Biomechanics of Joints and Orthopaedic Implants
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Lecture 34
Adaptive Bone Remodelling

Good morning everybody. Welcome to the first lecture of the seventh module on Adaptive Bone Remodeling.

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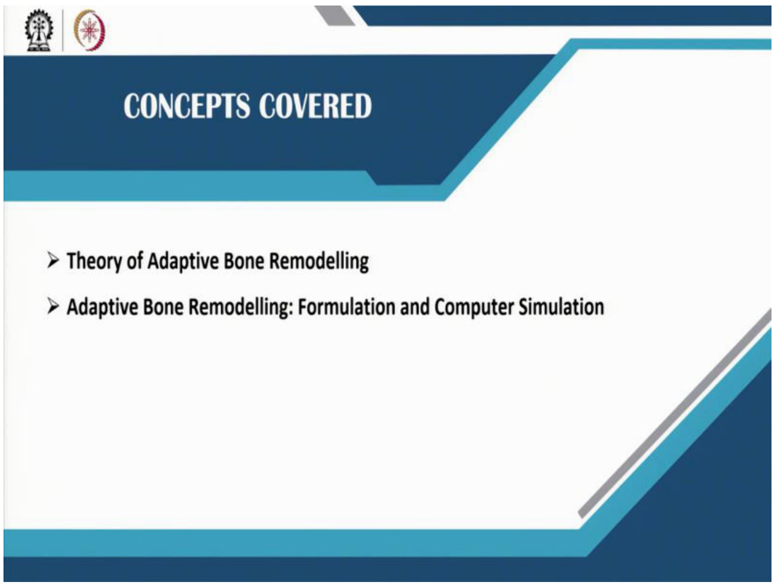

In this lecture, we will discuss the theory of adaptive bone remodeling, and thereafter, we will discuss the formulation and computer simulation of the adaptive bone remodelling process.

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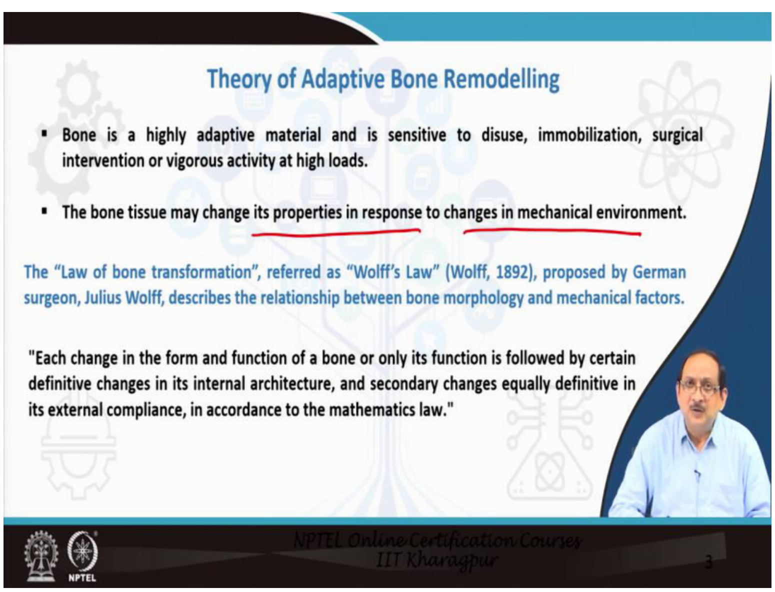

Now, as you know already that bone is a highly adaptive material. And is sensitive to disuse, immobilization, surgical intervention or vigorous activity at high loads. Bone tissue may change its properties in response to changes in the mechanical environment. The law of bone transformation, referred to as Wolff's law describes the relationship between bone morphology and mechanical factors.

So, the law states that each change in the form and function of a bone or only its function is followed by a certain definitive changes in its internal architecture. And secondary changes are equally definitive in its external compliance in accordance to the mathematics law.

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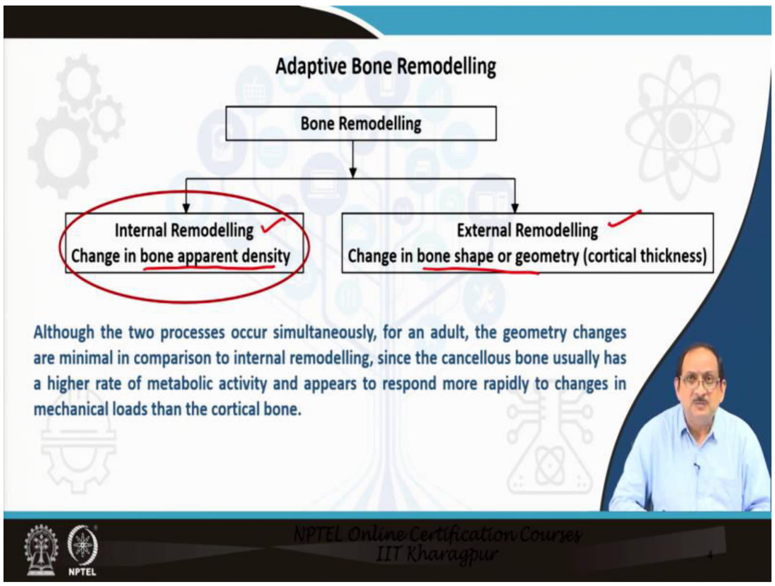

Now, Bone Remodelling can be broadly classified into internal remodelling and external remodelling. Now, internal remodelling involves a change in apparent bone density. In contrast, external remodelling refers to the bone shape or geometry changes, mainly the thickness of the cortical bone. Although the two processes occur simultaneously for an adult, the geometry changes are minimal in comparison to internal remodelling since the cancellous bone usually has a higher rate of metabolic activity.

