Biomaterials for Bone Tissue Engineering Applications
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Module 2

So I will briefly introduce now, to Bio Materials. So in last half an hour, I have mentioned that one of the core application areas for bio materials is orthopaedic applications and Patulic bone analogy materials.

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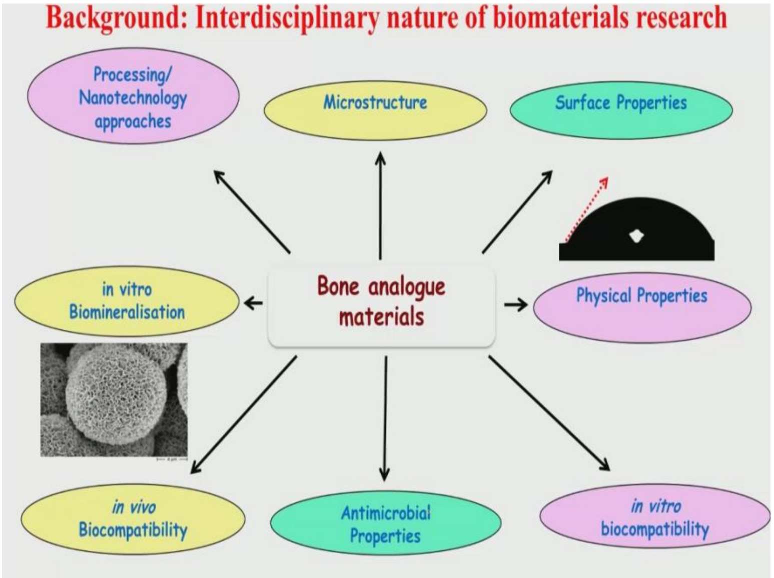

Now these slides essentially shows you that what are the different aspects, that one has to consider while developing these bone analog materials. So first one is the processing, of nano technology approaches like what are the, how to make these materials with bone mimicking micro structure.

Remember natural bone is a collagen, and hydroxyapatite based nano bio composites. So collagen is one kind of protein, what is this protein I will introduce you later. So you have to remember that collagen is one type of protein and also hydroxyapatite is inorganic inorganic part of the human natural bone and what is hydroxyapatite? Hydroxyapatite is a ceramic phase which is an inorganic phase and which is a particular stoichiometric composition, Ca10 calcium 10, PO for 6 (())(01.58) so in the natural bone hydroxyapatite nano platelets are disbursed in the collagen matrix.

Now this kind of unique structure is very difficult to mimic, in any of the synthetic materials, but people have made significant attempts to mimic artificial material as close as to that of the natural bone. So once this processing is done, then one can characterise the microstructure at multiple link cells both at two dimensional and three dimensional as well as micron scale, nano scale and so on. Now surface properties are important as I said that, bio compatibility or cell material interaction it is more surface mediated phenomena, so they are for what is, how does the surface property is in terms of with hydrophilic or hydrophobic property those are important.

A physical property in terms of strength properties, fracture toughness properties, elastic modular stiffness, is one of the major properties of relevance for the bio material application. In vitro compatibility I have defined briefly what is being; in vitro that is experiments which are conducted petri dishes glass wears, test tubes and so on. So those are like in virto experiments and traditionally in vitro, in the in vitro experiments, the cell level compatibility is established, that is followed by anti-microbial properties through this, to be evaluated using the various bacterial strains, both pathogenic strains like chephalochocai species or non-pathogenic strains and finally bio compatibility. Now in bio compatibility to be [asatu] and appropriate animal model.

Now since bone has hydroxide peptide, has one of the inorganic phase, so if some materials does not have hydroxide peptide as one of its micro structural constitute, one of the things that is very important to see whether this material can induce calcium phosphate nodule formation, when, that particular material is immersed in simulated body fluid of a certain time period. And this time period can be few days to few weeks. Now this is one of the examples that I have given where titanium which is a well-known bio compatible material and which is widely used clinically as, for different orthopaedic applications and among that various titanium alloys, titanium 6 present aluminium 4 present vanadium is perhaps the most widely used materials worldwide.

Now from the simple composition of titanium 6 percentage aluminium, 4 percentage vanadium one can well perceive that this does not have any hydroxyapatite as a second phase in the micro structure. However when the same titanium material is immersed in simulated body fluids, it can induce the calcium phosphate nodule formation as shown here. So this is a very nicely arranged nodules of several micro meter in diameter its perfectly more or less perfectly spherical shape.

More importantly one can notice that this nodule has a very fine level of pore structure, and you can see this is the micro porous structure this porosity is much much less than 1 micron and this kind of [nodu] hydroxyapatite nodule formation would essentially reflect on the ability of that specific material to induce bio mineralization. Biomineralization essentially means the ability of materials to form surface mineralised layer means surface layer infused with calcium phosphate like composition in simulated body fluids or in biologically relevant or physiologically relevant media.

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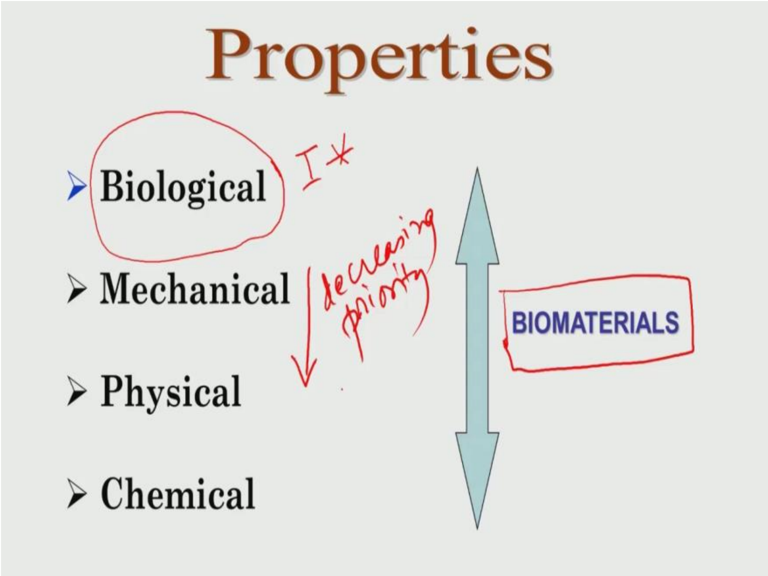

Now before I formally define the term biomaterials, I am trying to establish some link with the discussion I had few minutes ago and in that preceding discussion I have emphasised more and more that the material may have very superior combination of strained hardness (()))(07.42) of this properties. But if the material does not have acceptable biological properties or acceptable bio compatibility properties then that material should not be considered for biometrical applications.

