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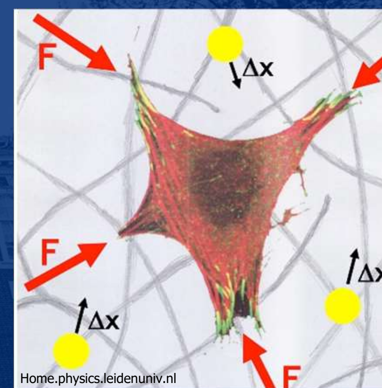
Cell and Tissue Engineering

Biomechanics of Bone and Cartilage



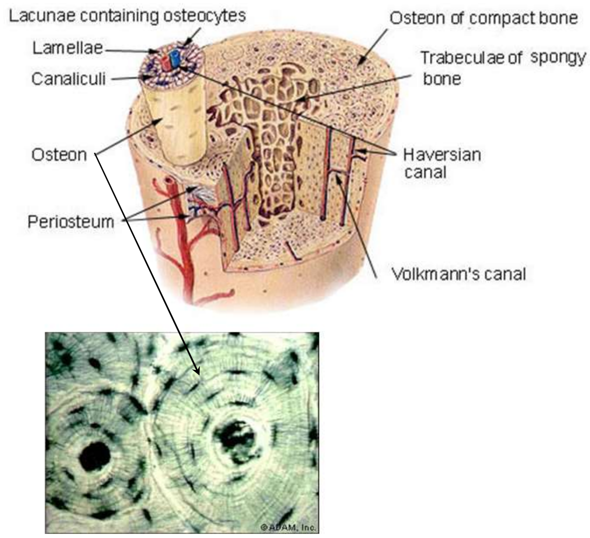
Welcome to Cell and Tissue Engineering.

We need these the models to help us understand the mechanical behavior of biological tissues. And we need to understand these behaviors so that we can **replicate** them in **engineered tissue.**

We just talked about specific model of mechanical behavior, now lets discuss the mechanical properties of some biological materials.

In this video, we will talk about the biomechanics of bone and cartilage

Biomechanics of bone



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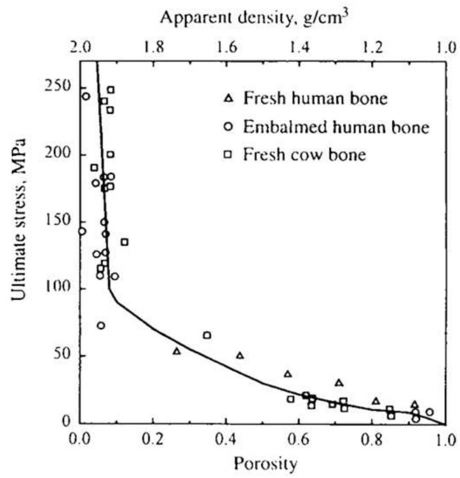
Wikipedia.org; Nytimes.com

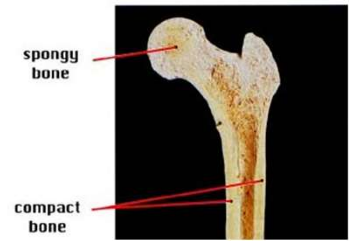
As you would expect bones are very strong and are mainly composed of mineral deposits (60%). Only 30% of bone is collagen matrix, leaving just 10% for water. This is quite different from the hydrostat muscles we saw previously which were **upwards** of 80% water.

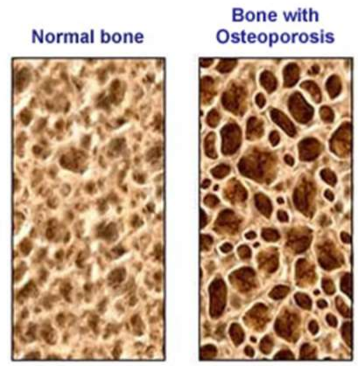
Bones are **highly vascularized** as you can see here, and as many of us have experienced first hand, they are quite adept at self-healing. Tissue engineers **love** to work on tissues that have self-healing abilities, because those tissues have regenerative capacities **built in**.

There are two bone structures – **compact/cortical** – that you can see here, and **spongy** or **trabecular** which is shown in the core of this schematic.

Biomechanics of bone







Porosity decreases bone stiffness and tensile strength

The differences in bone **microstructure** affect the mechanical properties of the different bone types.