Cancellous bone appears to respond more rapidly to changes in mechanical loads than the cortical bone. Hence, internal bone remodelling has been investigated more exhaustively.

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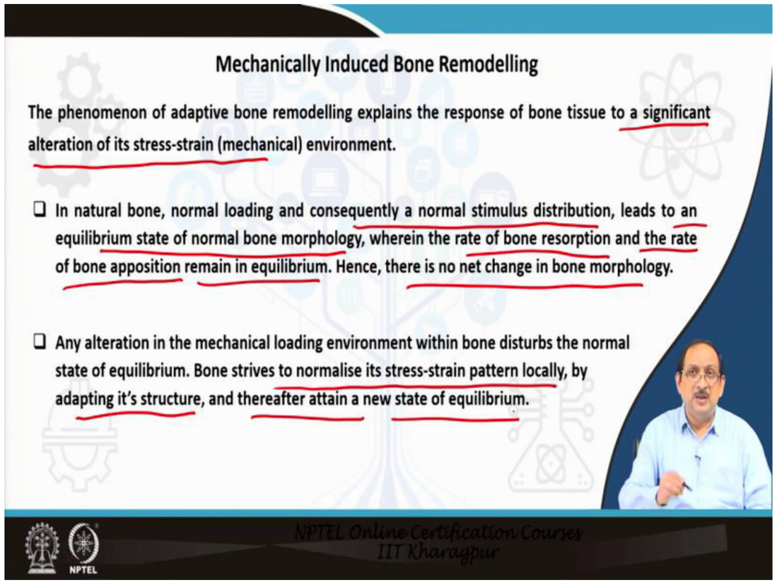

The phenomenon of adaptive bone remodelling explains the response of bone tissue to a significant alteration of its stress-strain environment that is the mechanical environment. In the case of natural bone, normal loading and consequently a normal stimulus distribution leads to an equilibrium state of normal bone morphology. The rate of bone resorption is a reduction in bone density, and the rate of bone apposition that is increasing in bone density remains in equilibrium. Hence, there is no net change in bone morphology.

Now, any alteration in the mechanical loading environment within the bone structure disturbs the normal state of equilibrium. Bone strives to normalize it stressed and patterned locally by adapting its structure and attaining a new equilibrium state.

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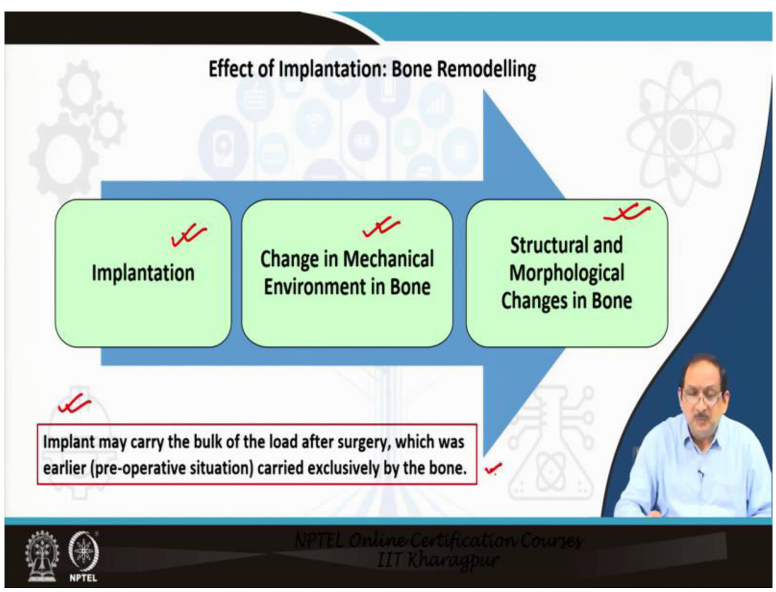

A classic example is the effect implantation. Now, implantation leads to changes in the mechanical environment within the bone structure, leading to structural and morphological changes in the bone. Now, as you already know that we have discussed the effect of stress-strain shielding. This leads to bone remodelling implant may carry the bulk of the load after surgery which was earlier that is in the pre-operative condition or situation was carried exclusively by the bone elements.

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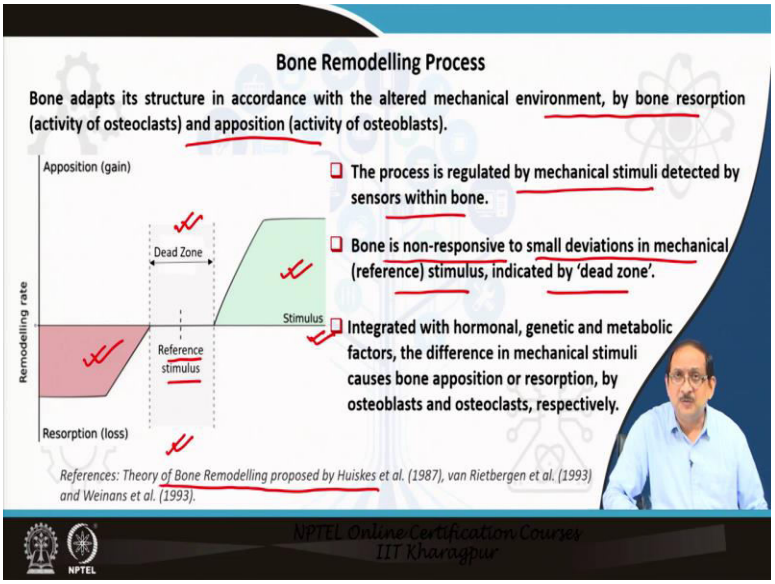

Let me present to you the process of bone remodelling. Now, as you already know, bone adapts its structure in accordance with the altered mechanical environment by the process of bone resorption, which is a reduction in bone density due to the activity of the osteoclasts and the process of bone apposition that is increase in bone density due to the activity of the osteoblasts. Now, the bone remodelling process is represented here in a figure presented in the slide.