So in other words, for a bio material to be defined, for a material to be classified as a bio material, it must have appreciable biological properties which can be qualitatively and quantitatively described to give us the confidence that yes indeed if the material is placed in a is placed in a Osseous system or in a human, in a particular human anatomy considers then that material would be compatible to the surrounding tissue structure or surrounding biological systems. So mechanical properties, so this is the first priority, priority Number one or I should mention it a star, just to emphasis again and again its importance in the context of biometrical applications.

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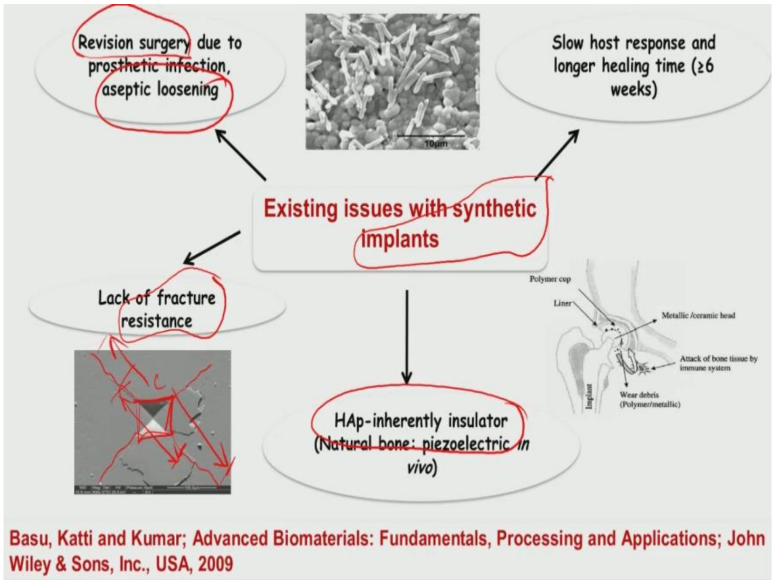

So this is in the order of decreasing priority. Mechanical properties, physical properties and decrease in priority. So other things which are important to mention at this stage, is that what are the issues with the synthetic implant materials like why researcher worldwide are constantly making attempts to discover new implantable biomaterials. Now the existing issues with the current used implant materials include, one is the division surgery that is primarily due to [aus] prosthetic infection or aseptic loosening and revision surgery means a patient has to undergo, again one surgery at the same anatomical sides, where the patient has already undergone the primary surgery.

The second one is that once a patient receives an implant materials typically most of the commercially available implants they show very slow host response and therefore longer healing time like 6 weeks are more required. Third one in the context of bio ceramics particularly hydroxyapatite is insulated materials whereas the natural bone has a piezoelectric property. And forth one is that fracture resistance property, ceramics are primarily week in terms of the fracture resistance property and just to give an example this is a weaker indent, you can indent on a material sub strait and the moment you try to make an intent there from the intend corners the extensive cracking takes place, now you can find out what is the length of this crack.

Let's say crack length is C, so larger the crack length more it reflects on the poor fracture resistance property of that material, smaller is the length, crack length, like one material has these much crack length and another material has such large crack length so certainly the material with large crack length, that material is not able to resist the crack propagation when it is being intended at identical load compared to the material which shows very small crack length.

So this kind of qualitative comparison tells you that ceramic which are the inherent and when they would be used or they would be suited for biometrical applications. One is to particular see that whether the crack fracture resistance properties are sufficiently good. Otherwise it will not be clinically acceptable by medical practitioners. This perhaps is one of the most significant reasons that why clinicians often do not prefer ceramic based implants, if metallic or biometric implants can provide similar clinical efficacy.

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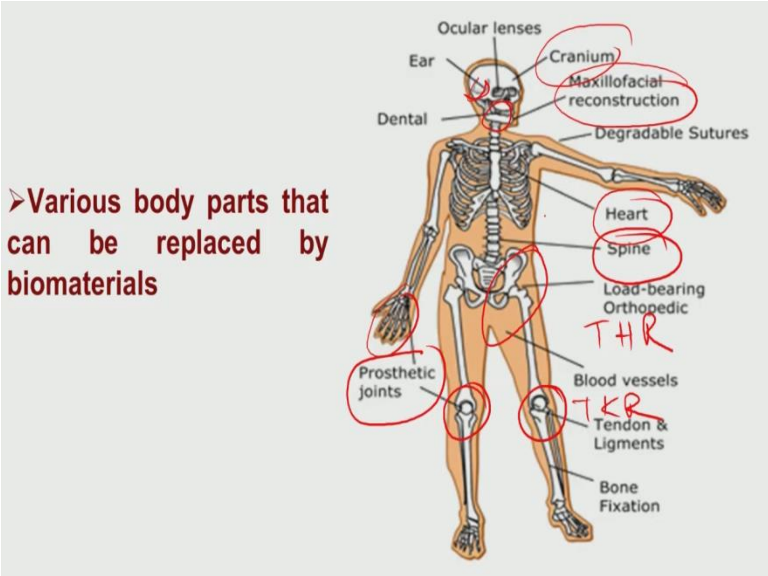

This is a human skeletal system, just to show you that what are the different places that biomaterials can be used so these are the finger joints here, different prosthetic, this is the knee joints, this is the load bearing, one of the popular load bearing joints THS, THA total Hip joint replacement, this is TKR, TKR stands for total knee replacement, knee joint replacement.

Spines, in the sine people use titanium and currently people are considering to use tantalum also. In the cranium and micro maxillofacial constants also people are using biomaterials. In the ear cochlear implants, in the cochlear implants people use certain electrodes, which are bio compatible in nature, dental materials as I told you before, the dental materials people use titanium 6, aluminum 4, vanadium, as a dental implant and over which one can use the crown material which can be zirconia and other bio ceramic materials or alumina.