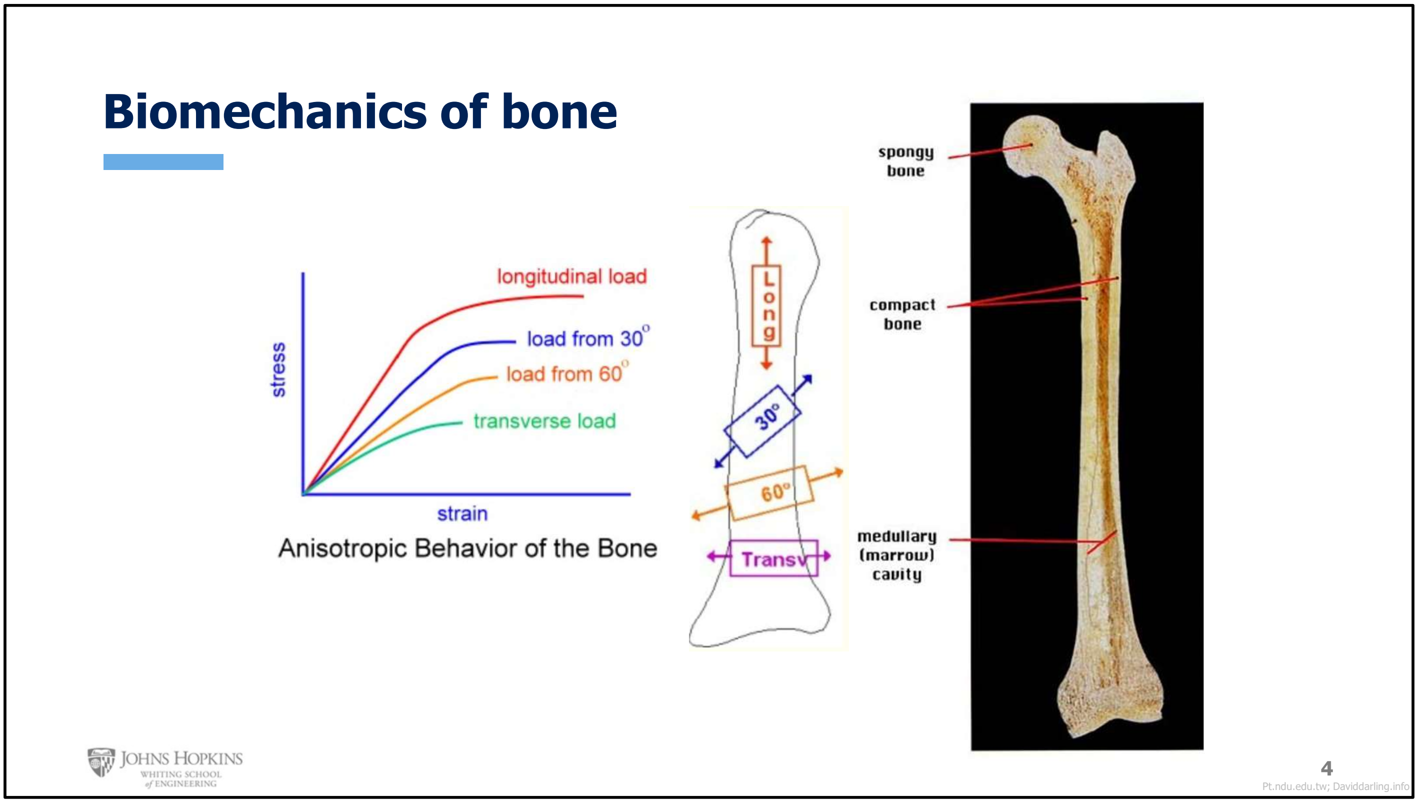
With **increased** porosity, there is **decreased stiffness** and **ultimate tensile stress.**

This graph show you how fast the **drop off** is in tensile stress, as porosity is increased in bone.

This drop off is the same for fresh or preserved human bone and is even the same in other species – here you see cow.

So, as you would expect, trabecular bone is not as strong as **cortical** bone. In fact, this is why it is more common to fracture the **ends** of your long bones which are trabecular in structure.

One natural cause of increased bone porosity is **osteoporosis** – this is when the creation of new bone does not keep up with the removal of old bone. Patients with this condition have weak and brittle bones – and subsequently an increased risk for fracture.

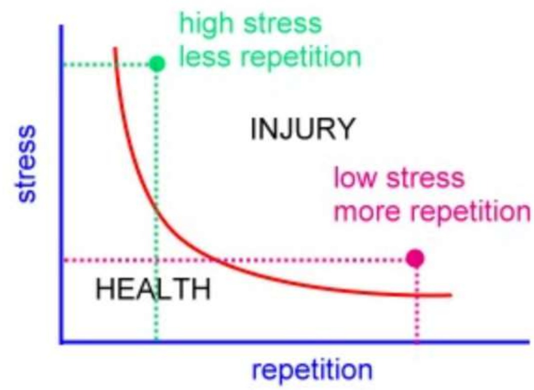


Like many biological materials, bone is **anisotropic**. This means that depending on the orientation of the stress, the strain (and therefore the perceived modulus) will be different.

