Biomedical Ultrasound: Fundamentals of Imaging and Micromachined Transducers

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Lecture: 48

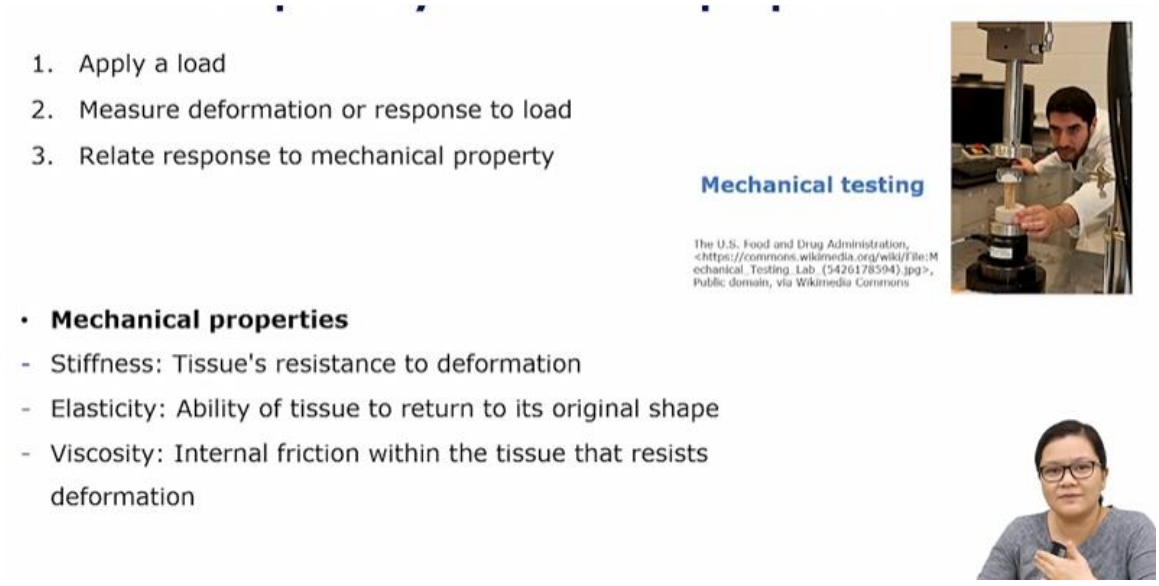
Ultrasound Elastography

Hello. In today's lecture, I will be introducing ultrasound elastography. So let's begin by understanding what is elastography and why is it needed? So we know that pathology alters tissue mechanics. So if a person has any injuries, inflammation, fibrosis, which is a buildup of extracellular matrix proteins in the tissue, and tumors, which can lead to cancer, typically, when these diseases are diagnosed, the patient would present themselves into the clinic, and the first thing the clinician would do is to palpate different regions of your body to see, to assess whether there are any changes in the mechanical properties of your tissue. So this type of procedure is called manual palpation. So you can see in this image here on the left, that a boy who is a patient is lying down and the nurse is palpating the abdominal area, probably looking for any variations in the location and the stiffness of the organs within that area.

Also on the image on the right, this is typically a procedure in which if you present yourself with some sort of cold, typically the lymph nodes, which are these glands below your neck can get inflamed. They get inflamed when there is a certain inflammation or an infection in your body. So what the doctor or nurse typically do is, they feel these areas to see if there are any enlargement or any stiffness changes in those glands.

So it's been well known for hundreds of years that the biomechanics of tissue can change whenever there is an injury or disease. The clinicians would use this manual palpation method to be able to gauge the severity of this disease. In terms of quantifying the

mechanical properties of tissues, as we know, manual palpation typically looks into the stiffness from a superficial point of view. But if you want to exactly quantify what the stiffness of the tissue is, then typically what is done is that, you would apply some sort of load onto the tissue. You can measure the deformation or the response to the load, and then relate the response to a certain mechanical property.



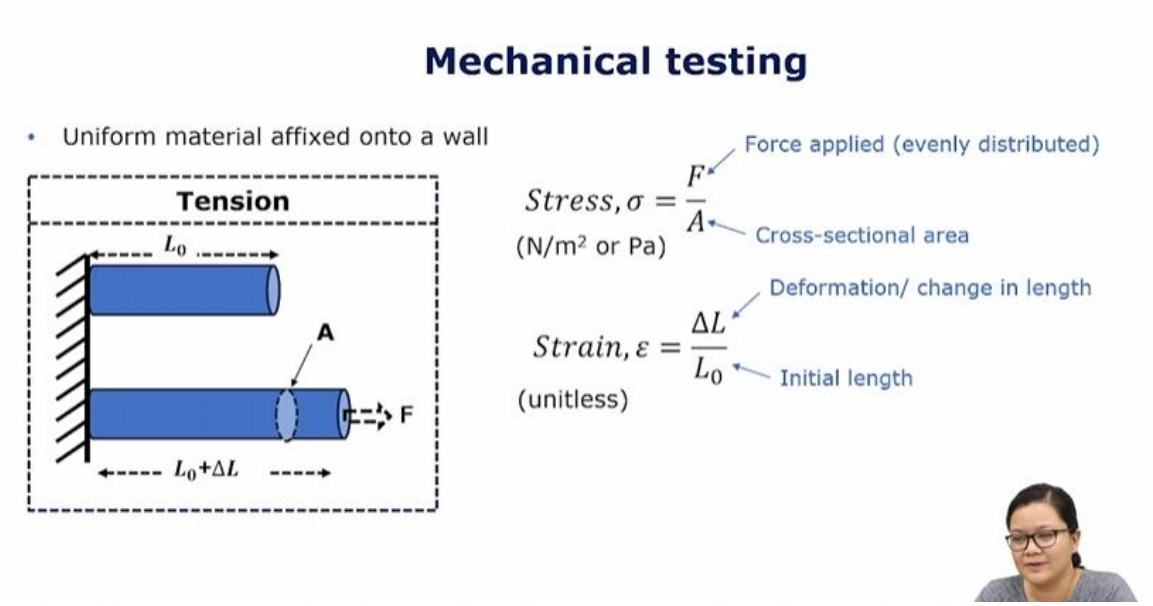
What is typically done in labs is that you would get a sample of a tissue that's either excised from a cadaver or even tissue constructs that are made, you would then put them onto a mechanical testing device, such as this that you can see here. And what this mechanical testing device allows you to do is, to apply a deformation onto the tissue, and then it allows the person to measure exactly how the tissue responds to that deformation.

There are several mechanical properties that are of interest, such as stiffness. Stiffness is the tissue's resistance to deformation. The stiffer the tissue, the higher it is likely to resist that deformation.

Another one is elasticity. Elasticity is the ability of the tissue to return to its original shape. So for example, if you have a rubber band which is fairly elastic, If you stretch it and you stretch and deform, you release it and then it will come back to its original configuration.

Viscosity is another parameter, and that's a measure of the internal friction within the tissue that resists the deformation. Typically, the viscosity term is more applicable to liquids. However, your body is made up of mostly water, and therefore your body is estimated as a viscoelastic type of medium.

Let's just give you an overview of different mechanical testing techniques that are being used currently. So here's just an example of a tensile testing type experiment where let's say you have your uniform material that is represented by this cylinder.



It's a very simplistic example of the tissue. but one can do this type of experiment. You affix that material onto a wall, and then you apply some sort of a tensile force that will stretch that tissue. So then the original length of this tissue is denoted by L_0. And when you stretch, and apply that force, the tissue deforms. In this case, the tissue will lengthen by an increment of ΔL.