The process is regulated by the mechanical stimuli detected by sensors within the bone. Please note that bone is not responsive or non-responsive to slight deviations in mechanical stimulus indicated by the dead zone and marked here in the figure. In the figure, you can see the reference stimulus, which is the stimulus that corresponds to the bone in the intact condition. Now, in the x-axis, we have the stimulus.

If the remodelling signal or the remodelling stimulus is less than the reference stimulus and the dead zone range, then it will cause bone resorption as indicated by the pink area. Now, if the remodelling signal is greater than the reference stimulus and the range of the dead zone, then it will cause bone apposition. Now, the process of bone remodelling is based on the theory of bone remodelling proposed by the group of Huiskes van Rietbergen and the Harry Weinans

Now, integrated with the hormonal, genetic, and metabolic factors, the difference in mechanical stimuli causes bone apposition or bone resorption by the activity of osteoblasts and osteoclasts, respectively.

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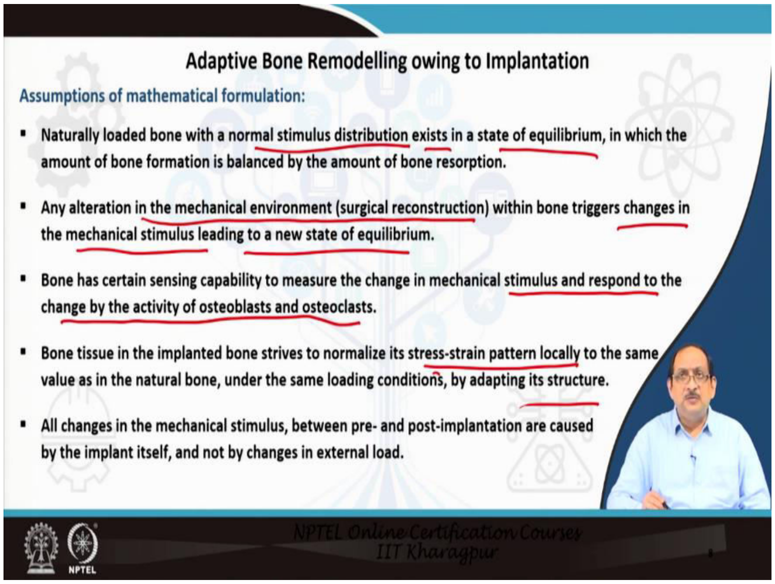

Let us discuss the assumptions of the mathematical formulation of the bone remodelling process. Naturally loaded bone with a normal stimulus distribution exists in a state of equilibrium. As stated earlier, the amount of bone formation is balanced or equal to the amount of bone resorption. Any alteration in the mechanical environment, say due to surgical reconstruction within the bone, triggers changes in the mechanical stimulus leading to a new state of equilibrium.

Bone has a certain sensing capability to measure the change in mechanical stimulus and respond to the difference by the activity of osteoblasts and osteoclasts. Bone tissue in the body planted bone strives to normalize its stress-strain pattern locally to the same value as the natural bone under the same loading conditions by adapting its structure.

The implant itself causes all changes in the mechanical stimulus between pre and post-implantation and not by the changes in the external load. So, based on these assumptions, the mathematical formulation of bone remodelling has been taken up.

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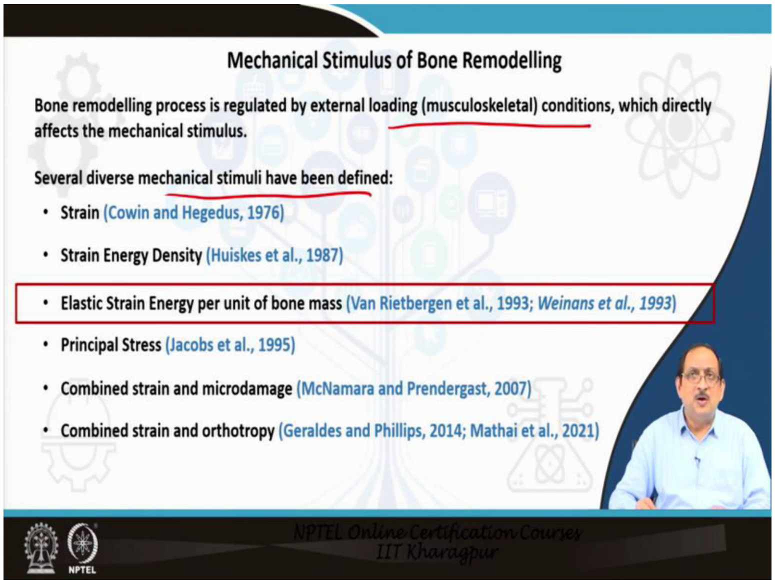

The bone remodelling process is regulated by the external loading, due to the musculoskeletal loading conditions, that directly affect the mechanical stimulus. Now, over the years, several diverse mechanical stimuli have been proposed and defined. So, the mechanical stimulus is now listed here in this slide. So, these mechanical stimuli are strain, strain energy density, elastic strain energy per unit of bone mass, principle stress, combined strain and microdamage, combined strain and orthotropy.

However, the elastic strain energy per unit of bone mass has been most commonly used as a mechanical stimulus in pre-prosthetic bone remodelling investigations.