And titanium 6 percent 4 percent vanadium which is used in dental implants, we are currently investigating how one can put that hydroxyapatite coating to provide this kind of implant better osseointigration at the same time one can also put some (())(14:02) like carbon coating to reduce the frictional properties of this implant material, so lesser the friction, lesser the pain, the patients will experience and it will be good health care, it will lead to better health care.

Heart also, for different cardio vascular applications like stents and so on, people use nickel titanium alloys, in the heart valves people use Teflon, diamond like carbon coated, titanium 6 aluminium, 4 percent vanadium heart valve application.

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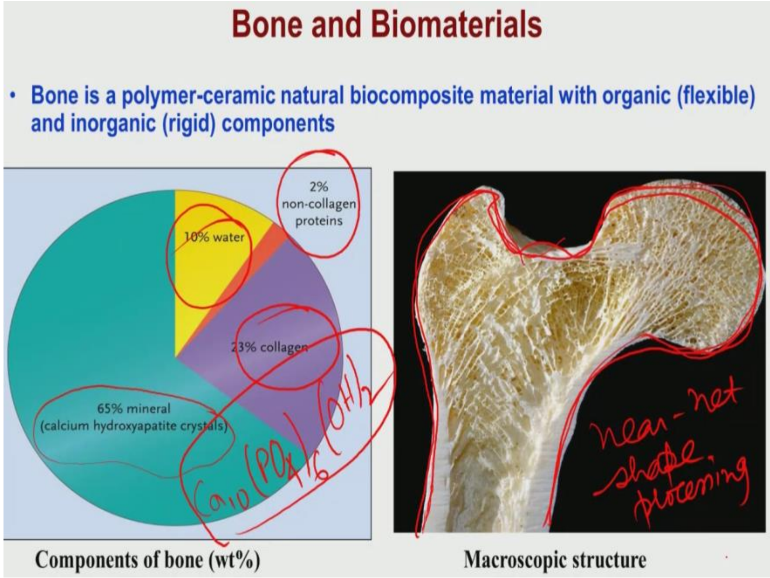

Ok now I have briefly mentioned about the natural bone composition. Here it show you some numbers and this numbers are important for you to realise that what is the relative percentage of different composition, different constituents. First one is that 65 percent mineral component that is calcium hydroxyapatite twisters are typically these calcium hydroxyapatite has this stoichiometric composition as I mentioned earlier.

Let me write down these for your knowledge calcium 10, PO 4 whole 6, OH whole 2. 23 percent is collagen. Collagen has different types, collagen type one to collagen type 9 and collagen 10 is also there. But we have most of the collagen type 1, and then we have 2 percentage non collagenous protein and 10 percent water

The other things I would like to bring to your attention are that this is a rough microscopic structure of a part of a long bone. What you can see is that this bone, does not have a very regular geometric shape and size, means you cannot describe this bone structure using a regular cylindrical shaped or rectangular shaped or square shaped in fact it is a very non uniform shape and size.

Therefore any material you like to replace full bone structure this material should have sufficient missing ability so you can shape this material to a particular shape and these materials, so therefore one thing that one can address is that knee and knee shape processing that means you take the, you can’t see that the design file of the bone to be replaced and then you expect the design file to eh additive manufacturing machine and this additive manufacturing machine will compose this design file into capital N number of layers, alternating layers and there you can just use this layer by layer fabrication technique.

I thought it was important for you to realise that bone has a very regular structure therefore the material if it is to be replaced, it has to replace the bone, and then it has to also be processed or manufactured into that specific shape and size.

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Cortical bone properties and Biomaterials

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 (HAp)	40-300	300-900	80-120	0.6-1

HAp is the most biocompatible and bioactive material

Mean time the properties the cortical bone so there are two types of typical bone; one is cortical bone structure, cancellous structure. So cortical bones has a range of properties like tinsel strength 60 to 160 mega Pascal which is not very high. Elastic modular since 3 to 80 giga pascal. So 60 to 160 mega pascal strenght is lower than many of the metallic materials tinsel strength, for example, stainless steel has tinsel strength more than 500 mega pascal. Fracture toughness also, the bone because it has a collagen and hydroxyapatite both phases are there. It is 2 to 12 MP square root meter. Now titanium for example as you can see, titanium has a much higher tinsel strength of the bone that is good.

Composition strength of 1bone is 130 to 180 mega pascal which is, which can, which is lower than many of the ceramic materials because if you from material science back ground you would know that composition strength of any ceramic is 8 times that of the tin size strength of that given ceramics.

Meaning that also the tinsel strength of hydroxyapatite can be as low as 40 mega pascal but composition strength of the same hydroxyl composition can be as high as 300 mega pascal, so it is more than close to 8 times higher than tinsel strength. Elastic modular of hydroxyapatite for that matter in any ceramic material can be very high like 120 giga pascal for example, in hydroxyapatite.

The major problem with hydroxyapatite like ceramics is that, poor facture toughness like point 61 MP square metre. So these therefore demands that fracture toughness o these kind of materials be improved significantly so that not only reaches the lower limit of the cortical bone properties that is 2 MP square metre but it also should be as close to the higher upper limit of the natural bone fracture toughness of this 12 MP square root metre.

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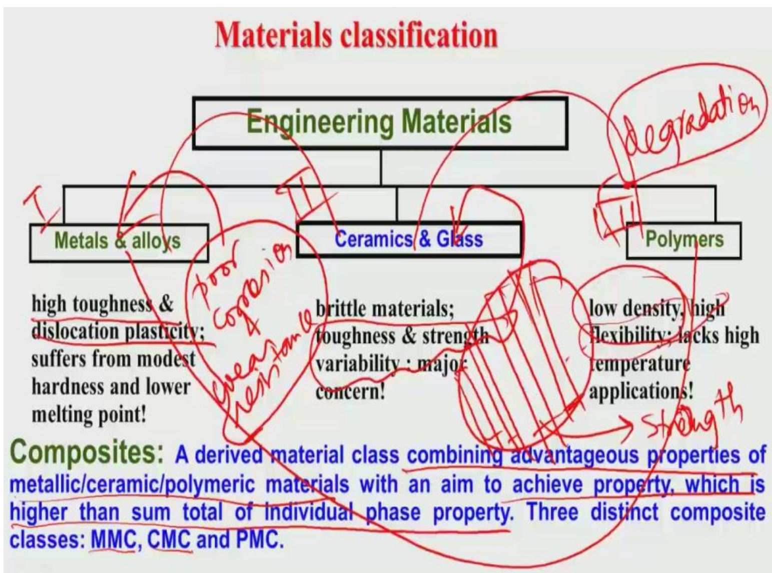

Little bit introduction to engineering materials metals and alloys ceramic implants and polymers. So these are the three primary material classes that entire engineering materials can be classified to and each of this material class has its own advantages as well as disadvantages. Now advantages include that high fracture toughness and dislocation plasticity. But disadvantages include that poor corrosion and wire resistance. Because many of these materials when implanted they will experience physiological medium and then typically in human physiology called medium the PH temperature is not uniform, the same throughout the body. So they dynamically change.