So the stress that is applied onto the material is denoted by the σ parameter here, typically in Nm^{-2} or in Pa. And that equals to the force that is applied onto the material divided by its cross-sectional area. So for this cylindrical material here, the cross-sectional area would just be a circle. So

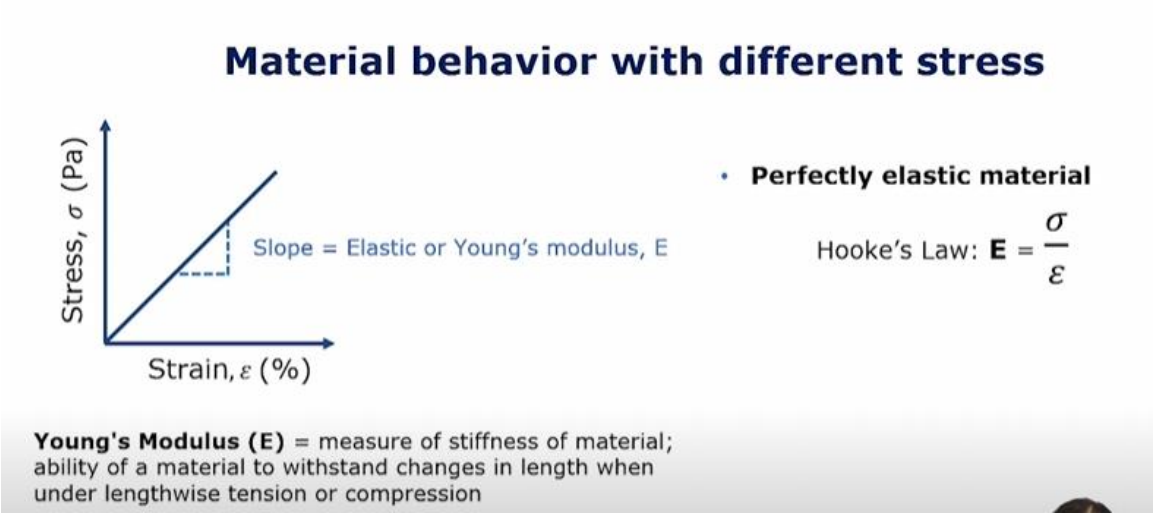
$$stress = \frac{force}{cross\ sectional\ area}$$

And in terms of the measure of deformation or displacement of that material, we usually utilize strain as our parameter here, where it's denoted by ε, and

$$\text{Strain}, \varepsilon = \frac{\Delta L}{L_0}$$

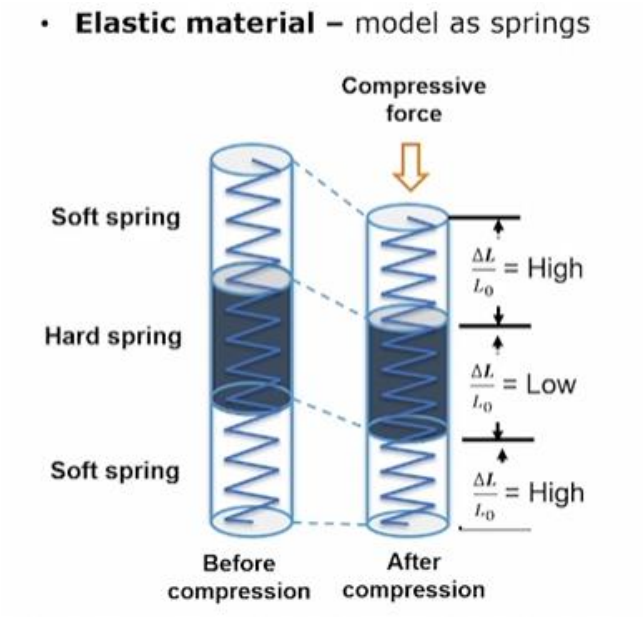
So if you apply a certain stress to the material, and then you keep increasing that stress, then the strain will also increase linearly if you have a perfect elastic material. So you might remember from your previous physics class, about Hooke's law. So here for a perfect elastic material, Hooke's law says that:

$$Young's\ modulus\ =\ stress\ /\ strain.$$



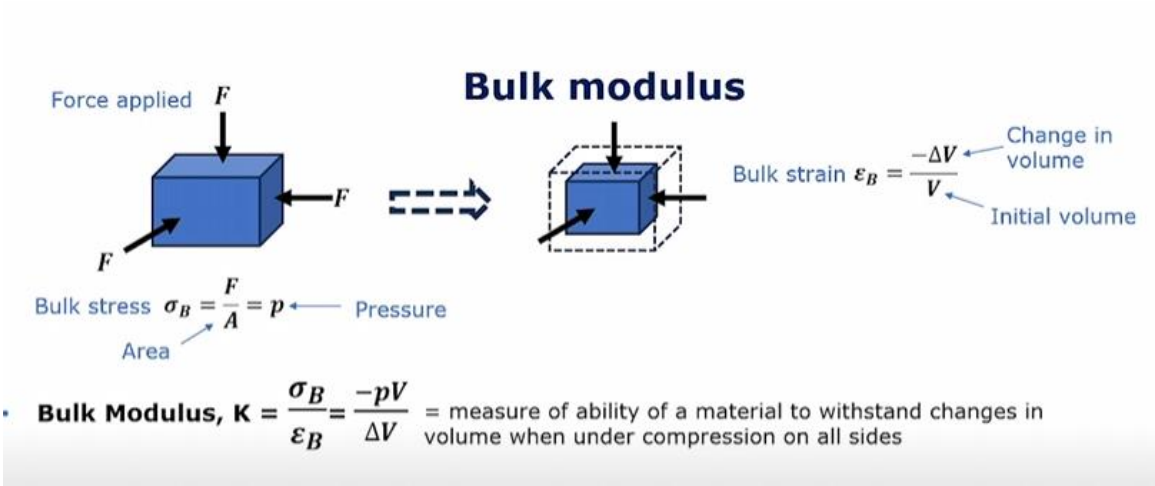
And we know from this stress-strain curve, assuming that you are within the linear elastic regime, then the slope of the stress-strain curve is the elastic or the Young's modulus, denoted by E here. Now, of course, if you keep stretching the material, the material behavior will change. There will be some other deformation or plastic deformation that will occur. And what that means is that if you stretch the material, it will not go back to its original position. There's also another situation where you keep increasing the stress that you're applying into the material that will cause the material to break. So that is related to yield point. But in this case, in terms of material behavior, we're quantifying it using the elastic modulus. So then here we assume that we're still in the linear elastic regime. So again, the Young's modulus is a measure of the stiffness of the material. It's the ability of the material to withstand any changes in length when under tension or even compression.

So in the previous example, we talked about tensile tests, but you can also get the elastic material or the Young's modulus using compression tests. So typically an elastic material is modeled as a spring. Like a spring, if you stretch it and then you release it, it will go back to its original position. So here's just an example of, let's say, a material that is modeled as one layer having a soft spring, a middle layer having hard spring, and then the bottom layer as being represented by a soft spring. This is how it looks before compression, as shown in the left figure.



Now if you apply some sort of compressive force onto that material, you would get strains associated with each of these regions. And we know that for a softer spring, the strain would be much higher than a stiffer or a harder spring, as you can see in the figure on the right.

Another parameter of interest is the bulk modulus. So the bulk modulus is the ability of the material to withstand changes in volume when under compression from all sides. So you can see the figure, in which a compressive force is applied on all sides of a cuboidal material.