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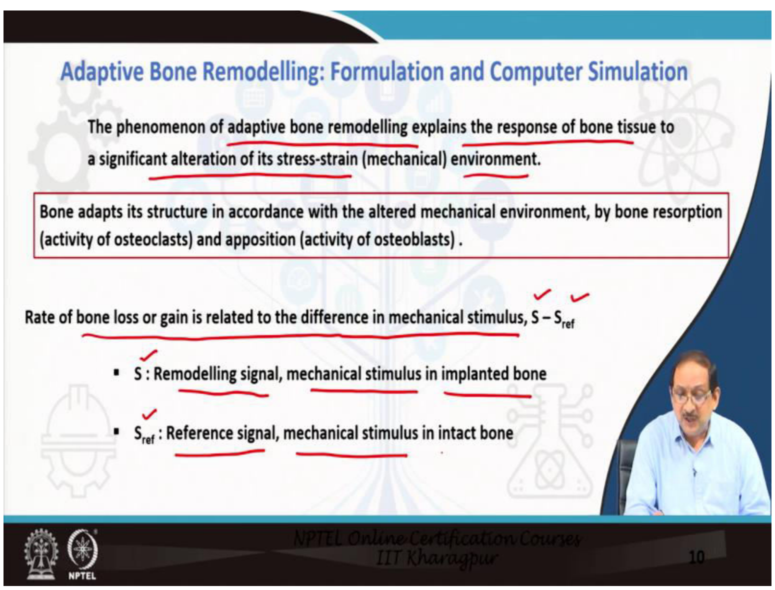

Let us now discuss the second topic on the mathematical formulation and computer simulation of the process of adaptive bone remodelling. The phenomenon of adaptive bone remodelling explains the response of bone tissue to a significant alteration of its stress-strain environment that is the mechanical environment. Now, bone adapts its structure in accordance with the altered mechanical environment by the process of bone resorption that is a decrease or reduction in bone density and the process of bone apposition that is an increase in bone density.

Now, the rate of bone loss or gain is related to the difference in mechanical stimulus, the difference between the S and S_{ref}. S is the remodelling signal that is the mechanical signal corresponding to the implanted bone structure. At the same time, S_{ref} is the reference signal of the mechanical stimulus corresponding to the intact bone structure or condition.

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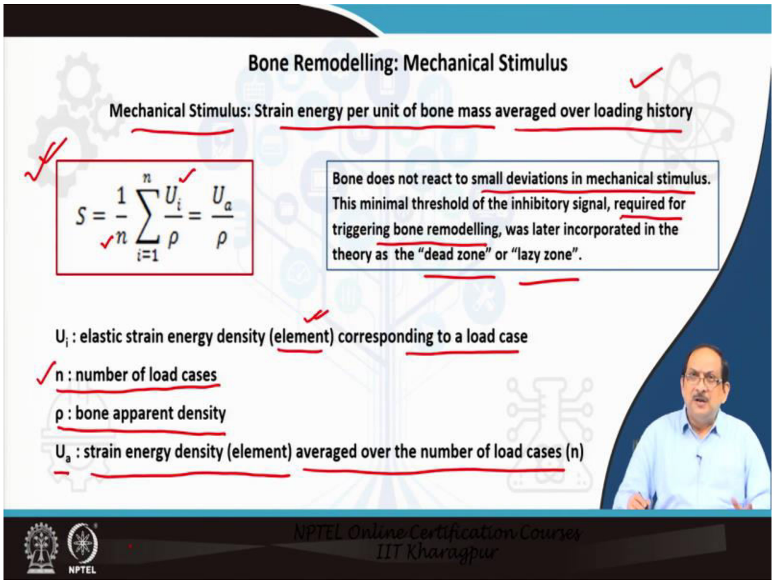

Now, mechanical stimulus is defined as the strain energy per unit of bone mass averaged over the loading history. This can be mathematically represented here, as mentioned in the slide where Ui is the elastic strain energy density of a bone element corresponding to a load case. So, there may be a number of load cases in a loading history or representing a loading history represented by n in the mathematical expression.

Now, ρ is the apparent bone density, and U_a is the strain energy density of an element averaged over the number of load cases. Now, as indicated briefly earlier, that bone does not react to slight deviations in the mechanical stimulus. This minimal threshold of the inhibitory signal required for triggering bone remodelling was later incorporated in the theory of bone remodelling as the dead zone or lazy zone, as indicated earlier in the figure, that presented the bone remodelling process.

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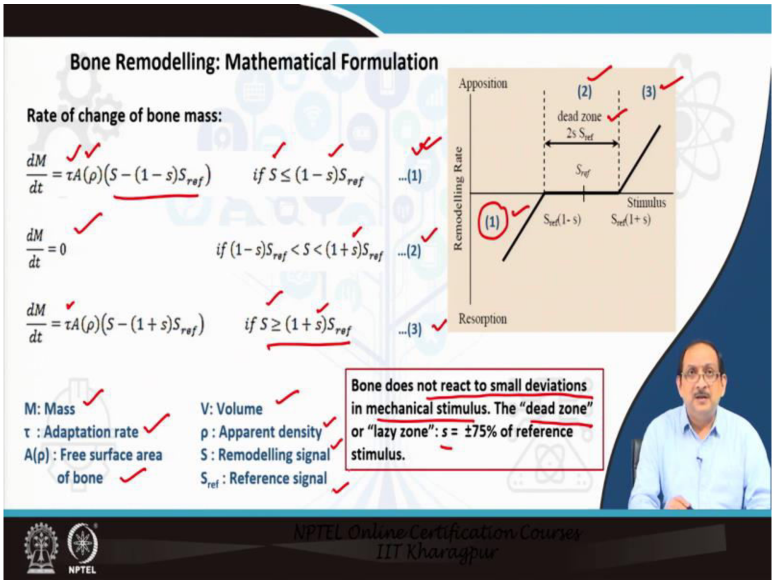

Now, let us come to the governing equations of the bone remodelling process. Now, hearing the rate of change of bone mass is proportional to the difference in mechanical stimulus before and after implantation. The governing equation includes the difference in mechanical stimulus before and after implantation and the threshold range of the dead zone or the lazy zone, as indicated in the figure.