Now under dynamic change in this PH and so on, this materials would experience the corrosion and wire related phenomenon particularly at the articulating joints] so therefore this degradation of material property is quite obvious and that has been an issue for the metals and alloys. Now for ceramics as I said fracture toughness is an important limitation for ceramics because they are brittle in nature.

Another one is the strength reliability. Strength reliability meaning, if you take 20 samples of alumina biomaterials from the same large disc of Alumina. For example there is a large alumina disk and you have 20 samples which is got from this alumina like that, now each will have a different strength value, simple because strength depends on the crack size and crack size distribution in the structure.

So each sample may be having, although they have uniform composition alumina but each sample maybe having different crack density and as a result the strength would be different. A polymer is another important material class which is used for biomaterial applications. It has a very low density because it is made up of carbon, hydrogen, oxygen, nitrogen and it also has high flexibility. And the disadvantage of the polymers also can be degradation and erosion in the physiological environment and also polymers do not have a great combination of the mechanical properties in terms of the strength properties in terms of the fracture toughness properties and so on.

So therefore in order to combine the advantages properties of the three material classes one is metals, two is ceramics, three is polymers, you can combine either metals and ceramics, you can combine either metals or polymers, or you can combine metals and, sorry ceramics and polymers or one can combine metals and polymers as well.

So the three classes of materials, they are three classes of composite materials which take advantages of the good properties of the three primary classes with an end point objectives to achieve a property which is higher than the simple sum of the individual phase properties lead to the development of three distinct classes of composites which are metal matrix composites abbreviated as MMC ceramic matrices composite abbreviated as CMC, polymer matrix composites abbreviated as PMC.

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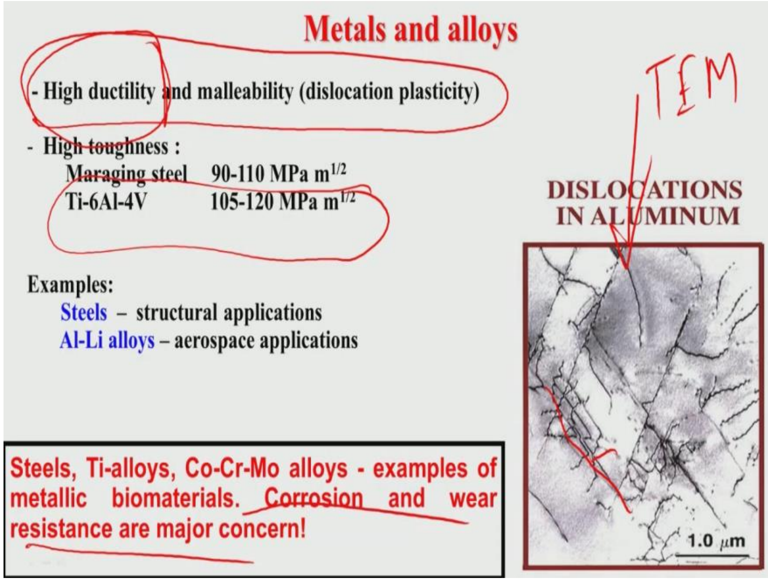

So just a quick introduction to metals and alloys. I reiterate here that they are widely used for various engineering applications as well as bio medical applications because of their good ductility property. Good ductility means it has good plastic deformation properties and that allows the metals to be shaped into different size and shapes. Some of the materials which is important for biomedical applications like titanium 6 percent aluminium 4 percent vanadium. It has a very high fracture toughness like 105 to 120 MP square metres which is orders of magnitude higher than that of the ceramics materials.

Corrosion and wire are the primary concerns, this is the TM image, transmission electron microscopy image of aluminium just to show how the dislocation credits are there and this is the dislocation lines in the materials.

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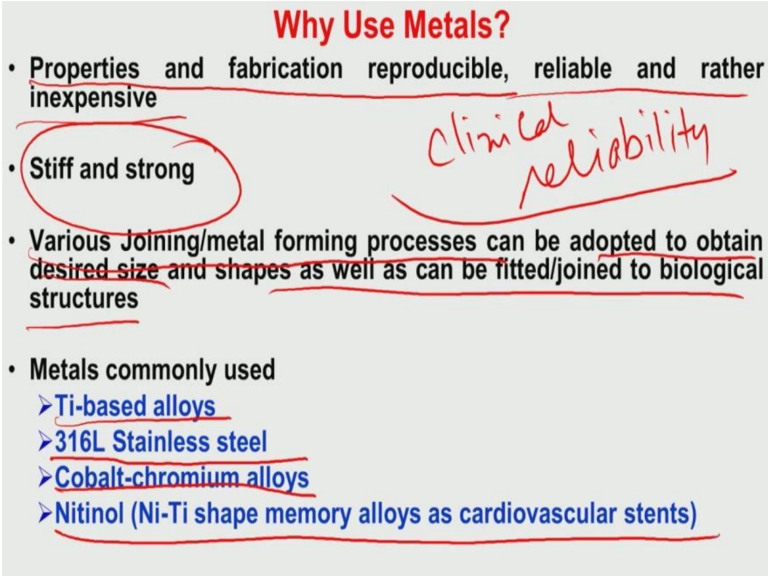

So why use material for biomedical applications. They have elasticity plus they are strong. The most important thing that perhaps gains a lot of clinical acceptance is that properties of fabrication are reproducible that means if you take stainless steel materials from different sources you can actually weld these stainless steel materials you can screw out of it, you can make a plate out of it, you can join it, but they will have, if it is a stainless steel material, if it is the same grade of materials it will have a very reliable properties. The property will not vary from sample to sample which is otherwise the case for ceramic materials so essentially clinical reliability is much more for metallic base material as compared to other classes of materials.