So this is similar to when you drop an object into the ocean. As you go deeper into the ocean, the pressure at deeper regions of the ocean will get much, more, and eventually, as the object is going down deeper depths into the ocean, it will feel a lot of compressive force due to that higher pressure deep in the ocean. So basically, it also depends on the

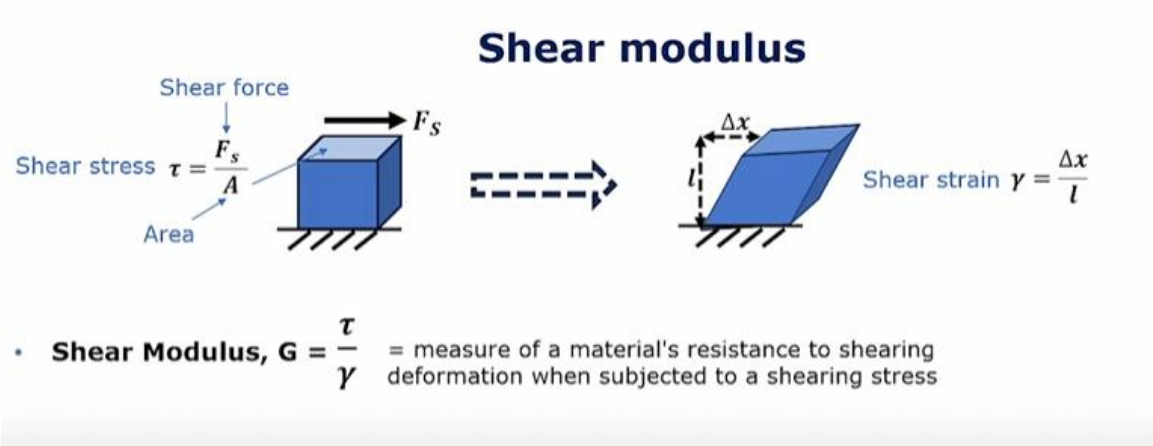
bulk modulus of that object to be able to withstand those pressures. So here, as you are applying that force, you will also be measuring some sort of strain. This is called bulk strain. And what the bulk strain is, that it encompasses of the change in volume divided by the initial volume of that object.

$$\text{Bulk strain}, \varepsilon_B = \frac{-\Delta V}{V}$$

So the bulk modulus is also an important parameter. It's the bulk stress divided by the bulk strain. And you can equalize that to the negative pressure times the initial volume divided by the change in volume.

$$\text{Bulk modulus}, \mathrm{K} = \frac{\sigma_B}{\varepsilon_B} = \frac{-pV}{\Delta V}$$

Another important parameter when we're talking about properties of tissues is the shear modulus. Here, let's imagine an object that is affixed to the bottom and a force is being applied on the lateral direction on the top surface of an object. So you're applying a shear stress, and it's denoted by the term τ. That equals to the shear force divided by the cross-sectional of this top section of the object.



And as you were applying that force, the object will shear, and it will go into this deformed configuration. The top portion will displace by a distance Δx here, and the shear strain, which is denoted by γ, is calculated,

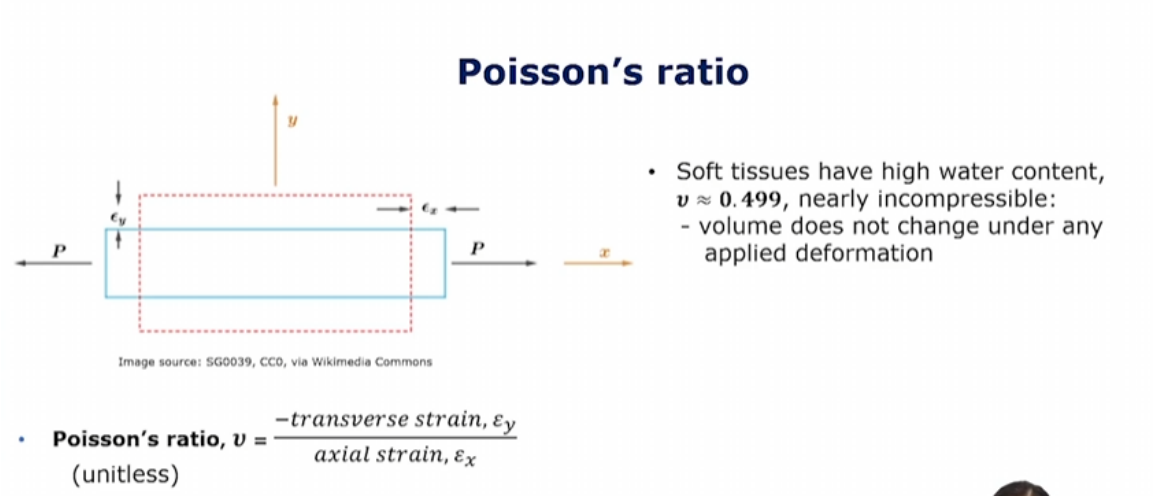
$$\gamma = \Delta x / l$$

Where, l is the height of this object. So you can measure shear modulus as well. Shear modulus is typically denoted as G, and that equals,

$$G = \tau / \gamma$$

Shear modulus is the measure of the material's resistance to shear deformation when subjected to a stress.

Another important parameter that we consider is the Poisson's ratio. And it's basically the ratio of the transverse strain divided by the axial strain.

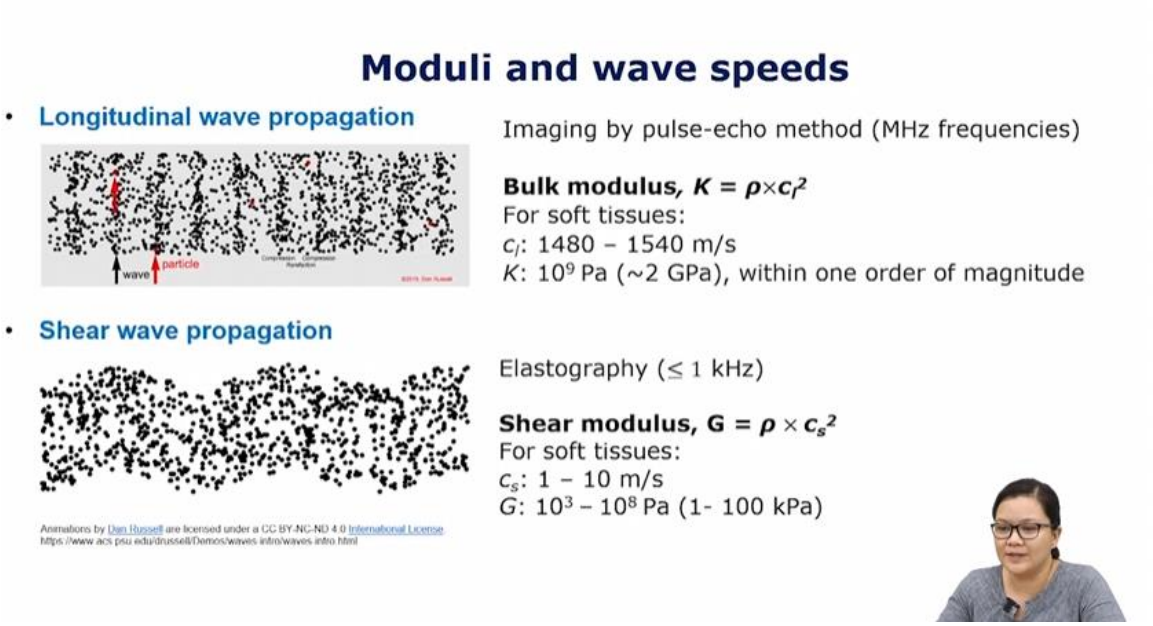


So if you could imagine, if the red box was the initial tissue and then if you apply a certain force that will cause a tensile deformation, the Y part or the lateral width of the object will also decrease as you are stretching the material in this axial, X direction.

