Medical Biomaterials
Prof. Mukesh Doble
Department of Biotechnology
Indian Institute of Technology, Madras

Lecture – 24
Metallic Biomaterials

Welcome to the course on medical biomaterials, we will continue on this metals that is the metallic biomaterials we have been talking about metals their advantages and so on yesterday, we will continue on that.

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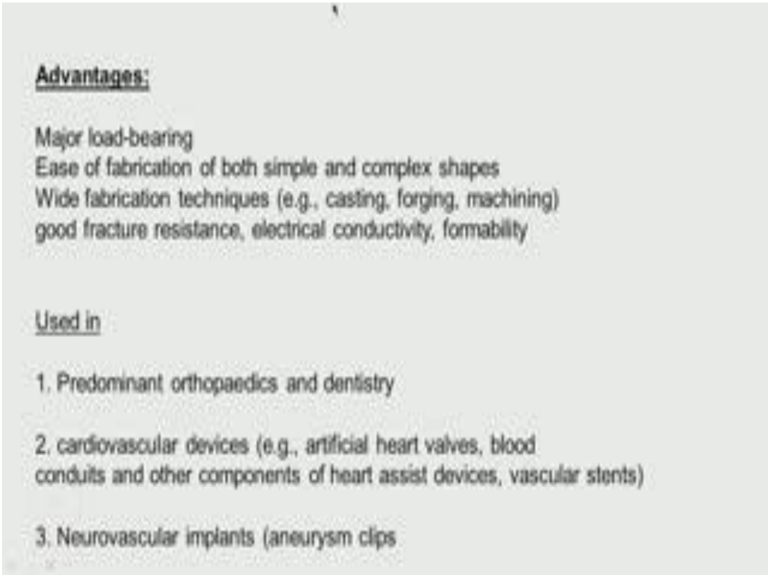

So, metals they are able to carry maximum amount of load when compared to say polymers or ceramics. So, where ever you have load bearing applications like joints like foot leg metals are very good these are fabrication metals have been used for several thousands of years. So, is a fabrication is there you can make very simple or we can make any complex shapes there are several fabrication techniques things like casting forging machining and. So, on actually good fracture resistance they have very good electrical conductivity especially if you are talking about lead wires gold is quite commonly used they can be made formed into any shape there are used in predominant in orthopedic and dentistry hmm cardio vascular devices like artificial heart valves blood conduits heart assist devices vascular stents also in neurovascular implants I showed you some pictures for example, if look at this these are titanium cages you made up of pure titanium. So, these are used in a segmental bone defects.

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So, they have less weight and compared to solid piece. So, you can fill it up with allograft is from the same patient bone fillings and then they are placed here and this type of approach is adopted if the gap between the bone is too much will that is called a long segment bone, we will talk about that later.

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So, titanium is widely used stainless steel bone plates titanium bone plates as you can see in this pictures titanium bone plates are stainless bone plates are used and they are connected to the broken bone using nails here as you can see in the x-ray picture.

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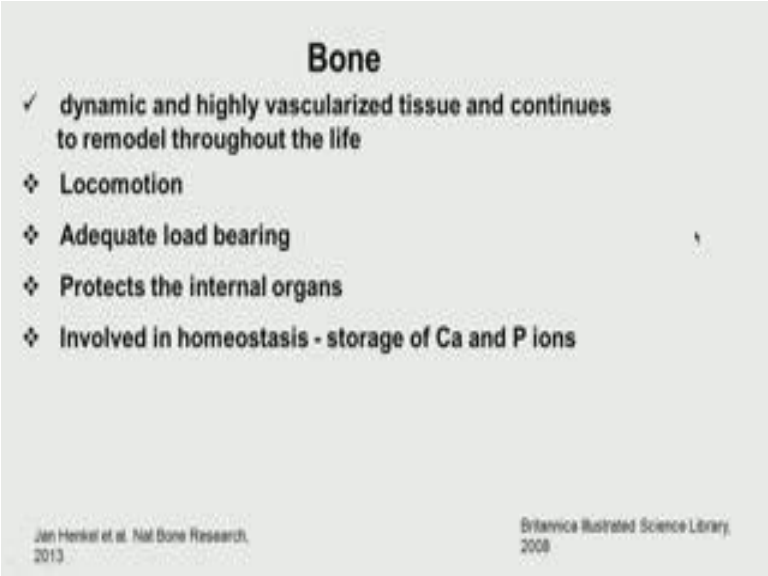

So, bone orthopedic is one big area where metals are used. So, we need to little bit understand this called the bone it is a dynamic and highly vascularized tissue and it keeps to continue remodel throughout the life; that means, bone can grow throughout the life get remodeled they are involved quite a lot of locomotion; that means, when you move your foot and leg and arms and rotate your arms.

They take a lot of load, they are able to as you can see some of the weight lifters in Olympics; they are able to carry several times their body weight; they protect the internal organ like your heart, lungs, they are all protected by these bones they are involved in homeostasis; that means, they store calcium potassium ions and they get liberated from time to time for the bodily functions.