I mentioned it here, the third point like various joining or metal forming process can be adopted to obtain desired size and shapes and be fitted or joined to biological structures means Osseous bone structures. Commonly used materials titanium based alloys, titanium aluminium 4 vanadium 6 percent of 4 vanadium then titanium aluminium niobium, titanium aluminium zirconium 306, low carbon stainless steel alloys so add on chromium nickel, cobalt chrome alloys which is used also from knee joint replacement, nitinol that is nickel titanium based shap memory alloys which is used for cardio vascular stents. So these are the different examples of the metallic plates which are introduced in these applications. You can see this holes right, here. These holes mean it has to be used by drilling.

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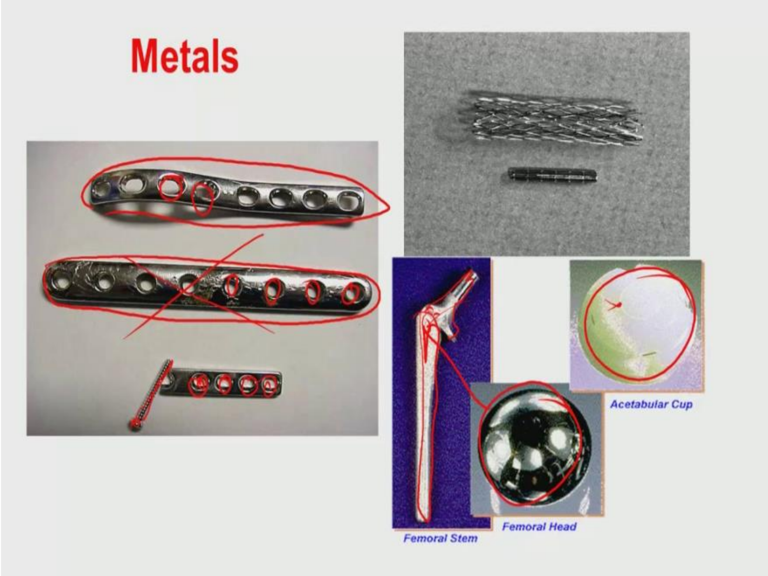

Now if you imagine using this long plate as which is made of some ceramics? The moment you try to make a hole to the ceramic plate this entire plate will simple fracture to tow pieces. Simple because it will not be able to sustain the drilling into stresses and it causes significant cracking and fracture. Also you can see that in a nail this is just to fix the plate into a trauma surgery and various other orthopaedic surgical applications. This nails can go into the hole and then can be fitted into tissue or bone structure. This is a simple example of the femoral stem as well as this total hip joint replacement here you will have femoral ball head, that is fitted here, and your acetabular socket which is going inside.

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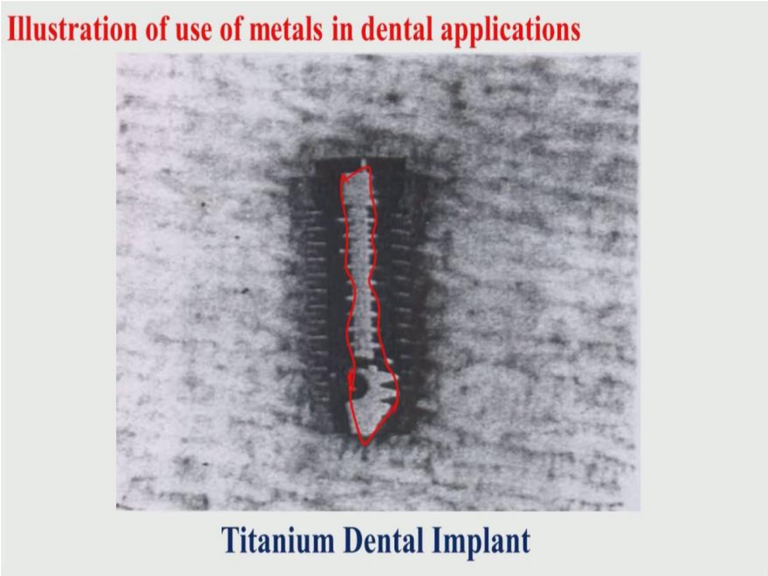

I mention couple of times, that we can use these titanium screws and this titanium screws have different threads, and this threads titanium 6 aluminium 4 percent vanadium it can be used for dental (())(27:41) applications.

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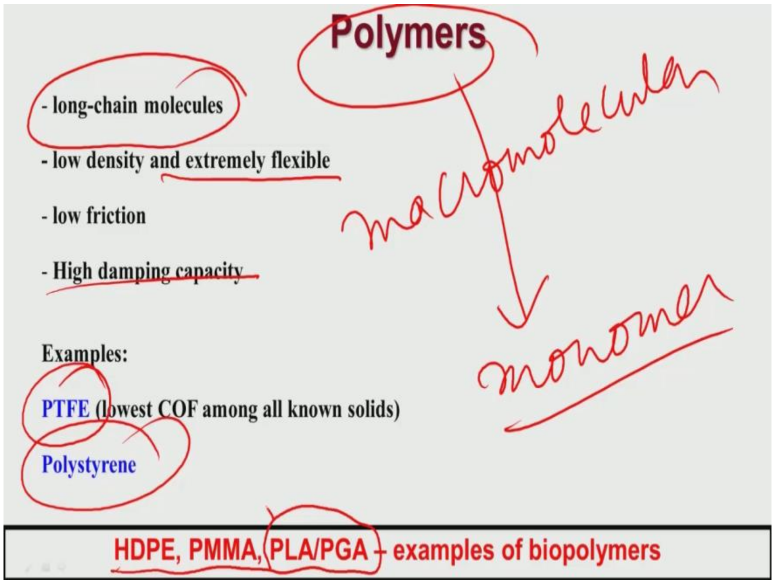

Next one is polymers, now polymers are characterised by long chain molecules it is a macro molecular structure and macro molecular structure essentially mean that it has this polymers essentially combination of several monomers which is joined together. Now depending on monomer, it is very flexible it has also high damping capacity popular example poly tetra fluoro ethylene, polystyrene and so on. Other biomedical evaluent polymers are PLA/PGA that is Poly lactic acid Poly glycolic acid, biodegradable polymers, you have poly methyl methacrylate that is bone cement it is largely used high density polyethylene this was another popular example of bio polymers.