So the transverse strain (ε_y) and the axial strain (ε_x) is denoted as here. And typically, soft tissues have a higher water content. So the Poisson's ratio is typically around 0.4999, It's considered a nearly incompressible material.

So what it means to be incompressible is that the volume does not change under any applied deformation, similar to water. Water is incompressible. If you compress water, it will also deform in another direction, but the volume of the water will not change. So tissues are typically assumed as nearly incompressible.

Now let's put together the concepts of the modulus and the wave sound speeds that we encounter in ultrasound. So we've already talked about longitudinal wave propagation. As a review, this is when the particles in the tissue or the material oscillate parallel to the direction of the wave propagation.



Now, this is typically used in imaging by the pulse echo method. And the frequencies associated with this is around MHz frequencies. So the bulk modulus, which we denote by K,

$$K = \rho c_l^2$$

So for soft tissues, the longitudinal sound speeds range around 1480 to 1540 m/s. And the bulk modulus range on the order of GPa, so in the order of 10^9 Pa, typically around 2 GPas, but within this one order of magnitude. When we talk about shear wave propagation, this type of wave is mainly used for elastography. So with shear waves, what happens in there is that the particles oscillate perpendicular to the direction of the wave propagation. And typically the frequencies of shear waves are less than 1 kHz.

The shear modulus now, which is our material parameter G, equals the density times the shear wave speed to the squared.

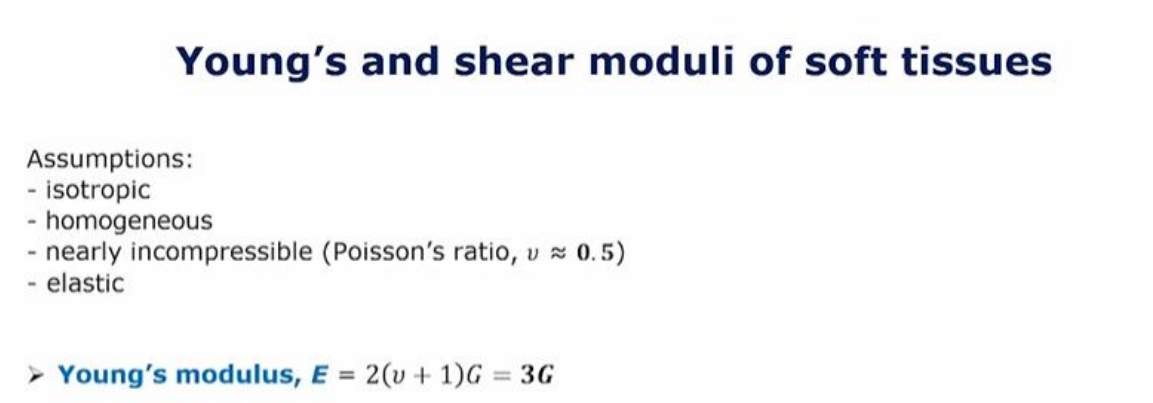
$$G = \rho c_s^2$$

So for soft tissues, the shear wave speed ranges in the order of 1 to 10 m/s, while the shear modulus ranges on the order of 10^3 - 10^8 Pa, or one to 100 kPa. So this is over almost five orders of magnitude. And the reason why the field of elastography itself utilizes shear wave instead of longitudinal waves to get the modulus properties, is because of this wide range of shear moduli. That will allow you to differentiate different types of tissues, especially which is important for tissue diagnosis.

Now, in elastography, the Young's and shear moduli of soft tissues are typically interchanged, and that's because of certain assumptions. So if you assume that the media

is isotropic, meaning that the material response is the same in both directions, or in all of the directions, and if you assume that the material is homogeneous and nearly incompressible, so that's why we talked about the Poisson's ratio, So an incompressible material has a Poisson's ratio of about 0.5. Soft tissues are typically assumed to be 0.499, very close to 0.5. And if you assume that the material is elastic, then the Young's modulus can be related to the shear wave speed or the shear modulus by this equation here. where the Young's modulus is three times the shear modulus.

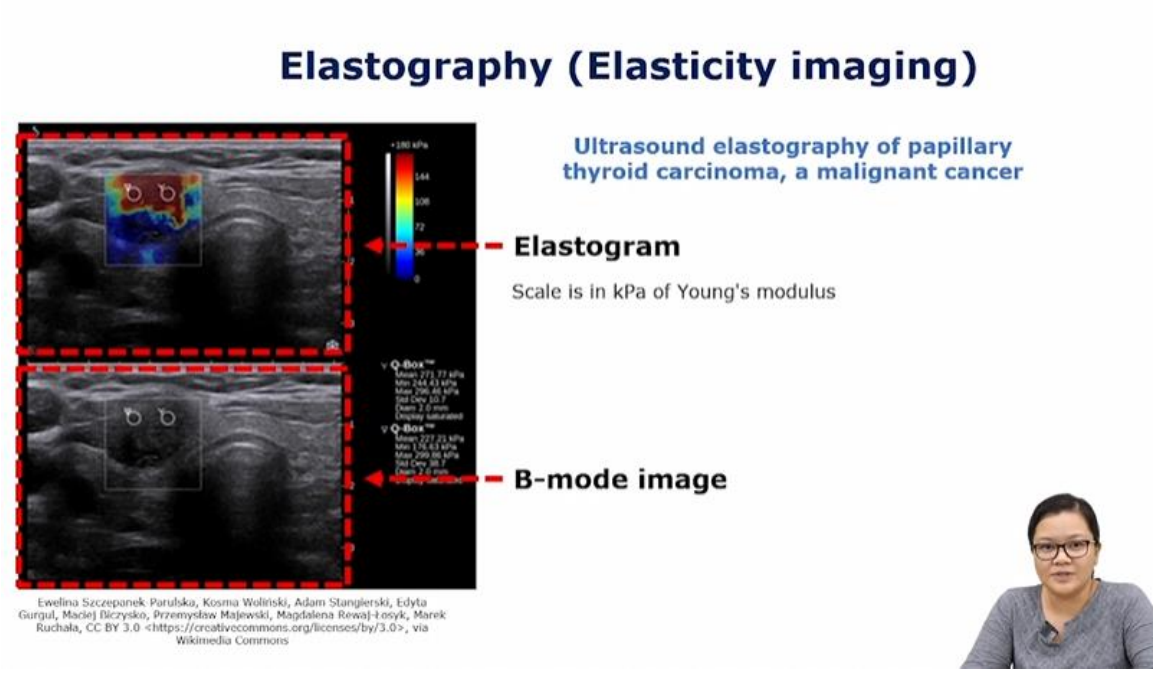
$$E = 3G$$



Now, this is the general expression for the relationship between Young's modulus and the shear modulus. But if you plug in 0.5 in this equation, it becomes three times the shear modulus.

So in elastography, we typically use the shear modulus. Now if you would like to estimate what the Young's modulus is, then under these assumptions, which are fairly simplistic assumptions of the material, then the relationship between the Young's and shear modulus is just by a factor of three. So we'll talk more about this when we get into shear wave elastography.