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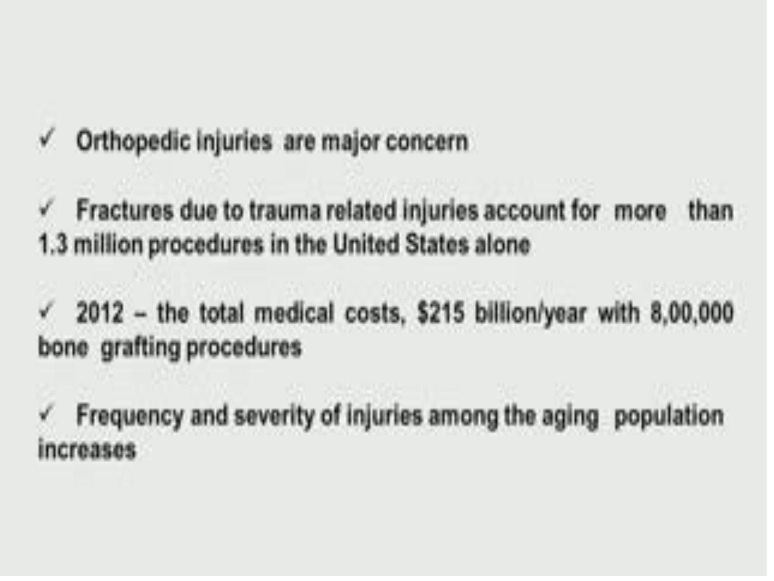

So, but then fractures are a big concern orthopedic injuries that is called happens because an accidents sports age related young people. So, all these happen. So, bones break. So, it is a very big issue orthopedic injuries fractures due to trauma related injuries account for more than 1.3 million procedures in US alone then can you imagine if you take the global it could be about 50 times more than this that is a big number then total medical cost 200 and 15 billion per year with 8 lakhs bone grafting procedures.

So, again you can see it is a big business the medical cost. So, orthopedic injuries bone fractures replacements filling up of bone crafting. So, that is a very large chunk of medical costs and again ages as the population like some other western countries the population slowing aging. So, aged related injuries osteoporosis injuries because of frequent falls. So, all these can lead to orthopedic implant or orthopedic surgeries. So, what is this long bone segmental defect?

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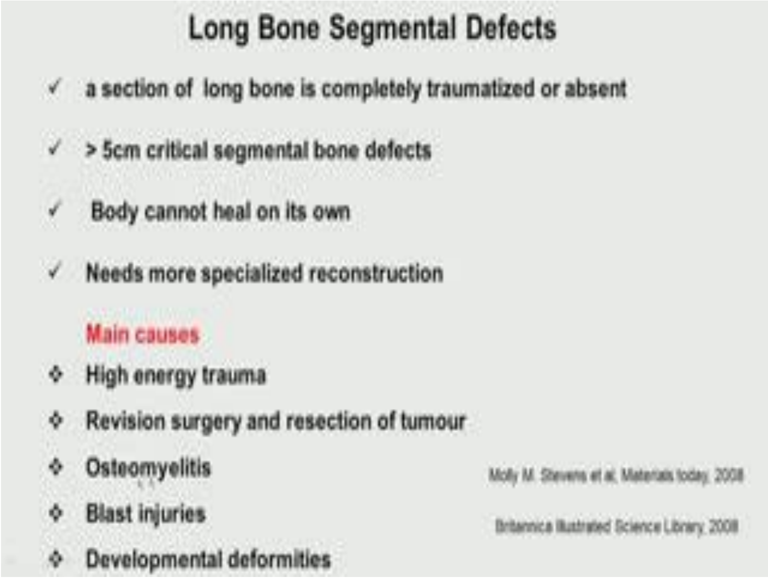

So, a long bone a section of long bone is completely traumatized or absent this can happen because of congenital decease from birth or this can happen because there has been an injury and it is not possible to fix that portion. So, that there is a big gap it can because there is an inflammation infection. So, the part of a bone has to be removed or cancerous bone that has to be removed. So, it needs to be filled up. So, anything above 5 centimeter is called critical segmental bone defect so that the body cannot heal by itself. So, the gap is smaller than this of course, the bones can grow and they can fill up, but then if it is larger what we do.

So, we need to involve by a lot of biomaterials. So, it needs specialized reconstruction as it is called. So, what are the main causes high energy trauma accidents revision surgery or removal of tumor Osteomyelitis blast related injuries developmental deformities; that means, because congenital all this lead to this long bone segmental defect that is defect in the bone gap in the bone which is longer than 5 centimeter.

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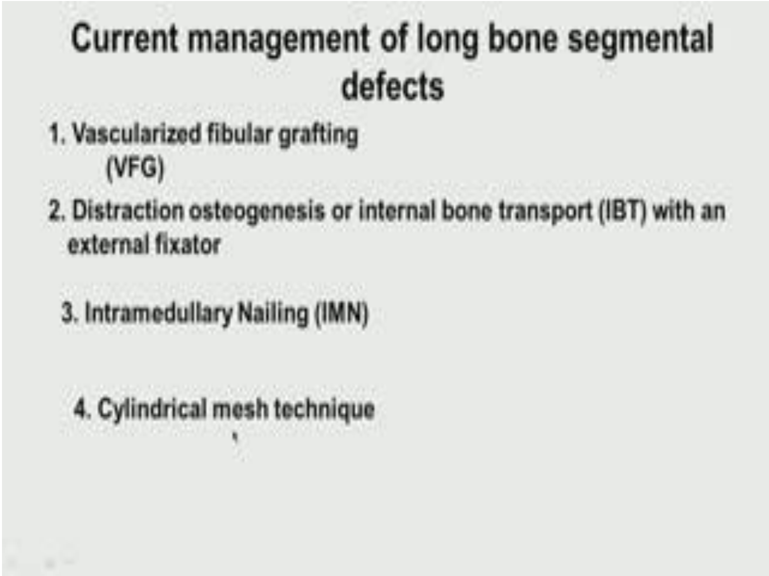

So, how do they do it now vascularized fibular grafting? So, they graft it in between distraction Osteogenesis or internal bone transport with an external fixator; they will externally pull the bones and then allow those extended portion to grow and. So, on they keep on doing that and it may take about six seven months for the bone to grow. So, they use an external fixator and keep doing that is a very difficult surgery and sometimes the both the bones may grow, but they do not exactly meet and then again there are problems another approach using intramedular nail. So, there is a long nail which runs through the bone from one end to another and then the remaining portion may be filled up.