Now, the governing equations of the bone remodelling process consist of three equations corresponding to different conditions, as indicated here in this slide. The first case I am discussing refers to the condition when the remodelling signal S is less than the reference stimulus. So, this governing equation refers to bone resorption, as indicated in the figure. The second equation corresponds to the value of remodelling signal S located in the dead zone.

So, let me erase it here. So, the second equation refers to the dead zone indicating no remodelling that is

$$\frac{\mathrm{dM}}{\mathrm{dt}} = 0$$

The third equation refers to the condition when the remodelling signal is greater than the reference stimulus as indicated by the condition specified here. So, these three equation summarizes the bone remodelling process. So, as discussed earlier, bone does not react to small deviations in the mechanical stimulus.

And this is indicated by the dead zone on the lazy zone. Generally, s represented in all the equations, the s refers to the definition of ±75 per cent of the reference stimulus that means on either side, ±75 per cent of the reference stimulus defines the range of the dead zone. The time-dependent progressive bone density changes also depend on bone's available free surface area indicated by A(ρ) in the equation.

And indicate defined here by a(ρ) as the free surface area of bone. The process also depends on the adaptation rate as indicated by τ in the equation. The free surface area of bone, the adaptation rate and the time step will be discussed in the following slides. So, the other variables here are mass of bone: m, the volume of bone: v, apparent density: ρ, remodelling signal: S and the reference signal: S_{ref}.

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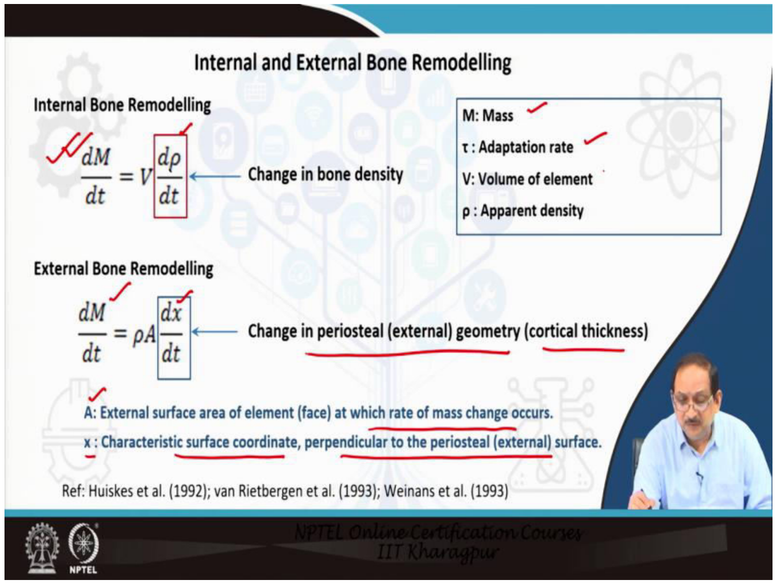

In the case of internal bone remodelling, the rate of change of bone mass is now expressed mathematically as a rate of change of bone density, considering the bone element volume to be constant. Whereas in the case of external remodelling, the rate of change of bone mass is expressed as a rate of change of periosteal geometry.

So, here in A refers to the external surface area of an element at which the rate of mass change occurs. And x denotes the characteristic surface coordinate perpendicular to the periosteal or the external surface. Now, the theory of adaptive bone remodelling is based on the published works of ref Huiskes van Rietbergen and Harry Weinans. So, here also bone mass is indicated by M Adaptation rate is τ. The volume of the bone element is V, and the apparent density of the bone element is denoted by ρ.

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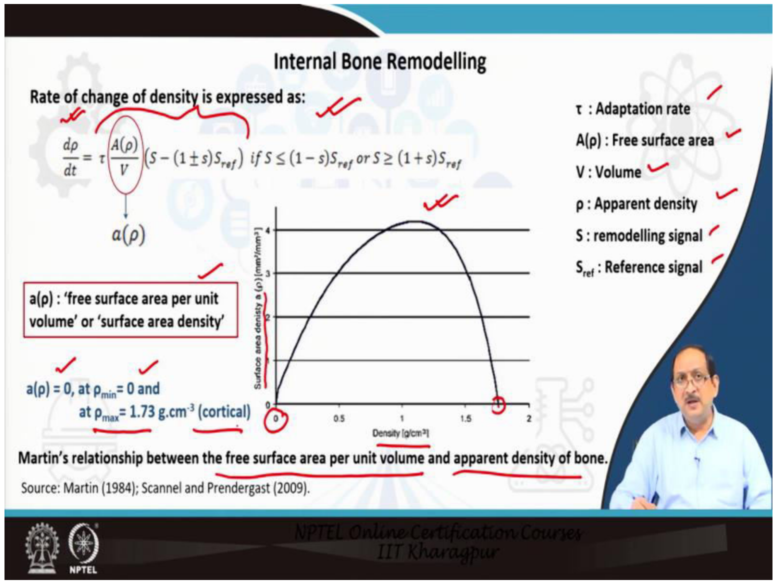

So, the governing equation can be expressed in a more general form indicated here in the slide. So, the governing equation for the internal bone remodelling as indicated here in the slide. So on the left-hand side, we have the ($d\rho/dt$), rate of change of bone density. And on the right-hand side, we have the expression consisting of the difference in the mechanical stimulus of the remodelling signal and the reference signal.

And it contains the other parameters such as the adaptation rate, the free surface area: $A(\rho)$, the volume of the element: V, the apparent density of the bone element, the remodelling signal and the reference signal. Now, the term $A(\rho)$ divided by V is a term which is known as the free surface area per unit volume or surface area density. There is a Martins' relationship between the free surface area per unit volume or the surface area density that is $a(\rho)$ as indicated in the figure.

And the apparent bone density is plotted along the x-axis. So, this curve defines a relationship between the free surface area per unit volume and the apparent density of bone. Now, it may be noted that $a(\rho)$ is equal to 0 at the minimum and maximum bone density. So, the minimum is 0, and the maximum density corresponds to the cortical bone density of 1.73 gm/cm^3.