Now, elastography in general has another term for it called as elasticity imaging. So imaging the elastic properties of tissues. Now it's more of like imaging the mechanical properties of tissues because we don't only get the shear modulus. We can also plot the map as a function of the shear wave speed as well as viscosity. So just giving you an example of what an elastography or an elastogram looks like. So here we plot the B-mode in the image below. There are some carcinoma regions around the location marked in the box



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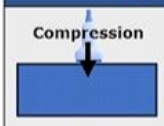
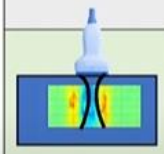
But you can see that sometimes in B-mode images, tissues appear isoecoic or these tumors appear isoecoic relative to the background surrounding tissues. So it makes it challenging for the clinician to be able to determine exactly where the lesion is. And what elastography allows you to do is that, it allows you to give more contrast to your image. based on the mechanical property. So what you see here on the top is what's called an elastogram, an image of the elastic properties of tissue.

We have a scale bar here that's in terms of the Young's modulus. And what you can see in this map is a color map where red appears more stiff and then blue corresponds to a region that's less stiff. And for these type of cancer, typically the tumor appears more stiff than the surrounding tissue. So here you see that it's more red in this region. I've just shown you an example of one type of elastography technique but there are several types and I will show you a couple of these.

So the first method we'll discuss is strain imaging and what it does here is that you send a type of push or compression onto the tissue and you measure the deformation of the tissue similar to our compressive testing that I described earlier.

Ultrasound elastography methods

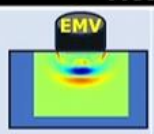
Method		Excitation Method	Technique	Measurements
	Strain Imaging	- Manual compression - Cardiovascular/ respiratory motion	Strain Elastography	▪ Strain or Normalized Strain ▪ Geometric Measures ▪ Strain Ratio
	Shear Wave Imaging	Acoustic Radiation Force Impulse (ARFI)	Point Shear Wave Speed Measurement Shear Wave Speed Imaging	▪ Shear Wave Speed (m/s) ▪ Young's Modulus (kPa)

Now the way this table is arranged is based on its excitation method, the name of the technique that is being used and what type of measurements it's being outputted. So for the strain imaging, you can either excite by manually compressing the material. You can either use the natural motion of the body. So for instance, the cardiovascular, the vascular pulsations, the respiratory motion as a person is breathing. So this technique uses strain elastography and a couple of the measurements that are shown here are normalized strain. Some geometric measures can be assessed in strain elastography and strain ratio. And we'll look at even others that are used to be able to assess tissues.

Now the next one is shear wave imaging. Now this utilizes the shear wave that is being generated into the tissue. You can create the shear wave using a transducer that will send an acoustic radiation force impulse. So we'll talk more about this in the next lecture. A couple of the techniques are point shear wave speed measurement and shear wave speed imaging. And that can give you the measurement outputs of shear wave speed. And if you apply our equation assuming isotropic homogeneous elastic medium, then you can also compute the Young's modulus.

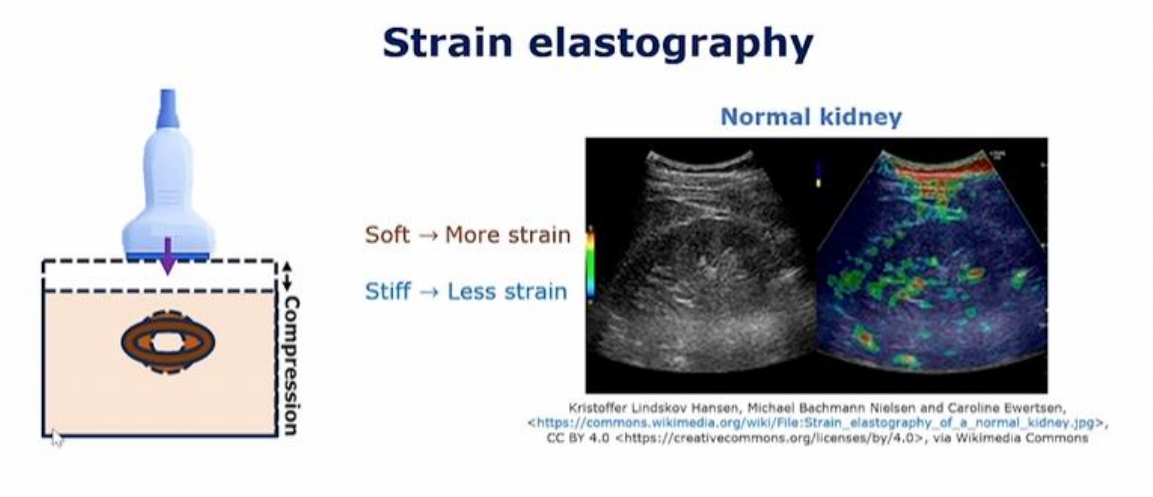
And the third set of techniques that we'll also discuss is the transient elastography technique. And in this case, the type of excitation method is external mechanical vibration systems.

Ultrasound elastography methods

Method		Excitation Method	Technique	Measurements
	Transient Elastography	External Mechanical Vibration (EMV)	Transient Elastography	▪ Young's Modulus (kPa)

So this is an electromechanical instrument where it vibrates the tissue and that causes propagation of shear waves inside the tissue. And this will allow you to measure the Young's modulus. So in the next lecture, we'll talk more about transient elastography.

Now let's first start with strain elastography. So as I had mentioned, what happens is that you first take an image of the material, which is the tissue, and then compress and then take another image right after compression.

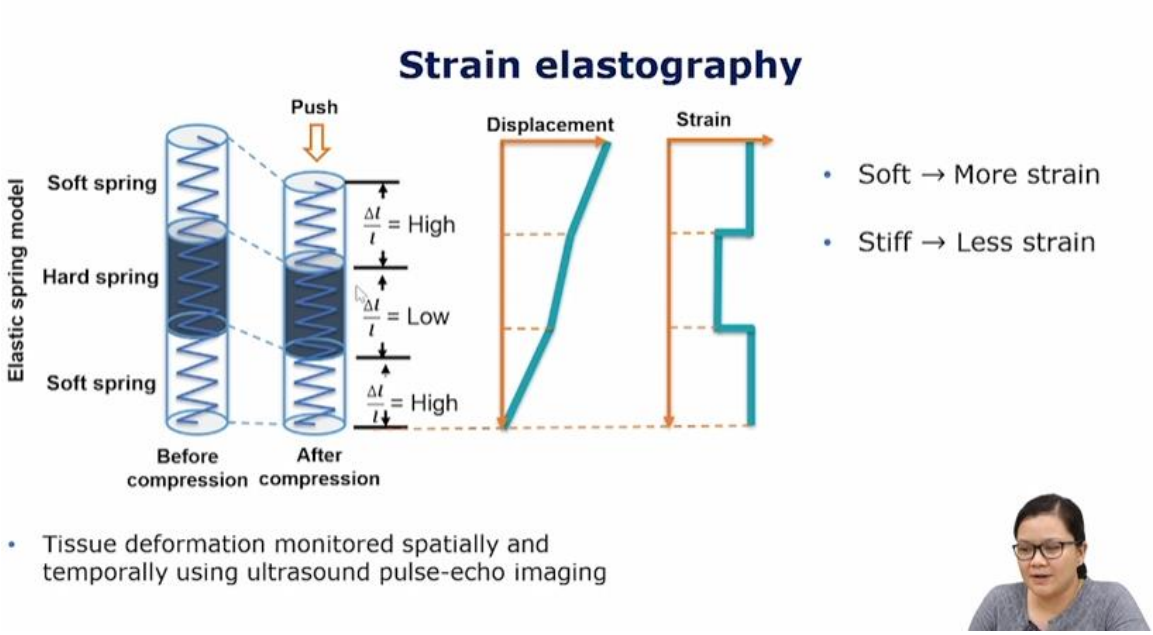


So you would take an image before and after compressing the tissue. You can also compress with your transducer itself. So you put the transducer on top of the material and compress it by hand. And based on that, you can create an image of the strain.