Cylindrical mesh technique; that means, they keep a mesh cylindrical mesh filling up the gap they may be fill it up with allograft as I showed you or that may fill it up with hydroxyapatite calcium sulphate and so on. So, that the gap gets filled bones start growing actually. So, these are some approach here actually. So, what are the properties material properties the biomaterial should process if they have to work in the area of bone.

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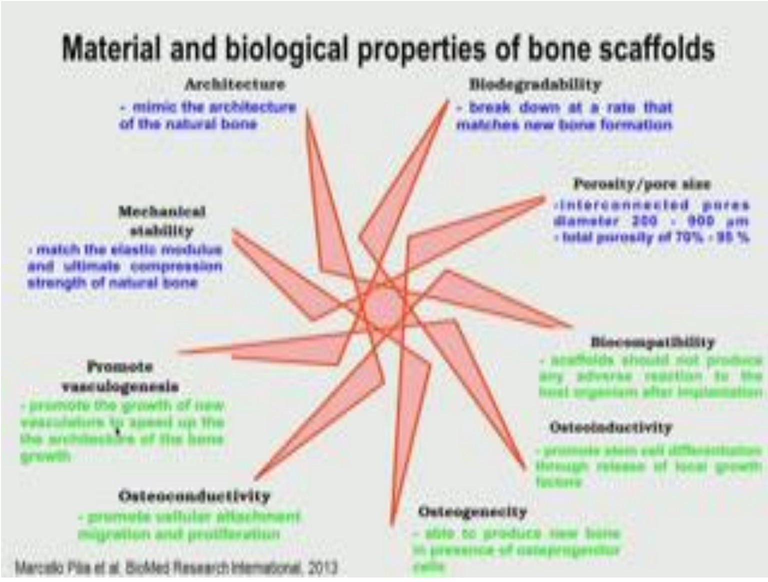

So, mechanical stability of course, that is the most important because bone is taking up lot of load they it should match the elastic modulus and ultimate compression strength of natural bone otherwise if they do not match if it is too much then there is something called stress shielding. So, they have to match stainless steel of course, does not match as I been telling you before titanium and newer versions of titanium are slowly the elastic modulus keeps going down and down. So, that they come closer to the values of the bone architecture they have to mimic the architecture of the natural bone. So, they have to exactly look like natural bone porosities and so on shape and so on.

Biodegradability; so, it will be very nice you keep this biomaterial once the bone has formed and completely disappears. So, it should match exactly the biodegradability should be exactly equal to the rate at which the bone is growing that is called biodegradability matching next is porosity you need to have lot of pores and they should be interconnected because we are talking about the blood flow and so many things ion flow. So, porosity should be around seventy to 95 percent diameter of the pore should be 200 to 900 micron and they all to be interconnected. So, that the tissues can grow nicely that is very very important next biocompatibility of course, they should not produce any adverse this is natural any biomaterial. So, this should not produce any adverse reaction to the host organism we are talked quite a lot about it biocompatibility.

Osteo inductivity; what is osteo inductive? Osteo as you know is related to bone. So, it should promote steam cell differentiation through release of local growth factors. So, it should allow the local cells to grow so; that means, it should able to release local growth factors may be if we coat the surfaces. So, that the release the factors then that is called osteo inductive; osteo genecity. So, it should able to produce new bone in the presence of osteo progenitor cells. So, that is called osteo genecity. So, it should produce new bone in the allow it should allow to produce new bone at the same time it should be able to release growth factors for the bone growth osteo conductivity it should promote cellular attachment migration proliferation because once you have the bone cell getting formed there could be migration there will be attachment to on with them and there will be proliferation. So, that should also be happening promote vasculogenesis thus means we need to allow growth of new vasculature; that means, we need to allow it for new blood vessels to grow go through in and complete the architecture of the bone.

So, lot of requirements for the material biomaterial if they has to be used for bone application please note we have introduced some new terms here osteo inductivity osteogenecity osteo conductivity what is this osteo conductivity it should promote cellular attachment migration proliferation; that means, cells should nicely attach proliferate and migrate osteogenecity it should produce new bone in the presence of the progenitor cells what is osteo inductivity it should help in the differentiation cell differentiation through release of some growth factors locally. So, all these are important the osteoinductivity, osteogenecity, osteoconductivity and then of course, it should allow blood vessels to form and penetrate to the pores. So, that finally, there is a good interconnection of the bed blood vessels that is also very very important.

So, we have the mechanical properties bio here and here biological properties here and here and then all properties related to the osteoinductivity, genecity and conductivity. So, it is quite a big challenge to develop materials for bone replacement.