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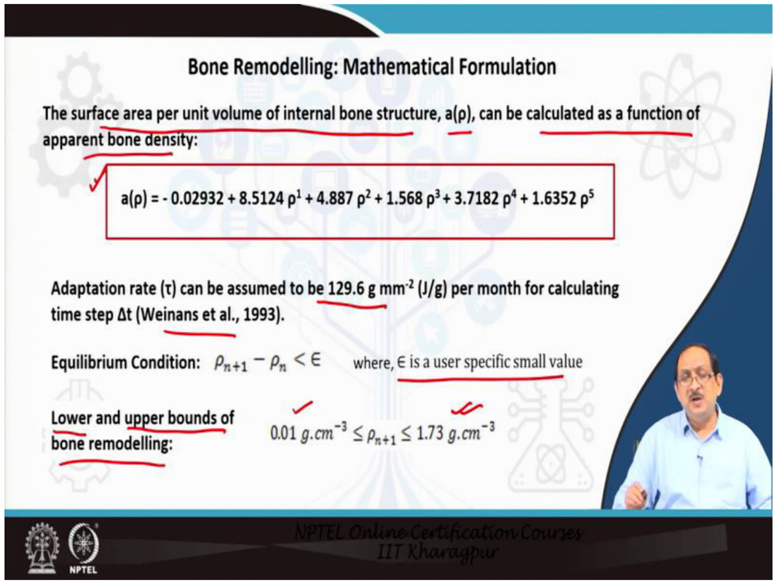

This curve can be mathematically represented as a polynomial based on which the surface area per unit volume of internal bones structure, surface area density a(ρ), can be calculated as a function of bone apparent density. Now, the adaptation rate tau is generally assumed to be a value proposed by the Weinans group for calculating the time step Δt.

The equilibrium condition of the iterative simulation of the bone remodelling process can be achieved when the difference in successive bone density values is less than a small user-defined value ϵ . This is a usual procedure for all iterative simulations.

The bone remodelling process stops at the bone density of the cortical bone that is 1.73 gm/cm^3. So, these are defined as the limits or the lower and upper bounds of the bone remodelling process.

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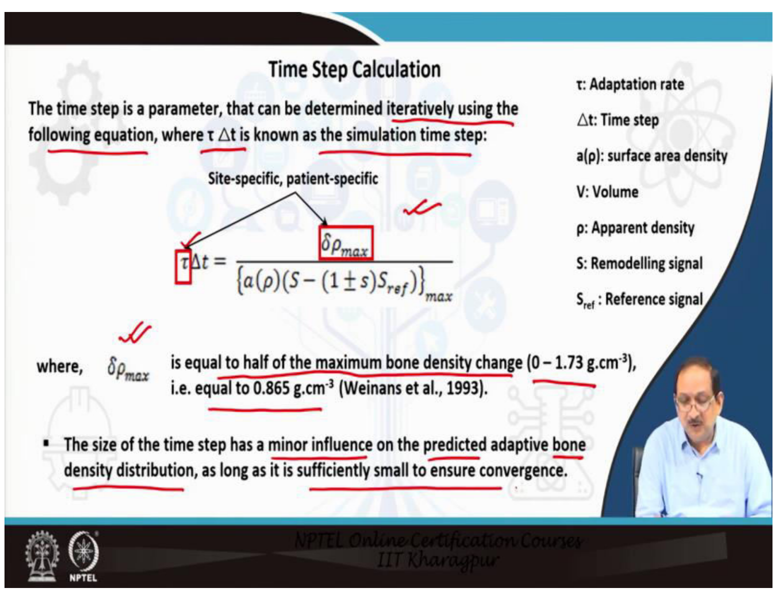

Now, let us discuss the time step calculation. Now, the time step is a parameter that can be determined iteratively using the following equation, where $\tau\Delta t$ is known as the simulation time step. Now, the expression for the simulation timestamp is given here is presented here in the slide. Where τ: the adaptation rate and the $\delta\rho_{max}$ actually may depend on site-specific and patient-specific data.

So, it may vary from site anatomic site to site, and it can also vary from patient to patient. Now, what is this $\delta\rho_{max}$? Now, $\delta\rho_{max}$ is equal to half of the maximum change in bone density. So, the maximum difference in bone density can be from 0 to 1.73, and $\delta\rho_{max}$ is equal to half of the maximum change in bone density equal to 0.865. However, this time step size has a minor influence on the predicted bone density distribution as long as it is sufficiently small to ensure convergence.

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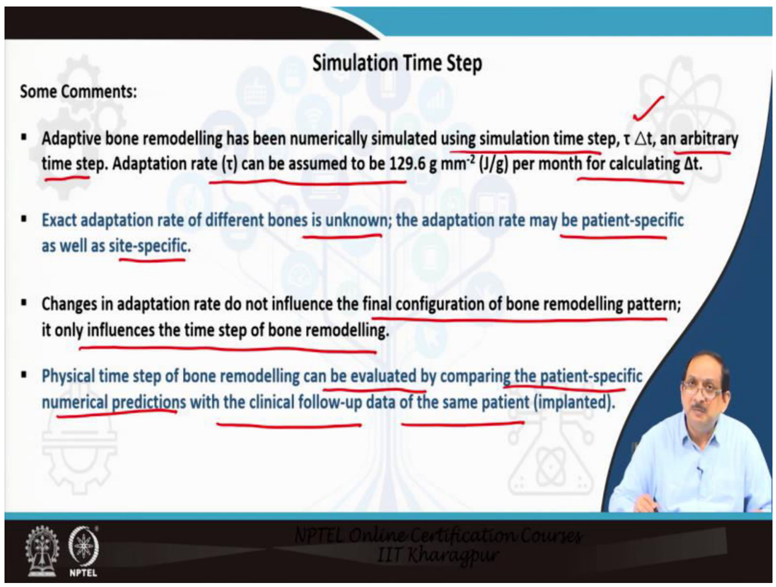

Now, I would like to summarize some comments about the simulation time step. Now, adaptive bone remodelling has been numerically simulated using a simulation time step that is $\tau \Delta t$, an arbitrary time step. Now, the adaptation rate as indicated earlier can be assumed as 129.6, and it can be used for calculating the Δt. Again, these are just values. The exact adaptation rate of different bones is unknown.