This leg bone has been designed by nature to resist force in the longitudinal direction – that's the way the bone is oriented when you walk. It is it much weaker in other directions, which is why it is more easily broken when hit in a perpendicular or transverse direction.

Trabecular bone is located at the ends. Note that bone is **mostly solid** and therefore the shape of these curves look similar to our **solid spring model from earlier.**

Biomechanics of bone



Fatigue of the Bone

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Pt.ndu.edu.tw; Musculoskeletalnetwork.com

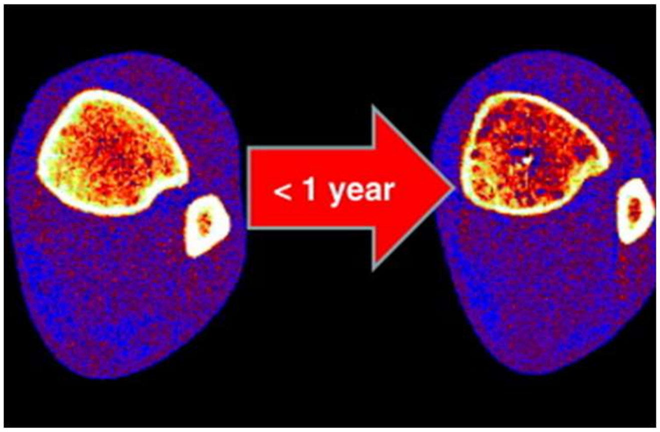
We all know what muscle fatigue feels like but did you know that you can also fatigue your bones?

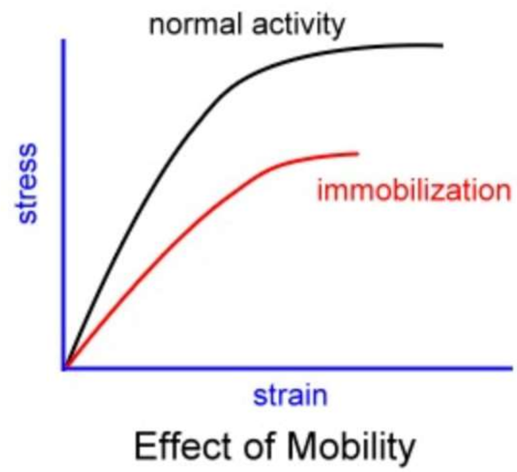
A single high stress event – the impact of a car door for example -- can result in fracture or injury.

However, when bone is subjected to cyclic loading – for example running a long distance, it can also fracture.

These low stress, high repetition fractures are the result of bone fatigue. Runners know these as **stress fractures**, and these fractures occur in the transverse direction – the weakest plane in cortical bone.

Biomechanics of bone





Pt.ndu.edu.tw

SO what's the treatment for a stress fracture or broken finger? Stop running, immobilize the bone in a cast or splint.

We immobilize our bones to allow for healing – however, we remove the normal cyclic loads that they are used to. Although we need immobilization to allow for alignment of the broken pieces and migration in the wound space there is a trade off. We foster growth at the defect site, and lose bone elsewhere.

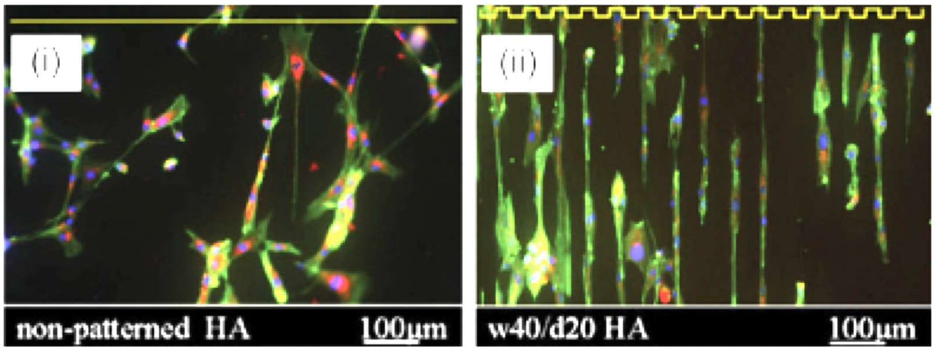
During bed rest you have about 1% bone loss per week