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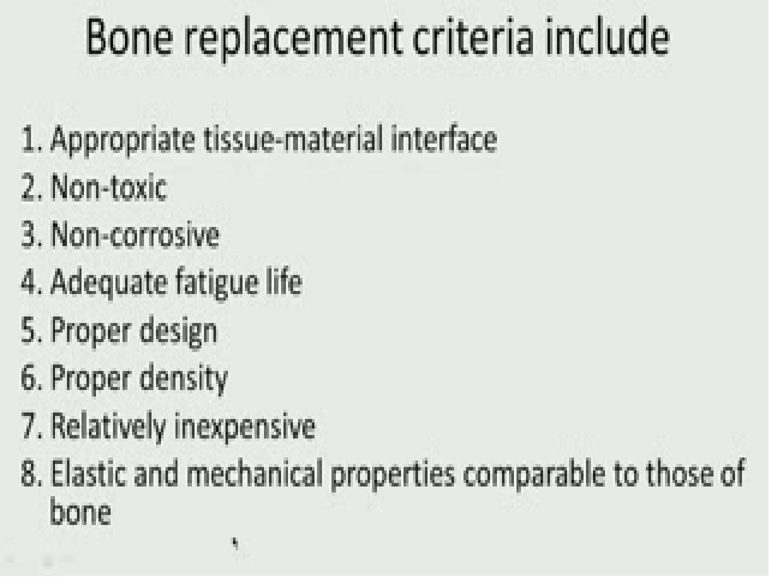

So, if you are talking about bone replacement there should be many criteria appropriate tissue material interfaces like a normal biomaterial requirement it should be non toxic of course, it should be non corrosive you do not want corrosion to happen, but that is problem because we use metals and when we are talking about stainless steel stainless steel can corrode adequate fatigue life it should because we are talking about a joint its flexing all the time. So, it should be able to have good fatigue life that is very important proper design of course, density is very important it should be of course, relatively inexpensive and then the elastic and mechanical properties comparable to that of the bone that is very very important.

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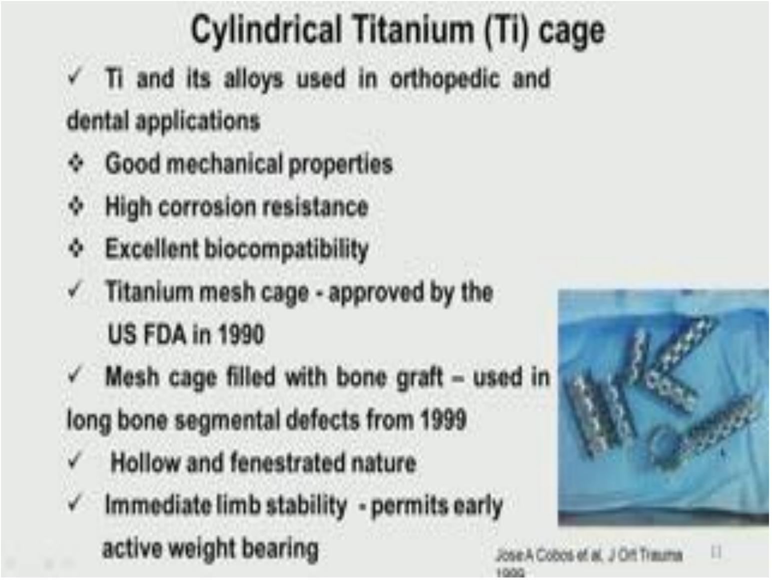

I have showed you these pictures the cylindrical titanium cage its used nowadays quite a lot specially when we are talking about long bone segmental defect that is greater than 5 centimeter defect the beauty of is this is a cage. So, its light weight; it is titanium has lot of biocompatible and osteo integration properties. So, one can fill this up with calcium sulpahte or hydroxyapatite or allografts of the host and then fill up the defective region.

So, titanium and titanium alloys orthopedic and dental good mechanical properties high corrosion resistance they do not corrode like stainless steel excellent biocompatible and this is approved by US FDA and from almost a year 1999 these type of long bone segmental defects are been addressed using this approach. So, it is an hollow fenestrated nature and it also able to take in the weight load of the individual and gives you the immediate limb stability that is the advantage of this type of cylindrical titanium cage and now a days there is even talk of can we use magnesium because magnesium cylinders they have they are bio resolvable; that means, ultimately they can completely disappear whereas, titanium will stay in the body.

So, magnesium whether it can be used is being looked at there are some research papers which talk about use of magnesium for long bone segmental bone defects.

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Common Reasons for Hip Replacement

Condition	Incidence
• osteoarthritis	60 %
• fracture-dislocations	11 %
• rheumatoid arthritis	7 %
• aseptic bone necrosis	7 %
• revision of previous hip operations	6 %

1 million hip replacements and 250,000 knee replacements are carried out per year

Now, hip again metal metallic biomaterials are used in this area why arthritis majority fracture dislocation rheumatoid arthritis asepctic bone necrosis; that means there are infections in the hip and there is death then revision that is from the previous operation. So, if you look here now again huge draw one million hip replacements and 250,000 knee replacements are carried out per year this is us data that is a big number. So, use of biomaterials metallic biomaterials in this area. So, again plays a very very important role.

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Requirements	If not fulfilled
Long fatigue life	Implant mechanical failure and revision surgery
Adequate strength	Implant failure, pain to patient and revision surgery
Modulus =that of bone	Stress shielding effect, loosening, failure, revision surgery
High wear resistance	Implant loosening, severe inflammatory response, destruction of the healthy bone Producing wear debris which can go to blood
High corrosion resistance	Releasing non compatible metallic ions and allergic reactions
Biocompatibility	Body reaction and adverse effects in the organic system
Osseointegration	Fibrous tissue between the bone and the implant, poor integration of the bone and implant and implant loosening

So, there are many requirement no it should have long fatigue life if does not have of course, it is going to have mechanical failure. So, one need to do revision surgery it is very painful time expensive consuming success rates goes down adequate strength; that means, if it is not taken there could be implant failure pain to patient and again revision surgery. So, modulus should be equal to that of bone that is a very point and that is why new designs of titanium are coming up. So, that the modulus of metal is not effecting the modulus of the bone otherwise if the modulus is high it is going to take stress shielding effects come into picture loosening can happen failure revision surgery will happen because the bone does not take in the load where because the metal takes in the load which has got higher modulus. So, the bone becomes loosed.