The adaptation rate may be patient-specific as well as site-specific as discussed earlier. Changes in adaptation rate do not influence the final configuration of the bone remodelling pattern. That is the bone remodelling pattern after attainment of equilibrium. It only affects the time step of bone remodelling. Now, the physical time step of bone remodelling can be evaluated by comparing the patient-specific numerical predictions with the clinical follow-up data of the same patient implanted with the same implant.

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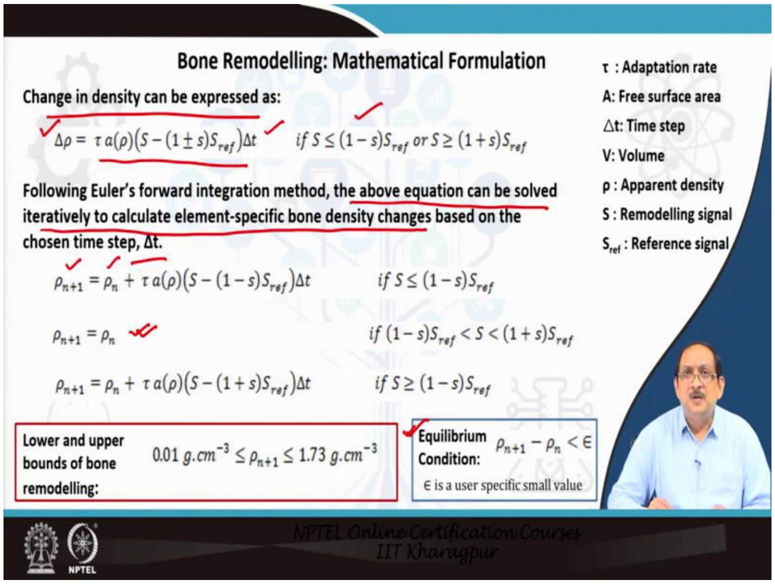

Now, let us rewrite the governing equation of the bone remodelling process.

Following Euler's forward integration method, the above equation can be solved iteratively to calculate elements specific bone density changes based on the chosen time step Δt. So, we can write the updated bone density as ρ_{n+1} and the previous bone density as ρ_n and rewrite the equations corresponding to the different conditions as explained earlier.

So, here you can see that ρ_{n+1} is equal to ρ_n because the remodelling signal falls within the dead zone. Hence, there is no bone remodelling. Let me reintroduce the lower and upper bounds of the bone remodelling process mentioned to you earlier. The equilibrium condition of bone remodelling indicated by the difference in successive values of bone density is less than a very small predefined value ϵ, as shown in the slide.

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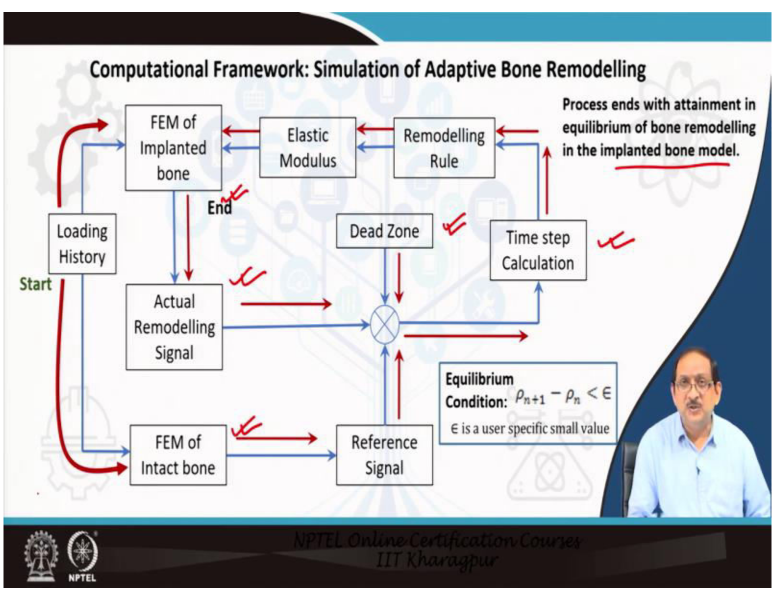

Let me now present to you the computational framework required for the adaptive bone remodelling process simulation. The remodelling theories can be incorporated in an iterative computational framework combined with finite element models and analysis to predict prosthetic adaptive bone remodelling. Now, let me discuss the steps in the computational framework.

So, first, we need two models, one corresponding to the intact bone a finite element model of the intact bone. And another is the finite element model of the implant-bone of the implanted bone. Please note that these two models are different but should be based on the same bone. Now, the simulation starts when we apply the loading history or the loading conditions to the finite element model of the intact bone.

In the first step, we simultaneously apply the loading history to the finite element model of the implanted bone. Now from the finite element analysis of the intact bone, we can calculate the reference stimulus of the reference signal, and from the finite element analysis of the implanted bone structure, we can calculate the remodelling signal. Once we have obtained the remodelling and reference signals, we can compare them with the dead zone.

Now, if it falls within the range of the dead zone, then there is no remodeling. If it falls beyond the threshold range of the dead zone, bone remodelling starts. So, we move forward in implementing the bone remodelling process the first step is to calculate the time step as indicated in the flowchart. So, following the time step calculation, we apply the remodelling rule based on the governing equations discussed earlier.