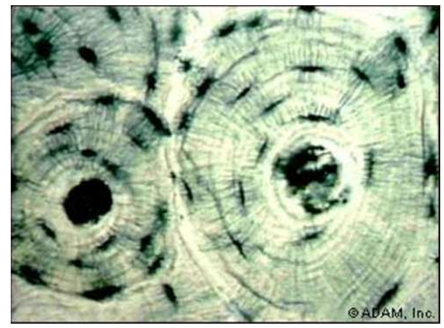
The image on the right is a CT scan the head of tibia bone. This patient was a weight lifter and had accumulated substantial bone mass– indicated by the bright yellow. An injury left him in a cast for several months, resulting in the loss of bone, shown on the left with decreased yellow intensity.

Looking at this stress strain curve, we can see that immobilized bone has a decreased Young's modulus and ultimate tensile strength.

Moderate loading is necessary to promote growth of both bone types - this growth is an increase in mineralization, mass and overall bone thickness. Without continuous loading through movement and exercise, these properties cannot be maintained. This is called Wolfe's law.

Biomechanics of bone





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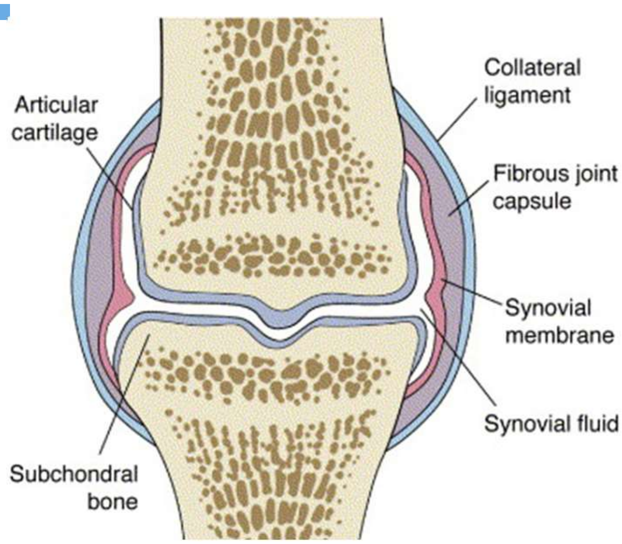
There have been great efforts in the field of bone tissue engineering. These efforts focus on programming and growing bone cells as well as recapitulating the mechanical behavior of bone. As you'll read about this week, one of the techniques that is being developed is the use of microtopographies to orient bone cells.

This allows researchers to **orient** cells. In this image on the far right and the prior diagrams, it is clear that bone is highly organized both in cells, matrix, and mineral components. This bone organization is what governs its mechanical properties. The study figures on the left here concluded that the narrow grooved channels were better for aligning bone cells and even increased the formation of gap junctions between osteoblasts.

Though bone has a natural ability for regeneration we can see that there is quite a bit of work to be done in generating bone tissue substitutes for critical sized defects and crush injuries.

Biomechanics of cartilage



~200,000 knee replacements in 2010

~ 1,065,000 in 2020

Expected to reach 3.5million by 2040

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van Weeren 2006; Advisory.com; Cleveland 2019

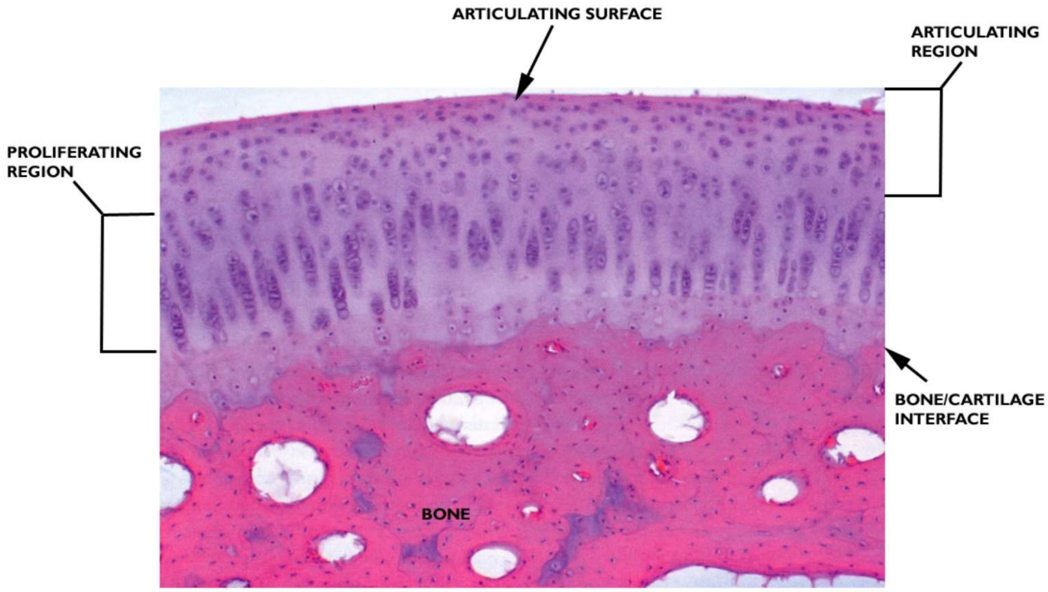
Other than setting bones, orthopedic surgeons are also in the practice of replacing joints. In fact joint replacements are so common that likely everyone in this course knows someone who has had one. This market shows you the reason this is a hot area of tissue engineering research.