High wear resistance if there is lot of joints varying implant loosening inflammatory responds destruction of the healthy bone the healthy bone also starts varying because of this it produces debris which can go to the blood and if a person has a toxicity relates to a say metal chromium or nickel then he or she is going to end up having other acute problems high corrosion resistance, so releasing non compatible metallic ions and allergic reactions. So, if the corrosion resistance is low its starts giving out lot of unwanted biocompatibility. So, if not fulfilled there could be adverse reaction in the system osteo integration otherwise what happens if that does not happen fibrous tissue between the bone and the implant; that means, there is no integration between metal and the bone there could be gap. So, there could be tissues formed poor integration of the bone and implant and implant loosening. So, the integration is not good there could be implant loosening.

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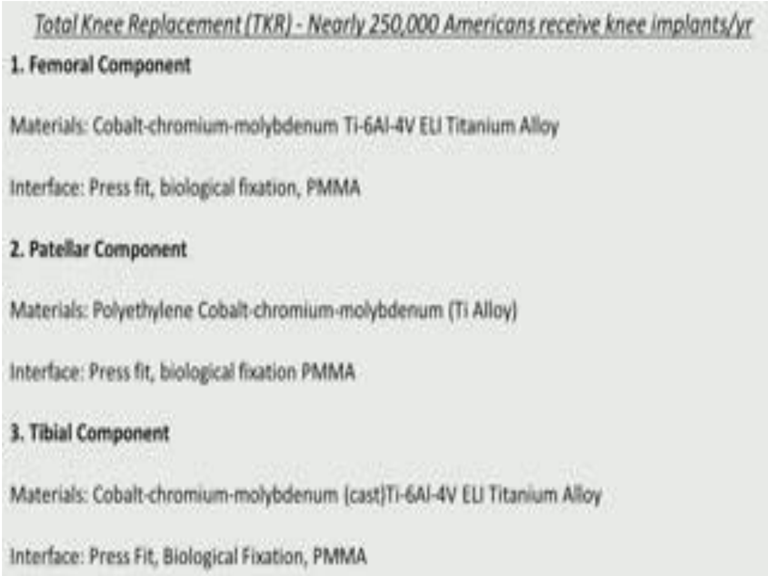

Total Knee Replacement (TKR) - Nearly 250,000 Americans receive knee implants/yr

1. Femoral Component

Materials: Cobalt-chromium-molybdenum Ti-6Al-4V ELI Titanium Alloy

Interface: Press fit, biological fixation, PMMA

2. Patellar Component

Materials: Polyethylene Cobalt-chromium-molybdenum (Ti Alloy)

Interface: Press fit, biological fixation PMMA

3. Tibial Component

Materials: Cobalt-chromium-molybdenum (cast)Ti-6Al-4V ELI Titanium Alloy

Interface: Press Fit, Biological Fixation, PMMA

So, as I said the total knee replacement, we are talking in terms of 250,000 persons in US getting knee replacement.

So, these knees; artificial knees contains a three different parts and we have metals we have polymers like polyethylene one is the femoral component. So, you can see cobalt chromium molybdenum titanium alloys are used here that is the femoral component. So, its fitted. So, you also have some poly using a poly methyl methacrylate fixing then we have the patellar component, so femoral component femoral component patellar component here polyethylene cobalt chromium molybdenum. So, this cobalt chromium molybdenum is coated with polyethylene to reduce the wear resistance otherwise it will be metal on metal.

So, there could be lot of wear and debris could be released. So, that is why they coat with polyethylene they fix again using PMMA because PMMA after all PMMA is used quite lot in dental application which acts as a adhesive then you have the Tibial component. So, we have materials cobalt chromium molybdenum titanium alloy again its fixed using PMMA you see. So, three components there are three components here and we are using cobalt chromium molybdenum titanium and then in here we are using polyethylene as a coating for interface. So, that it prevents the metal on metal rubbing it improves wear resistance.

So, this is how the total knee replacement biomaterials are used and predominantly you can see cobalt chromium molybdenum and PMMA is used as a fixating to both sides on both bones you have the knee coming in between.

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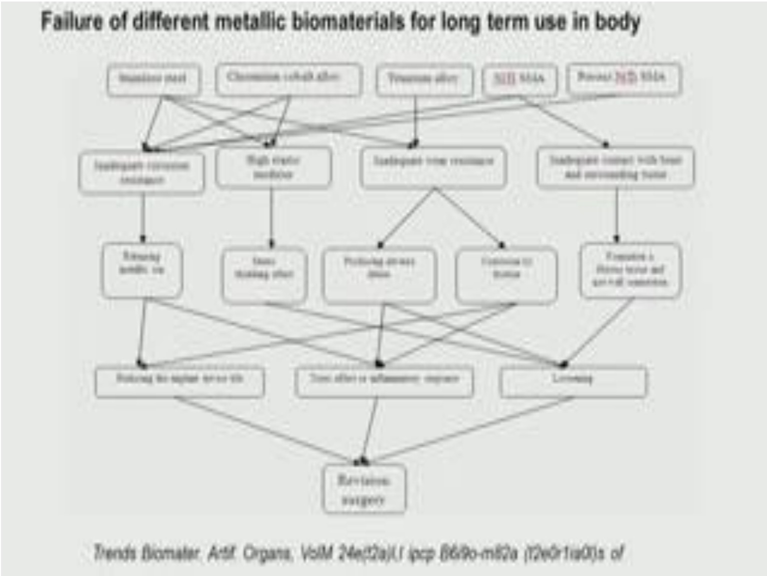