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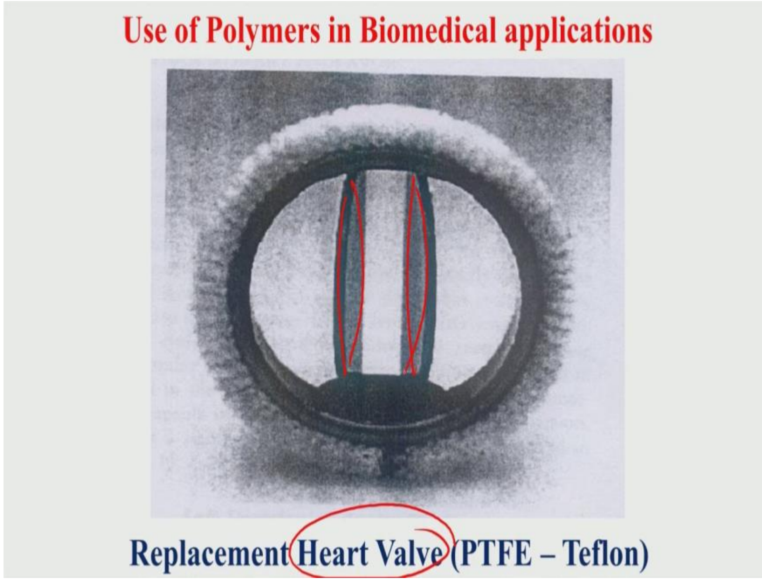

Cardio vascular applications, this is a very popular example of heart valve, this poly tetra fluoro ethylene so it is used for blood contacting devices do therefore thrombogenesis is one of the properties one is to check for.

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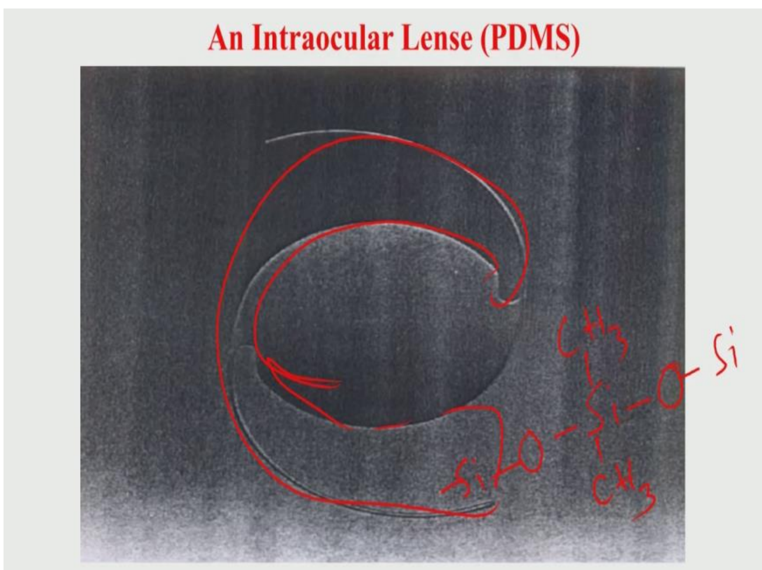

Intraocular lenses poly methyl methacrylate that is kind of used in the intraocular lenses so PMMA as well as PDMS Poly dimethylsiloxane so it is known an inorganic polymers because it does not have, it does not have a carbon hydrogen or carbon oxygen bonds instead of it has poly dimethylsiloxane, so dimethyl means two methyl group and then again silicon is there. And these poly dimethylsiloxane [eh] has received lot of attention for these intraocular lens applications.

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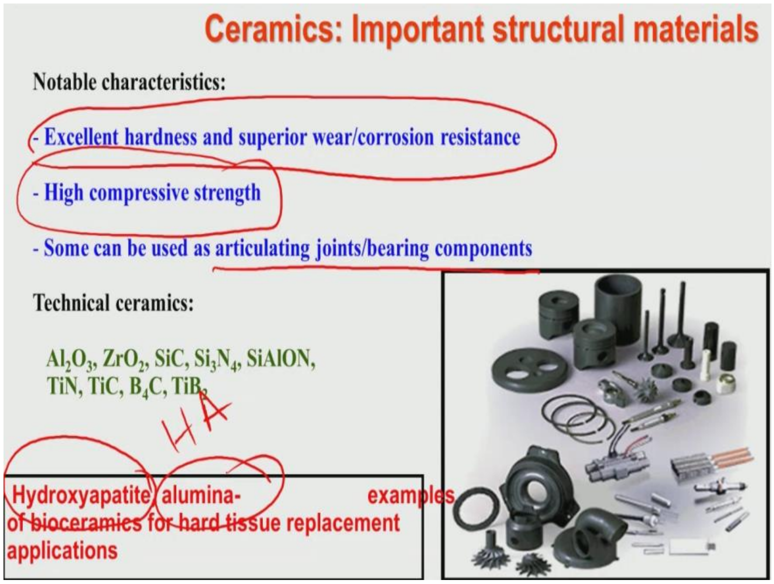

Now ceramics are one of the important material clauses simply because of the fact that is has an excellent combination of hardness and wear resistance properties and it is a large composite strength property, is it an unprecedented composite strength which is much higher than that of the metals. And it can be used as articulating joints and bearing components in combination with polymers and metals as well. Some of the popular examples of the bio ceramic materials hydroxyapatite HA which is quite widely used. Alumina also can be used in biomedical application.