The knee is an example of a **synovial joint** – a joint which is surrounded by a fibrous capsule. In between the bones of the joint there is a layer of articular cartilage and buffering that cartilage, acting as **lubrication** in that joint, there is synovial fluid.

The function of articular cartilage is to **distribute** and **dissipate** stresses during joint loading – so for a knee that would be walking, running or standing for example. It also functions to **reduce friction** between the bones. Unlike bone, cartilage has **very limited capacity** to repair – partially because it is **avascular**.

Rates of Total Joint Replacement in the United States: Future Projections to 2020–2040 Using the National Inpatient Sample
Jasvinder A. Singh, Shaohua Yu, Lang Chen, John D. Cleveland
The Journal of Rheumatology Apr
2019, jrheum.170990; **DOI:** 10.3899/jrheum.170990
https://www.jrheum.org/content/early/2019/04/09/jrheum.170990

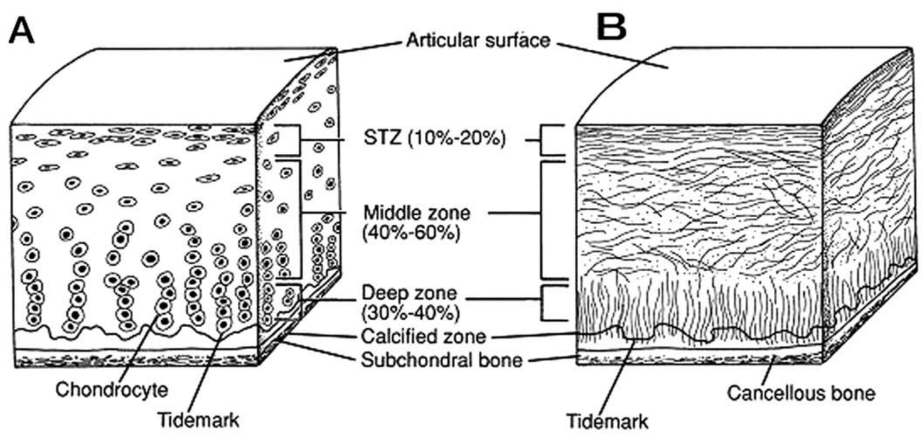
Biomechanics of cartilage



Just as with the other tissues we've discussed this semester, the **structure** of cartilage is related to its **function**.

IN this histological section of articular cartilage you can see that the structure changes with depth. There is **structural inhomogeneity** – changes in cellular, matrix and water content as you go from the surface to the bone interface.

Biomechanics of cartilage



Structural homogeneity across three zones:

Superficial zone
Middle zone
Deep zone

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Sph.sagepub.com

This inhomogeneity is so great that cartilage anatomy is actually broken down into zones.

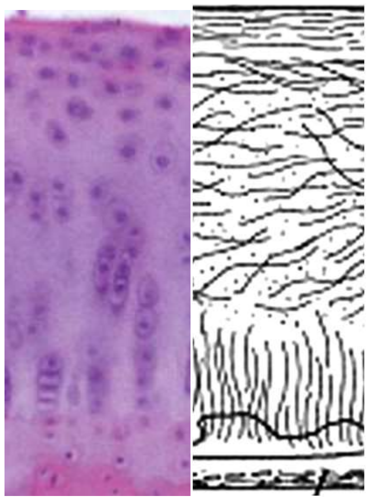
The top or **superficial zone** sits at the top by the articulating surface. This zone has the highest water and collagen content, the collagen fibers here are running **parallel** to the articulating surface

Transitioning down into the joint we come to the **middle zone,** where water content decreases and aggrecan – a cartilage-specific proteoglycan -- content is highest. Collagen fibers here have **a totally random orientation**.