So here what I show is an image of a normal kidney. On the left is the B-mode image and on the right is your strain image here. The color bar here is the measurements of strain. So soft material will have more strain because it's easier to displace. So it'll appear red in the image. and then a stiff material will have less strain, so appear more blue.

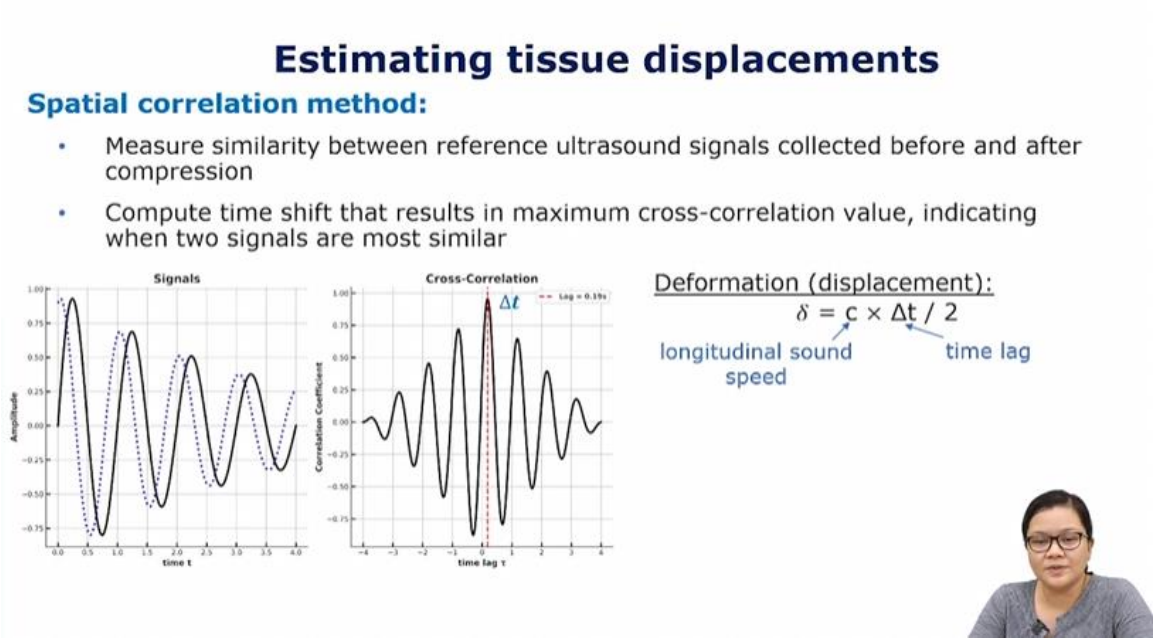
So this is of a normal kidney. You can see in the B-mode image delineation of that normal kidney. If there was any disease or injuries in the kidney, then one would be able to look at a strain image and see whether there are any differences in these stiffness or the strain of the tissue relative to a normal kidney.

So going back to our elastic spring model here. So when you apply the compression, again, you're assuming that the tissue is elastic.



So if you have a softer spring, it will displace more. And if you have a hard spring, it will displace less. And the spatial derivative of displacement is actually the strain. And so this is how you can relate the strain to the displacement of the tissue as you are applying the compression. Now, the tissue deformation is monitored spatially and temporally just using typical ultrasound pulse echo imaging. I will talk about three methods that are used to estimate tissue displacements.

So the first method is the spatial correlation method. And it measures the differences between the reference signal, which is before compression, and the ultrasound signal that you would get from the tissue after compression. And it uses the cross-correlation algorithm. You're computing a time shift in the signal. So for example, here on the left, we see the black signal.

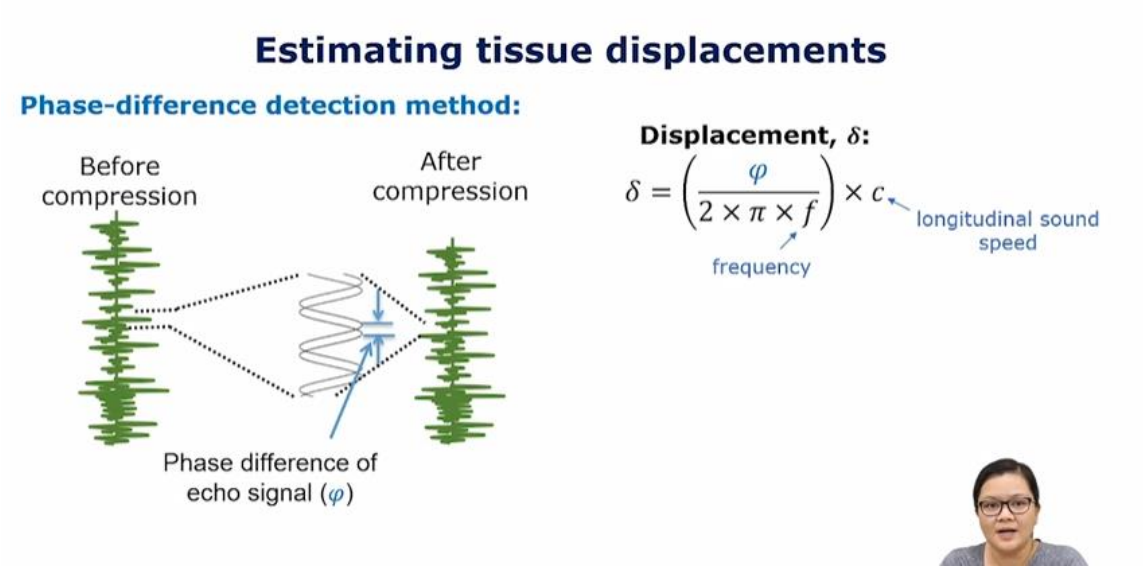


This is an amplitude as a function of time. The black curve corresponds to the post compression and the blue dotted is the pre compression signal. And you can see that there is some sort of shift in the signal during time. When you apply a cross correlation between these two signals, it will produce a cross correlation coefficient as a function of the time lag, something similar to the image on the right. And the peak of that correlation coefficient will get you the time lag Here in this case it's Δt. And then how you can compute the deformation or the displacement of the tissue is by using the range equation that we have discussed before.

$$\delta = c * \Delta t/2$$

Now this will be on the units of meters.

Another method is the phase difference detection method. So it looks into the differences in phase of a portion of the signal before and after compression. So you can see here, this is what a signal would look like before compression and after compression.



If you window a certain portion of the signal and look at the phase differences, then you can also compute the displacement based on the phase by using this equation.

$$\delta = \left(\frac{\varphi}{2 * \pi * f}\right) * c$$

So these are two methods to compute. Now there are trade-offs between each of these methods. So first, here I show the trade-offs with respect to real-time capability, as well as the amount of displacement that can be measured with the time shifts.