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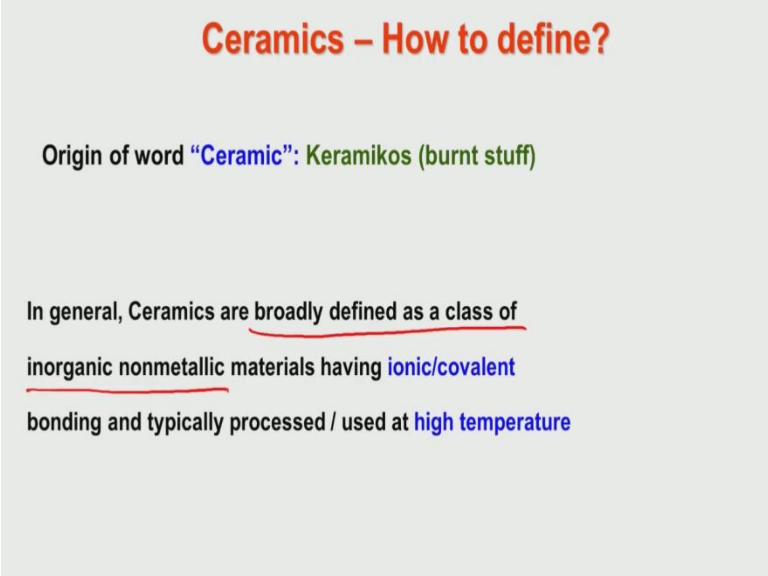

So this is a formal text book type of definition of ceramics like (())(30:24) has broadly defined as a class of inorganic non-metallic materials it has a combination of ionic and covalent bonding and typically it is processed at high temperature.

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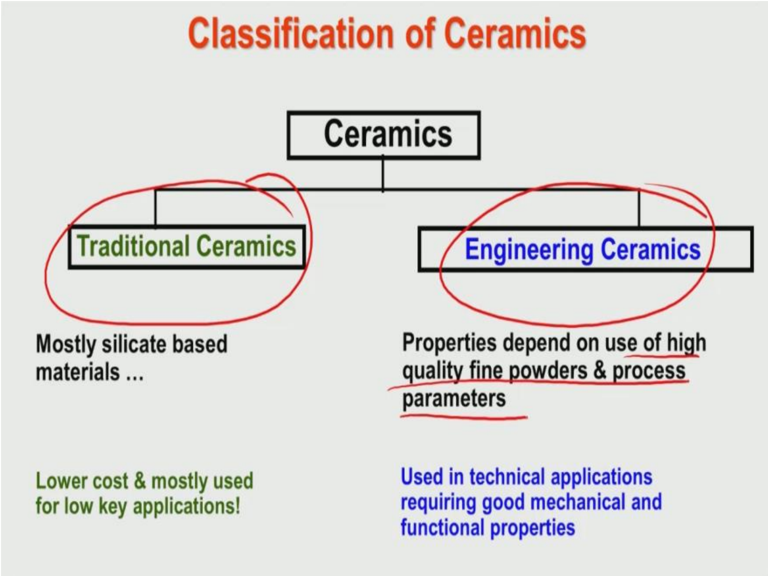

So there are two broad classifications one is the engineered ceramics one is the traditional ceramics. Engineered ceramics it depends on the use of high quality fine powders and process parameters and they are used for a variety of applications right from space shuttle tiles to artificial bone structure which we will discuss more and more in this course.

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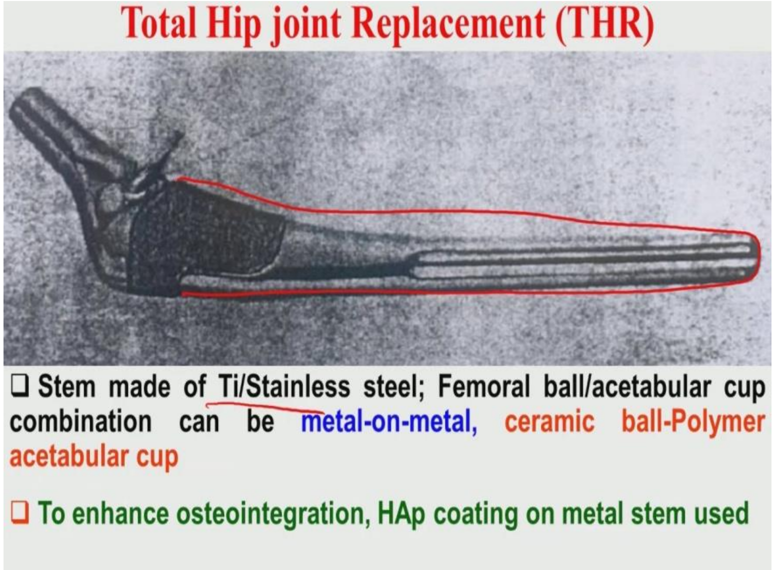

Now total hip joint replacement is one of the popular example of titanium stainless steel is used as the stem. Nowadays one of the developments is that one can use hydroxyapatite coatings on this titanium or stainless steel structures to make it more biocompatible on to have better osseointigration properties.

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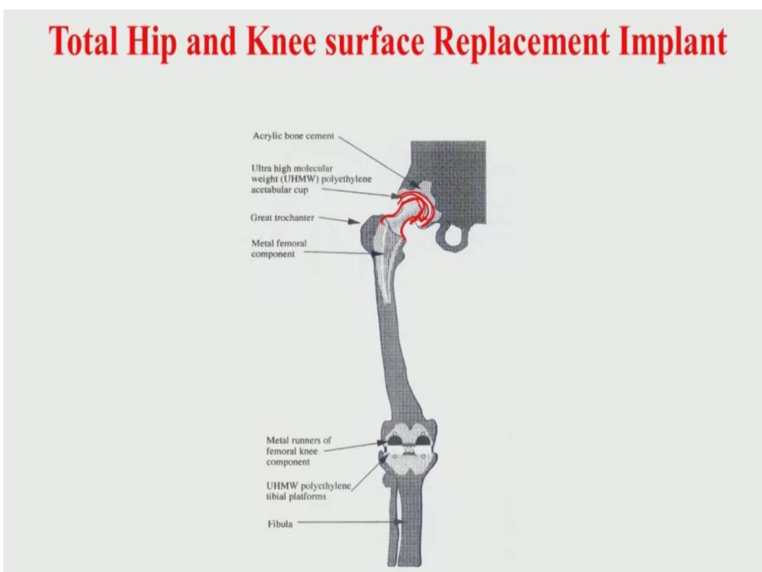

Now you have this metal metal so you have this femoral ball head here and there are tubular sockets. Now this femoral ball head structure can be made of a wire that is ceramic or polymer or metal.