In the **deep zone**, collagen fibers are arranged in bundles and **oriented perpendicular** to the articulating surface. These fibers insert into the calcified cartilage zone and subchondral bone below.

Biomechanics of cartilage

Articular surface



Subchondral bone

Biphasic material
Solid phase - matrix
Fluid phase - water

Anisotropic
Non-linear

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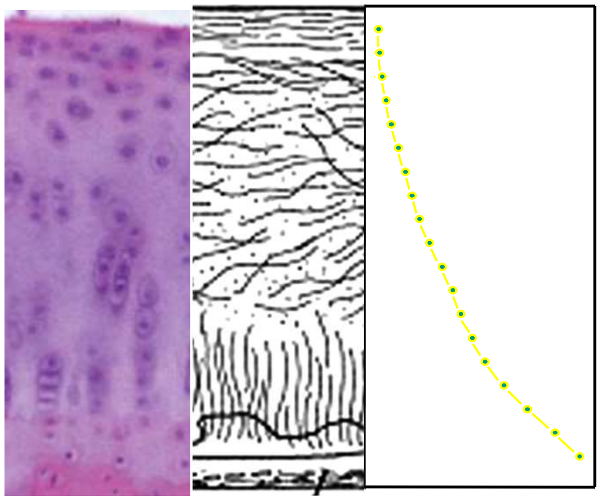
Although we have many zones, each zone has the same two phase components – a solid and a fluid phase. Similar to muscle the **fluid phase** of cartilage comprises roughly 70-80% of the materials total weight. The solid phase, which is mainly collagen and proteoglycans, makes up the rest.

Cells make up just about 2% by volume.

For this reason cartilage is considered a biphasic material. Like bone, it is anisotropic with mechanical properties that are directionally dependent and it is non-linear as we'll see a bit later.

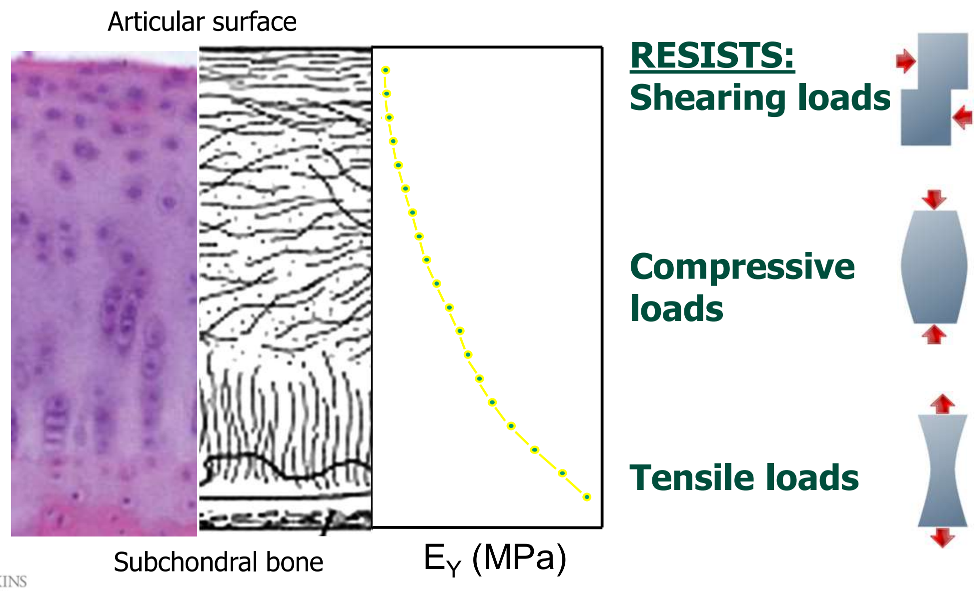
Biomechanics of cartilage



Young's modulus is a function of distance from the surface

If we look the zones again we see that the young's modulus changes with depth. That is the highest modulus is at the top of the material and the lowest is at the interface between the cartilage and bone.

Biomechanics of cartilage



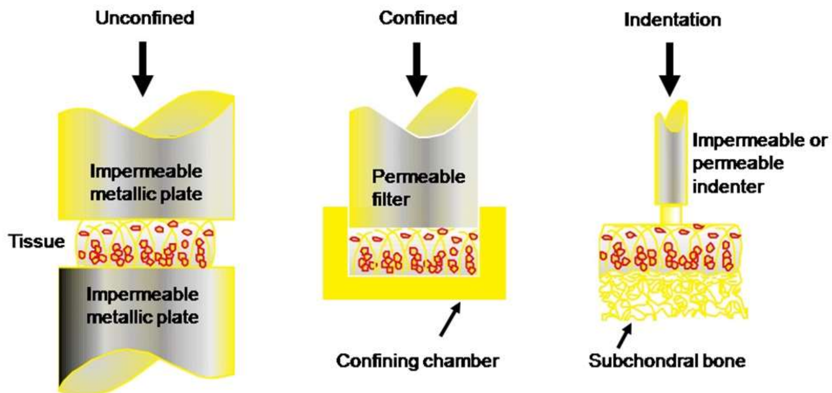
As the structure and modulus changes so does the function of the tissue.