So it looks very complicated what happens to various metallic biomaterials long term use in body. So, this was adapted from this particular reference trends in biomaterial artificial organs we have stainless steel we have chromium cobalt alloys titanium alloy nickel titanium porous nickel titanium stainless steel corrosion resistance is poor chromium cobalt also is poor titanium is highly non corrosion where as nickel also can have corrosion problems high elastic modulus again stainless steel has very high chromium cobalt has high elastic modulus titanium has a problem inadequate wear resistance stainless steel also have inadequate wear resistance. So, that is why chromium cobalt’s are used in the knee region.

Now, if you take nickel titanium inadequate contact with the bone and surrounding tissue. So, osteo integration does not happen here. So, if you have a inadequate corrosion. So, there is going to be release of metallic ions, so reduction in implant life toxic effect or in inflammatory response because you are releasing metallic ions. So, high elastic modulus you are going to have a high stress shielding. So, there is going to be loosening of the bone if there is going to be high wear resistance debris are produced corrosion by friction is going to happen again this can lead to device failure this can lead to inflammation this can lead to loosening.

So, the inadequate contact with the bone and surrounding tissues they are going to form fibrous tissues in between the gap. So, again there is going to be loosening because we do not have good osteo integration. So, all this can lead to revision surgery there is very interesting feature. So, you see titanium the main problem of titanium is inadequate wear resistance. So, they could produce some debris and corrosion and toxic effect otherwise stainless steel has got a lot of disadvantages and chromium cobalt also have some disadvantages although they are very good wear resistance the elastic modulus is high corrosion effects are also high. So, some of them have good advantages, but there are some bad there are disadvantages also.

So, it is like a challenge in selecting or balancing between the advantages and disadvantages of various materials.

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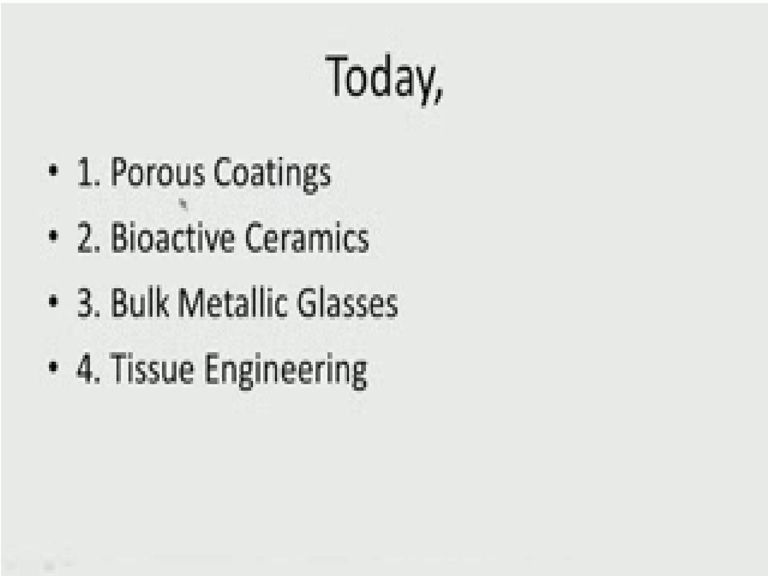

So, what do we they do porous coatings because we need to have good pores. So, that that issues the vascularization can happen they are using bio active ceramics the ceramics improve the osteo integration even bulk metallic glasses are being used these inorganic material they are highly biocompatible non toxic and they are bioactives. So, they allow the integration of the material with the bone, but one problem of some of the ceramics is they can lead to infection tissue engineering approach can I develop these tissues outside and brought inside. So, that can I grow the bone cells outside and then bring it and grow inside of course, infection and other contamination issues is to be talked about actually. So, if you look at the research current research especially in bone osteo integration these are some areas very good for research purposes.

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	Ceramic	Metal	Polymer
Hardness	VH	L	VL
Elastic modulus	VH	H	L
High temperature strength	H	L	VL
Thermal expansion	L	H	H
Ductility	L	H	H
Corrosion resistance	H	L	L
Resistance to wear	H	L	L
Electrical conductivity	B	H	L
Density	L	H	VL
Thermal conductivity	B	H	L

so we have us bone metals we have the polymers we will talk about polymers later we have the ceramics these are properties you are looking at hardness elastic modulus temperature strength thermal expansion ductility corrosion resistance resistance to wear electrical conductivity density thermal conductivity some of them are very high high, low low, high high, both low or high, we can also have very low. So, if we look at metals they have low hardness high elastic modulus.

High temp low temperature strength the high thermal expansion high ductility they have low corrosion resistance they have low resistance to wear they have high electrical conductivity high density high thermal conductivity. So, the metals have these properties and polymers have different and ceramics have different as you can see we at sometimes we need to have a miss mix and matched type of approach or coating of hmm non metals on top of metals to achieve the desired property that is how we need to do actually.

So, if you are interested in elastic modulus if you want very high then we go the ceramics or even in high metals, but polymers have much lower elastic modulus if you do not want any thermal expansion then of course, ceramic are very good because they are low if you want complete corrosion resistance of course, ceramics are the best resistance wear also is best density ceramics are low so; obviously, materials sizes high becomes very bulky polymers also low and very low. So, as you can see we have different physiochemical properties and you can have different grading of low very low high very high and so on actually when you go the mechanical properties.