So, once we calculate the updated value of the bone density, we can calculate a new value of the bone Young's modulus. Hence, we have an updated new implanted bone model to be analyzed again corresponding to or subject to the loading history as applied earlier. So, this process goes on iteratively until the process ends with attainment in the equilibrium of bone remodelling in the implanted bone model.

As discussed earlier, the equilibrium condition is reached when the difference in the successive values of bone density is less than a minimal value that is user-defined as indicated in the slide.

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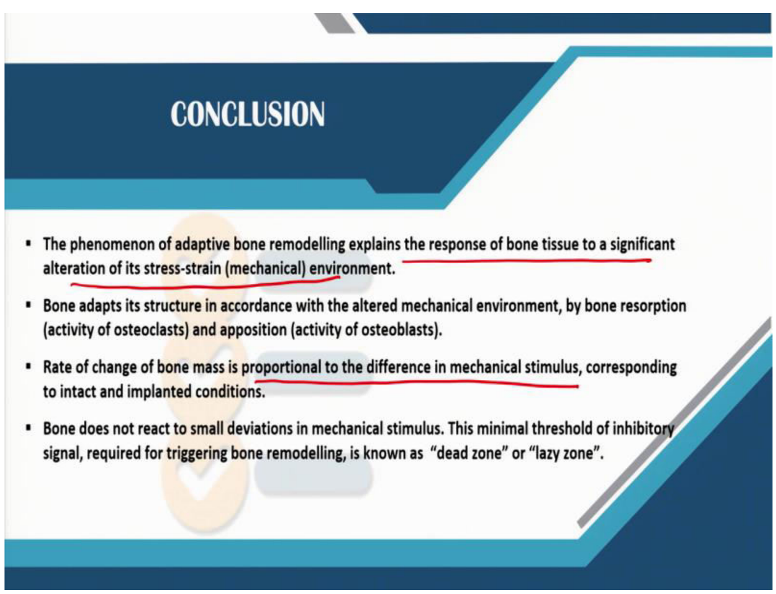

So, we conclude the study. The phenomenon of adaptive bone remodelling explains the response of bone tissue to a significant alteration in its stress-strain environment, that is, the mechanical environment. Bone adapts its structure in accordance with the altered mechanical environment by resorption. And bone apposition is due to the activity of osteoclasts and osteoblasts, respectively.

The rate of change of bone mass is proportional to the difference in mechanical stimulus corresponding to the intact and the implanted conditions. Bone does not react to small deviations in the mechanical stimulus. This minimal threshold of inhibitory signal required for triggering bone remodelling is known as the dead zone or lazy zone.

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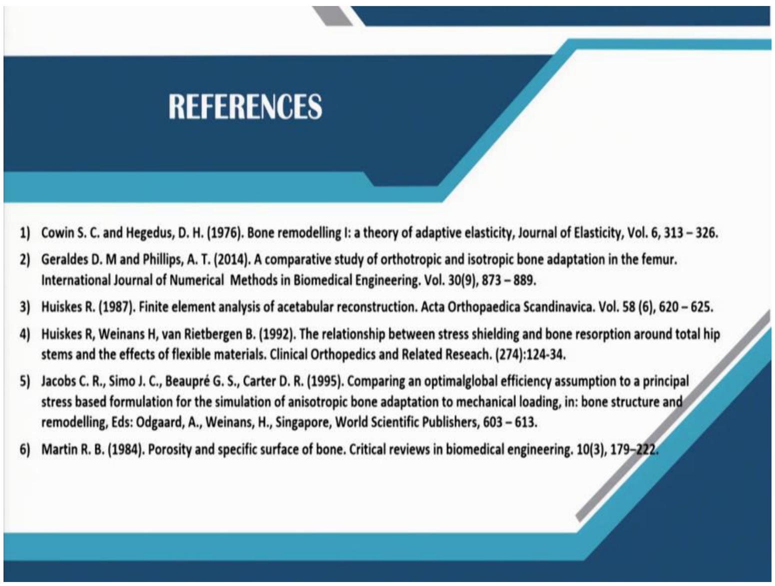

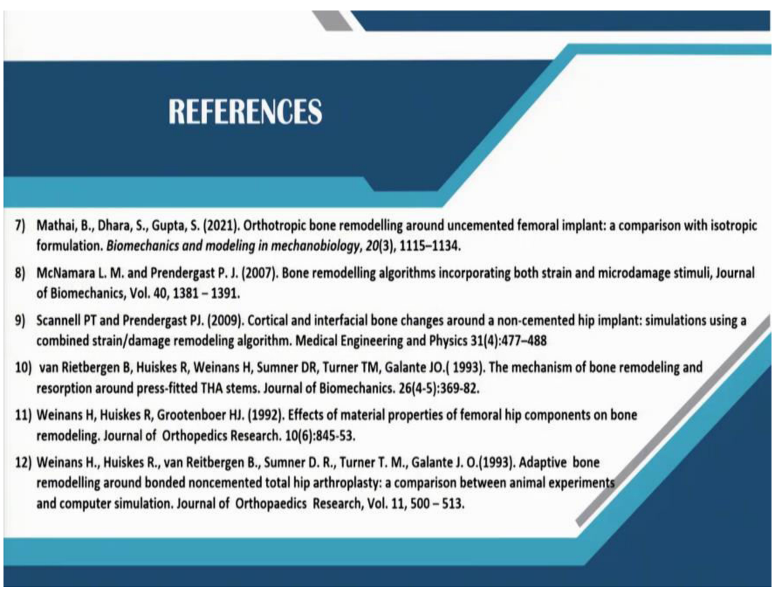

So, the list of references is indicated in two slides based on which the lecture has been prepared. I thank you for listening.