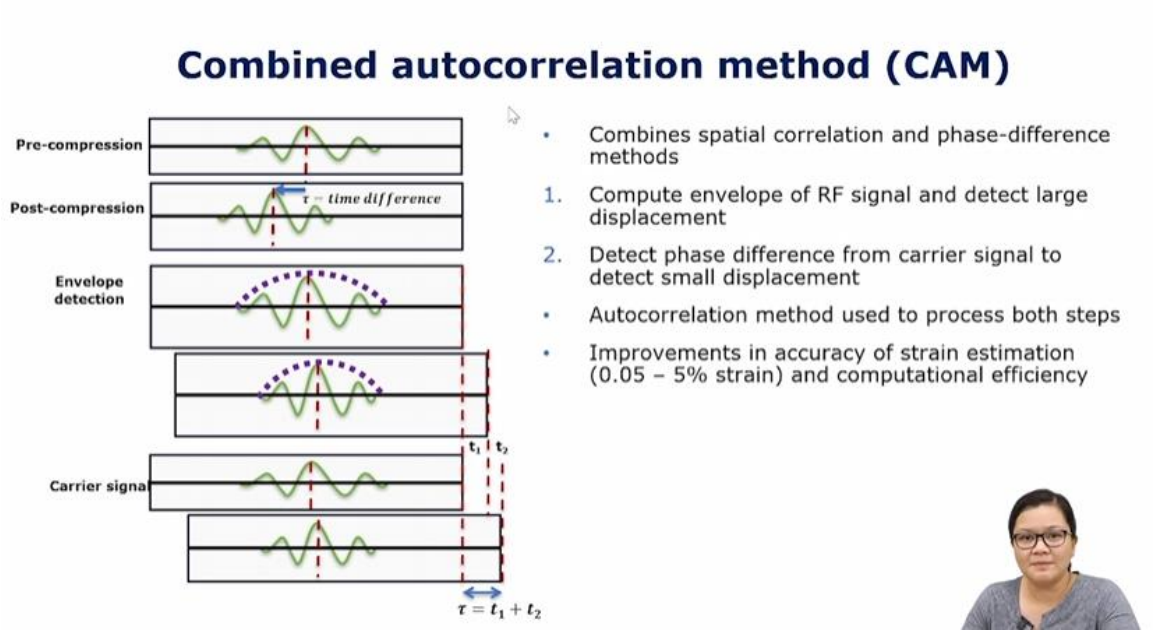
Estimating tissue displacements

	Spatial correlation method	Phase-difference method
Real-time capability	Computational complexity	High-speed operation
Displacement amount	Displacement exceeding wavelength possible	Up to half of excitation wavelength

So for example, for the spatial correlation method, it has really high computational complexity because you would have to calculate the correlation coefficient. Whereas the phase difference method, has a good high speed operation. So it's much faster than the spatial correlation method. The advantage of the spatial correlation method is that it can measure displacement exceeding the wavelength of the ultrasound. So another name for the spatial correlation method is actually speckle tracking method. This is widely used.

But the phase difference method, although it has better computational efficiency, it can only measure displacements up to half of an excitation wavelength. So what has been done now is to combine the benefits of both spatial correlation and the phase difference algorithms.

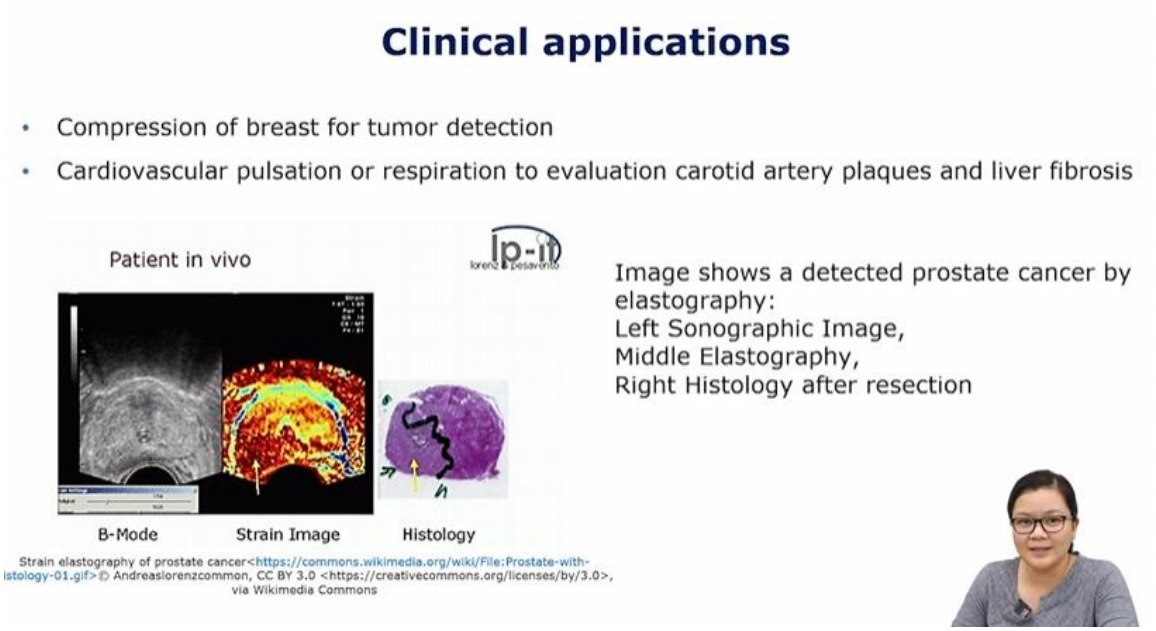
So now I will talk about this combined autocorrelation method that has been implemented into clinical scanners. So for example here, you have your signal before you compress the tissue and the signal after you compress the tissue.



There will be a time shift that will be computed. So to be able to do this combined autocorrelation method, first, you do a coarse estimation of the displacement. So this is similar to the speckle tracking algorithm, where in this case, you first compute the envelope of the signal. So we're going to detect the envelope , and then we would detect the envelope also for the post compression signal. And then what you would do is you would perform autocorrelation to be able to detect the large displacements.

Subsequently, if you look at the carrier signals here, you would detect the phase difference from the carrier signals' pre and post compression to be able to detect the smaller, less than half a wavelength, small displacements. So both these methods use the autocorrelation method. And what it has been found is that it improves the accuracy in strain estimation, and it has been able to measure strain within the range of 0.05 to 5% strain. Compared to the other two methods, it also has good computational efficiency. So this combined autocorrelation method is typically used in clinical scanners now. Now, there's been a lot of research and looking into other displacement tracking algorithms, but I would welcome you to look into those algorithms. However, they're beyond the scope of this course.

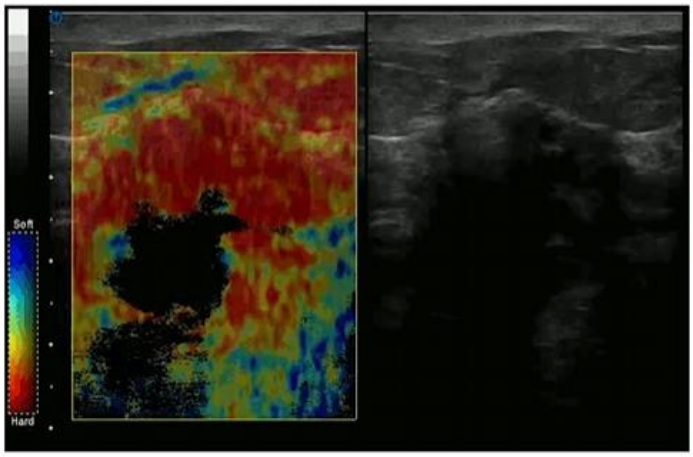
Looking into the clinical applications of strain elastography now. So strain elastography has been widely used for detecting breast tumors. It's clinically used currently. Also, you can utilize the cardiovascular pulsation or the pulsation of your blood vessels or either the respiratory process to be able to evaluate the stiffness of plaques in your carotid arteries or also monitor liver fibrosis.