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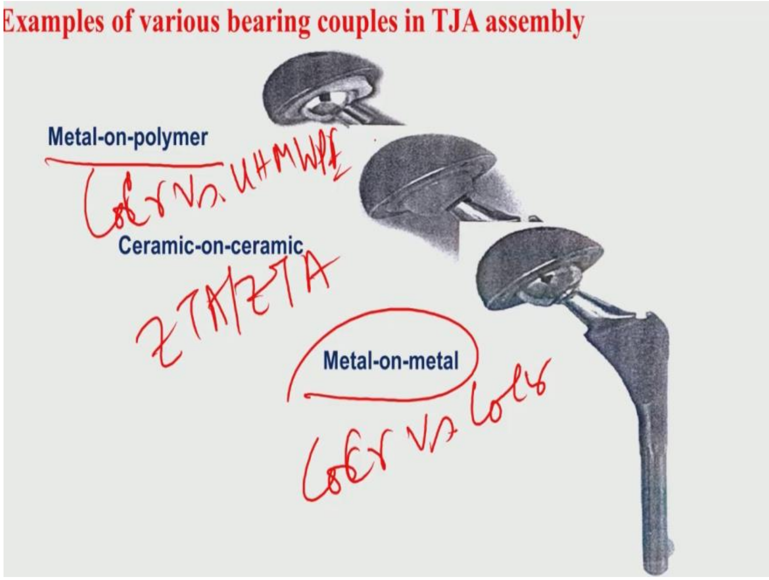

So therefore you can have polymer, you can have metal metal combination like cobalt chrome bars is cobalt chrome. You have ceramic and ceramic but that often cause lot of noise for example JTA toughened alumina Vs. Zirconia toughened alumina. Metal and polymers like you know you can have cobalt chrome Vs. ultra molecular polyethylene that is also clinically used or people have done lot of hip similar studies on this kind of materials.

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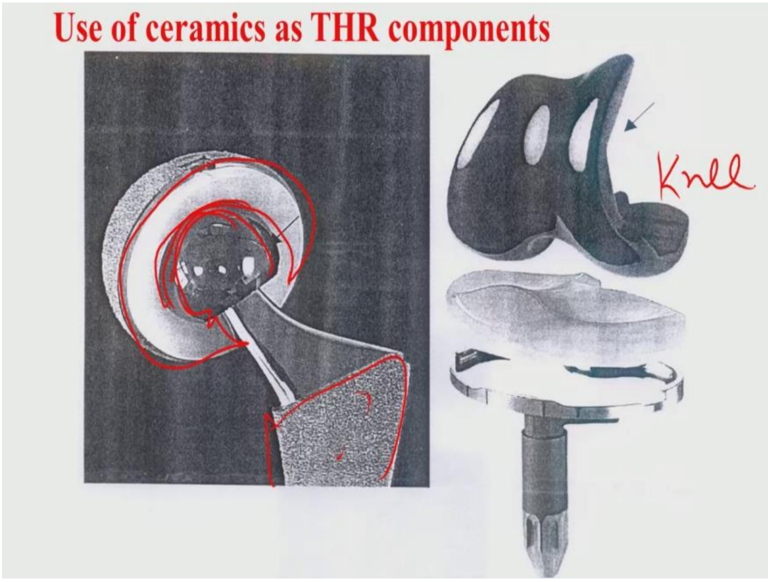

Now this shows that hydroxyapatite coatings this is your fumoral ball head which is going into the acetabular socket here and this is a knee replacement materials. So knee and hip you can see that the way the TBL component is femoral component replaced is characteristically different.

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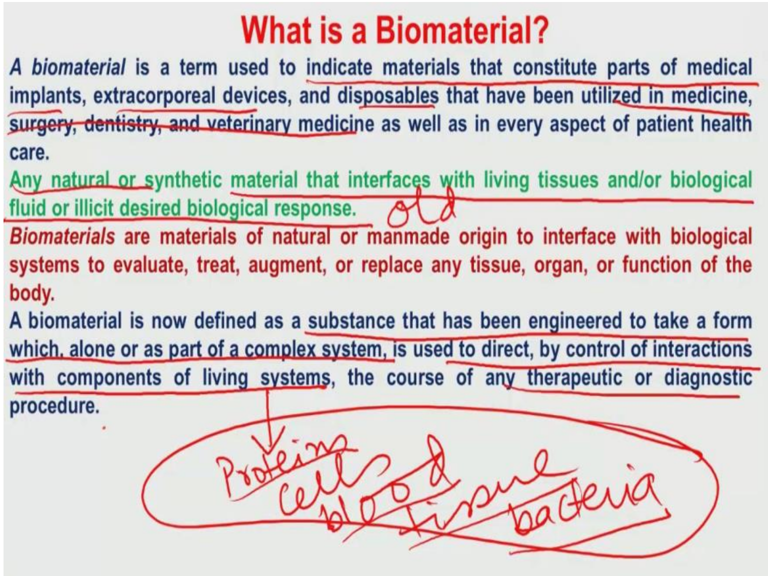

So before I finish today's lecture let me know define that what is mean by biomaterial. I will give you some 3, 4 definitions which I have taken from different text books which I have mentioned it at the beginning on this course. Biomaterial is a term used to indicate materials that constitute parts of medical implants extracorporeal devices and deposers that have been utilised in medicine. Surgery, dentistry and veterinary medicine.

Some text book type of definition is that any natural synthetic material that interfaces with living tissues or biological fluids or illicit biological response. This is a kind of very old definition. So modern definitions includes, the substance that has been engineered to take a form which alone or as a part of complex system is used to direct by control of interactions with components of living systems. By components of living system means proteins, cells, blood which is also in tissues as well as bacteria.

So once the material is implanted in the living system it has to interact with the proteins, protein absorption is a pre cursor to cell additions, cell proliferation then blood like it should have a good blood compatible hyeomocontaper, it should have a tissue compatibility and bacteria, bacteria material ideally material should not encourage the growth of bacteria because if the bacteria grows then it can cause bio fume formation then it can cause infection and it can ultimately lead revision surgery. And all this leads to the therapeutic or diagnostic procedure. So this is the formal definition of biomaterials and I hope, I would like to continue further on these topics in the next lecture. Thank you.