The top zone is built to resist **shear** forces – this is perhaps the most important function of articular cartilage.

The middle zone resists **compressive** loads and the lowest zones resisting **tensile** loads.

Biomechanics of cartilage

Indentation test
Unconfined compression test
Confined compression test



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Korhonen and Saarakkala, 2011

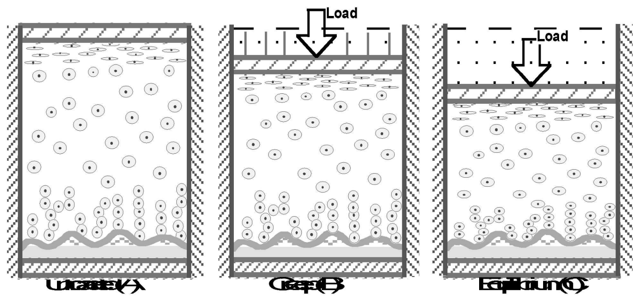
In order to calculate the modulus of cartilage and other biological materials – testing is done with mechanical loads. Compression testing is the most common type of testing for articular cartilage and is also the most relevant since cartilage is constantly bearing compressive loads in the body.

Other types modes are **tension, shearing and bending**. There are also a host of rheological tests to study the mechanical behaviors of fluids and gels that are discussed in your text.

As I said, here we are concerned with compression tests. There are several different types of compression tests **– indentation test, unconfined compression** where the tissue can expand **and confined compression** where the tissue cannot expand**..**

Biomechanics of cartilage

Confined compression test



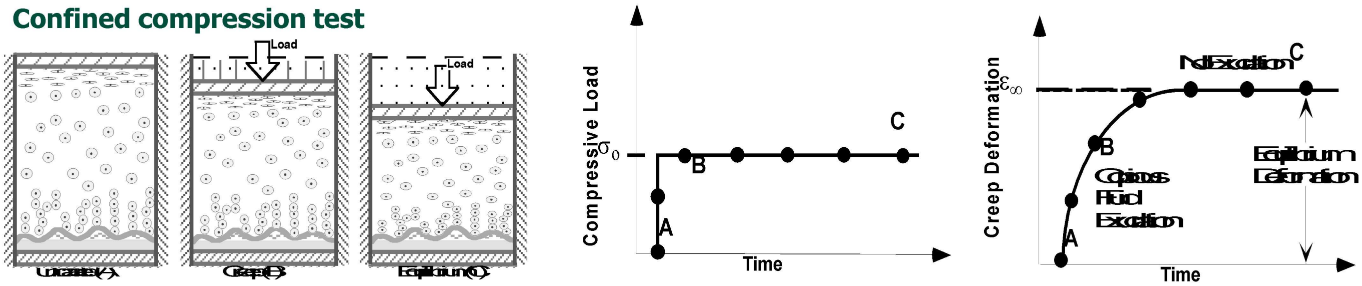
Here we are looking at a confined compression test for cartilage.

In this test the material – cartilage in this case-- is confined on three sides by solid impermeable walls. The top piston where the load is applied is permeable. When subjected to this compression test the load presses down on the cartilage and the fluid in cartilage flows through the permeable top piston.

Each zone within cartilage has a different composition and modulus but they all **contain fluid** – water that is. Although the middle zone is designed to resist compressive loads – cartilage does deform under pressure.

