accepted for biomaterial applications. This is the illustration of the use of a metal in dental applications. Like you know, this is the titanium, which is used widely in the load clearing like screws and all, in dental applications.

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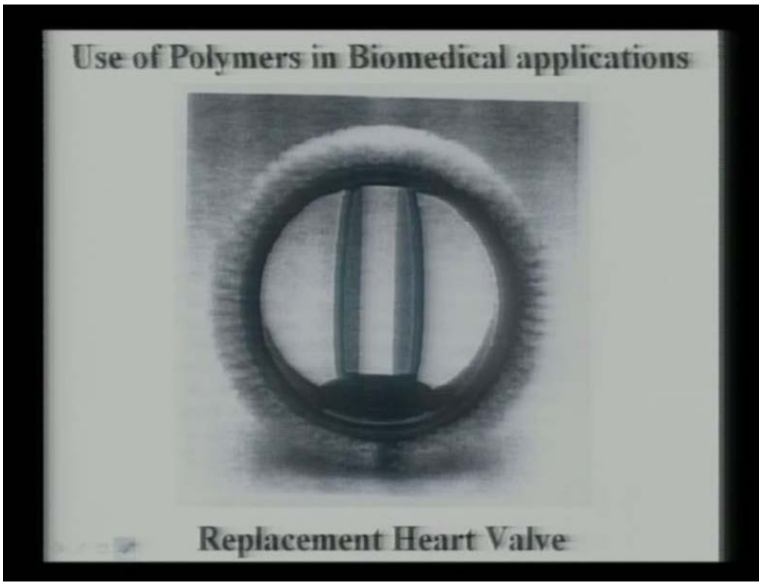

Also, this is like replacement heart valve. These are like, very light and for that, again, mechanical properties is not important. Again, the all the blast cell should not speak over here. So, this is the region where the valves can open, when the, when you are pumping the heart. So, the valves should be very light weight. Because of this light weight requirement, many polymeric based materials where density like PTFP, where density is like less than or equal to 1 gram per CC, they should be used. That is a reason, like diamond, like carbon coated materials or (( )) fluoric, like these should be used. These should not cause any thrombus formation. Thrombus formation means, like blood platelet, they come together; they form a platelet. These blood cells, so, this agglomeration of the blood cells, that should be avoided and this should be avoided at the maximum extent, for any heart valve applications.

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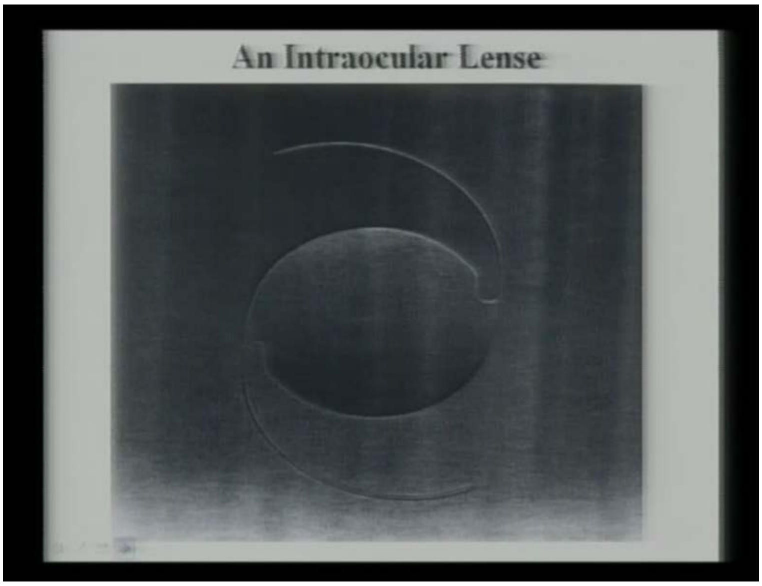

This is one of the examples of the intraocular lens, like poly methyl methanol layer and then silicon rubber. Those are the material; these are typically used for these different intraocular lens applications.

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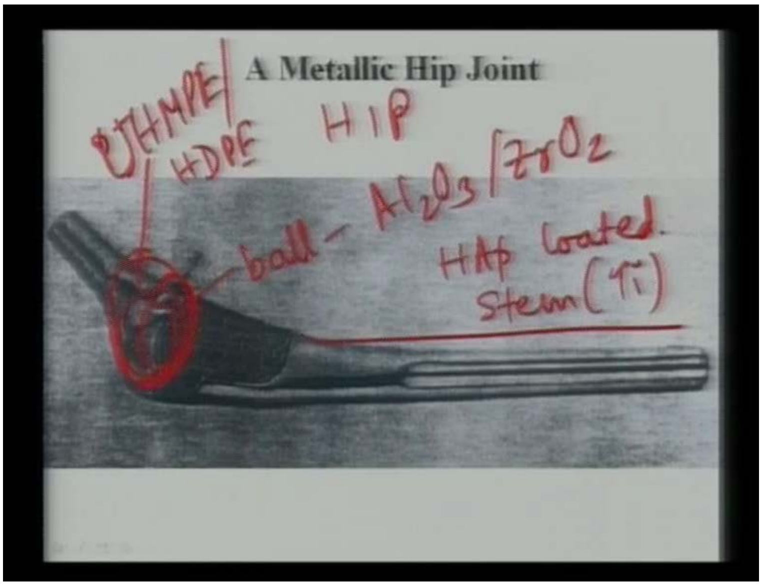

Now, this is a thing that I was mentioning new couple of minutes ago. Now, this is called stem. Now, this stem is typically made of titanium. On this titanium, you can put the hap coating also. Like you know, hap coated steel titanium also you can use. Now, this is the part, longer part of the structural part or load varying part of the stem total hip joint; so, hip replacement. Then, here you can use some ball and this ball can be femoral ball. That can be alumina or zinconia and again at the top here, this is the like some poly methyl methanol layer or alcohol molecular polyethylene. These are like acetabular cup things and this can be either (( )) polyethylene or high density polyethylene based material.

Now, these balls, they will make a small rotating movement here and they can experience some wear problem also. These balls will be fitted directly to this femoral stem, which is made of titanium. So, this is like one of the most popular examples, where the biomaterials have been successfully used.

This is the end of the lecture and tomorrow we will start with this other applications, like you know, some of the fundamental properties of the different materials, which you should know before we can realize that how different materials can be successful for different biometrical applications. Thank you.