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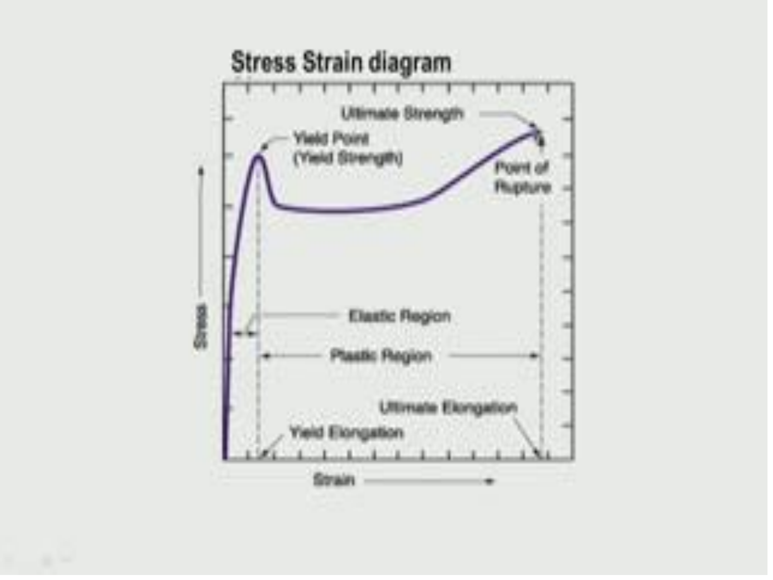

We remember this graph. So, metals especially if you draw a stress strain graph we have the elastic region where the stress and strain are related in a linear fashion here stress and strain are related in a linear passion then here we have the yield strength this region is coiled the plastic region. So, this elastic region and this is the plastic region and the slope is called the modulus and finally, it breaks here. So, this is the ultimate strength this is the yield strength yield strength ultimate strength for example, ceramics will not have a plastic region polymers will not have a lower modulus. So, it may go for polymers graph may look like this. So, this region is called the elastic region where the stress and strain are linearly related if you remember long time back and this is the plastic region. So, metals will nicely exhibit this type of graft the stress strain diagram.

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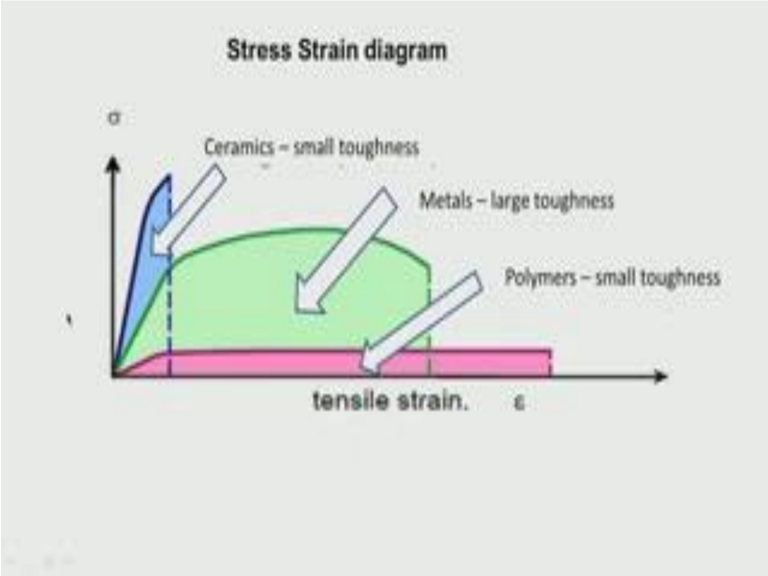

So, again same metals polymers ceramics. So, ceramics of course, do not have the plastic region they have only the very small elastic region modulus are very very high and as you can see polymers have the lowest modulus they are smallest toughness large toughness small toughness. So, this again this picture remember long time back we have been comparing polymers and ceramics in this fashion.

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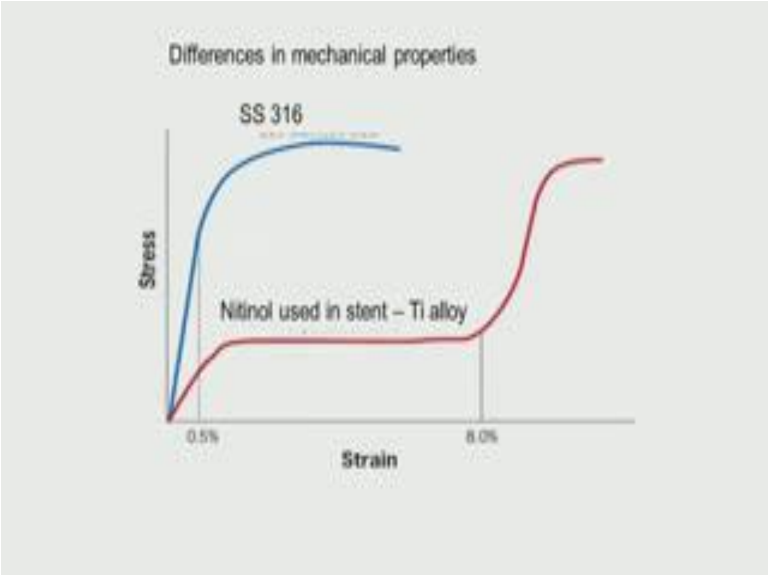

So, different metals have different types of stress strain diagram for example, stainless steel will look like this Nitinol is the titanium alloy it will look like this much lower and then goes like this Nitinol is a titanium alloy it is used in cardio vascular stents its got many good properties as you can see the modulus is extremely low therefore, metals can exhibit very large difference in stress strain and properties that is the advantage of metals we can have metal alloys. So, toe. So, many different combinations and then preparation methods and then there could be heat treatment method by which one could change these stress strain properties dramatically as you can see, stainless steel is very less very high if it go to titanium you may have a one lower and this particular alloy is much much lower. So, wide range of variations could be achieved as I said metals and their alloys preparation methods and again heat treatment methods and. So, on where as if you take polymers the; we cannot achieve this type of large differences in the stress strain behavior.