Biomechanics of cartilage

Confined compression test

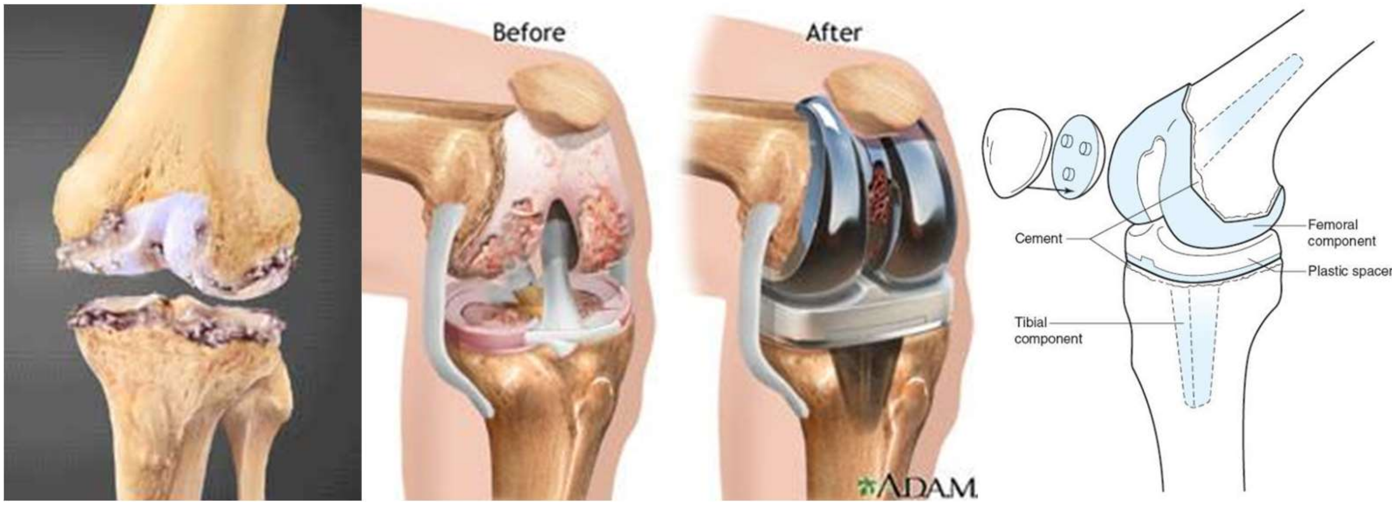


When the load is applied as **a step function** we see that the that the deformation is slow. Fluid leaves the tissue until the tissue reaches an equilibrium with the load.

This type of test can also be used to determine the permeability of the tissue by measuring the fluid flux out. The permeability of the tissue is related to the internal structure and porosity. Both the structure of the pores, and the degree of porosity which we saw earlier will influence the overall mechanical behavior the material.

We will revisit porosity in the next module on when we get into trafficking and delivery of molecules and cells in human body.

Biomechanics of cartilage



With what we've seen about cartilage biomechanics, are you at all surprised what an artificial knee replacement looks like?

Here you can see what a knee joint looks like when damaged – there is almost no articular cartilage left. Perhaps this patient has severe osteoarthritis or rheumatoid arthritis.

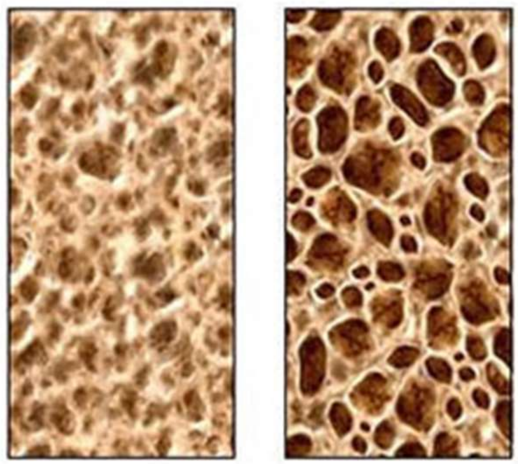
Instead of a soft, biphasic material,   knee replacements consist of two metal pieces placed on the end of either bone – here and here, and a polymeric spacer placed in between for lubrication.

One of the reasons that tissue engineered solutions aren't prevalent in the OR we heard earlier in this lecture – **cartilage does not regenerate well** in the body. There are too few cells (less than 2% volume) and the is no blood supply to bring stem cells and other nutrients.

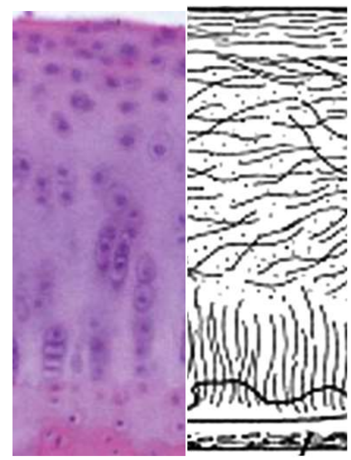
In future lectures we'll talk more specifically about tissue engineered cartilage, so stay tuned to hear about the alternatives to total knee replacement.

Review and rewind

Bone



Cartilage



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IN review this lecture discussed the mechanical properties of two biological materials – bone and cartilage and explored how the structure of these materials determines their mechanical functions.


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