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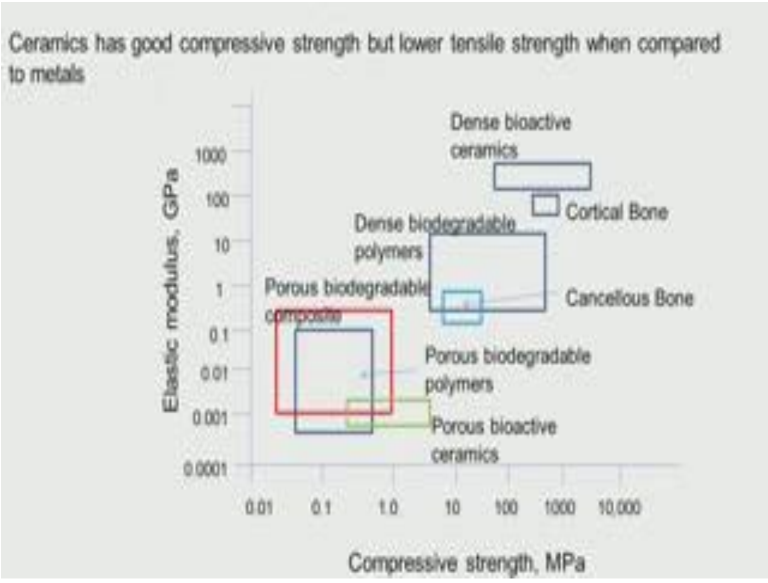

So, again this is a very interesting picture we will talk about this again we have a lot of difference between the compressive strength and the elastic modulus and let us not go into the ceramic part we will talk about that later, but as you can see the cortical bones have high elastic modulus and compressive strength cancellous bones are much lower. So, polymers are able to achieve some of these dense polymers biodegradable polymers and some of the bioactive ceramics could able to achieve will look at this diagram much later again once more again this is also very interesting picture and this was taken from this particular references called biomaterials by freeze casting.

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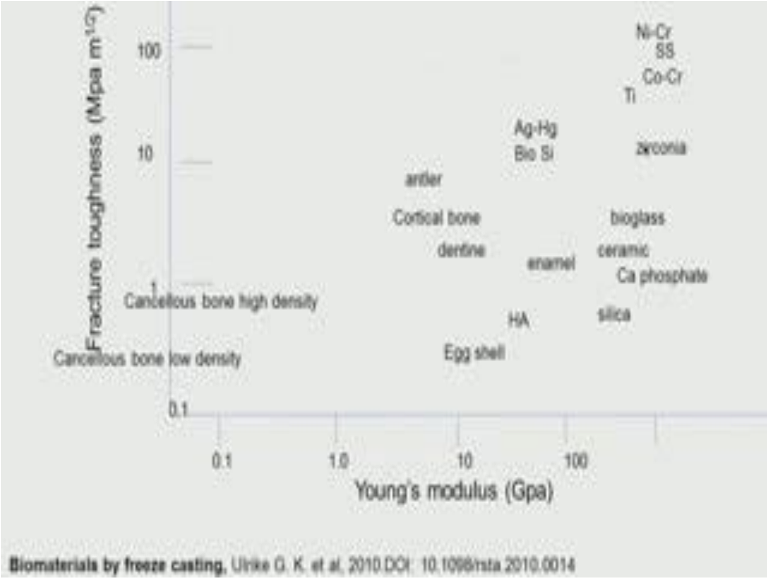

Nickel chromium stainless steel they have all come here this is the fracture toughness versus Young’s modulus fracture toughness is very very important. So, if there is a crack that is developed in the material how long does it last without completely breaking it is called fracture toughness where as we take say for example, bones cancellous bones low density high density they have very low fracture toughness as soon as there is a fracture it will immediately break whereas, as soon as there is a crack developed they will immediately break where as if you take these nickel ,metals even there is a crack they will not fracture for a very very long time that fracture toughness is very important. So, as I said these bones have very low egg shell here comes dentine this is the surface portion of your tooth cortical bone enamel they have quite low fracture toughness, so ceramic, calcium phosphate, silica, bioglass, mercurium, amalgam, bio silicate. So, they have much lower zirconia. So, some of the inorganic materials are coming here some of the bone and dental parts are coming here and the metals are coming here that is they have very high fracture toughness they have very high youngs modulus.

So, if you take these inorganic materials like bio glass ceramic they have very high youngs modulus, but their fracture toughness is quite low as you can see here right. So, they have very high Young’s modulus, but their fracture toughness. So, if there is a small crack developed immediately they can break just like your bones here now as you can see. So, this very interesting figure I would say which gives you nice idea about fracture toughness versus youngs modulus youngs modulus talks about the strength fracture toughness talks about if there is a defect developed or a crack developed how long how tough the material is even with a defect like a crack. So, we will talk about these issues in the next class as well.

Thank you very much for your time.