So another example here is ability to detect prostate tumor using strain elastography. So you can see here this is a B-mode image of a prostate with a tumor. It's very challenging, and difficult to see with an untrained eye exactly where the tumor is. But if you look at the strain image on the right, you can see a red region that has higher strain relative to the background, and it's much different to the surrounding tissues. And this, if you compare it with histology, this is a part where the tumor is. And basically one can correlate the strain and the histological sections to be able to exactly identify that this is a location where the tumor is.

Another application is elastography of invasive ductal carcinoma in the breast. So this is a nice image that shows you motion that's being applied in the ultrasound image of a tissue. And you can see the strain being calculated almost in real time. So these kinds of images can be able to help the clinician assess exactly where the tumor is.

Clinical applications



Strain elastography of invasive ductal carcinoma in breast

<https://commons.wikimedia.org/wiki/File:Manual_compression_elastography_of_invazive_ductal_carcinoma_00132.gif>© Nevit Dilmen, CC BY-SA 3.0 <https://creativecommons.org/licenses/by-sa/3.0>, via Wikimedia Commons

Now, strain elastography is fairly easy to use. It can provide strain images with almost pixel resolution. But there are several limitations to these techniques. So first, since one does manual compression, it is difficult to calculate the actual stress distribution that is inside the body. Therefore, it's typically considered as a qualitative technique. So it's also very challenging because of its nature.

Advantages and limitations of strain elastography

Advantages:

- Easy to use
- Provides strain images with high spatial resolution
- Detects single-pixel deformation

Limitations

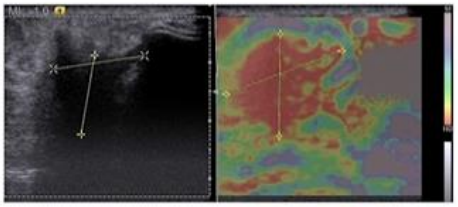
- Difficult to calculate stress distribution *in vivo* (inside body)
- Qualitative
- Difficult to perform quantitative comparisons between cases

It will be challenging to perform any quantitative comparisons between different cases from different patients. However, there are several efforts to be able to try to get some quantitative metrics from the strain elastography images. So I'm going to introduce some of the semi-quantitative metrics that are being used today. So some of these metrics include normalized strain, which is just a measure of the strain divided by the max strain.

Quantitative evaluation based on strain elastography

Semi-quantitative metrics

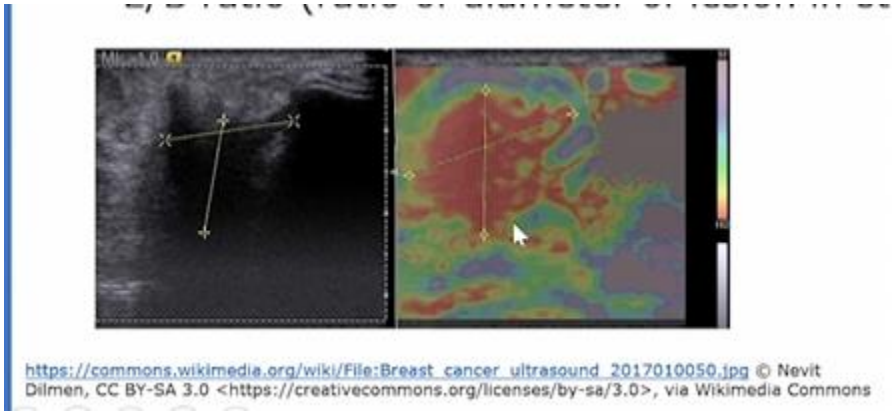
- Normalized strain (strain/max strain)
- Geometric measures (size or shape of low strain area)
- Strain ratio, SR = $\frac{Mean\ strain\ B\ (reference\ area)}{Mean\ strain\ A\ (lesion\ area)}$
- E/B ratio (ratio of diameter of lesion in strain image to its diameter in B-mode)



Typically, the strain will vary depending on the region. If a tumor or diseased region is there, then the strain will change. Also, some geometric measures can be gained from the strain elastography image. You can look at the size or the shape of a low strain area.

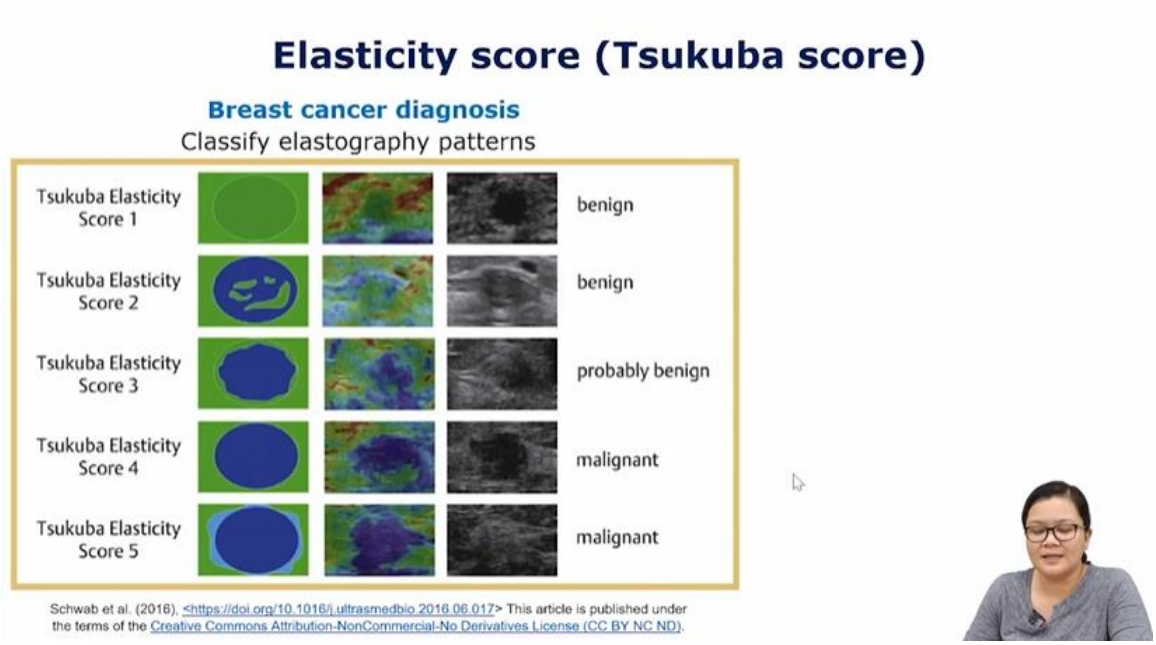
You can also calculate a strain ratio. And typically how that's calculated is you select a region outside of the tumor and a region inside of the tumor. So here, a mean strain of B is the reference area outside of the tumor. And the mean strain of A is actually the tumor lesion area. So depending on these strain ratios, it will change. You can detect whether the lesion is there.

And then you can also use the E to B ratio. This is the ratio of the diameter of the lesion in the strain image versus the diameter in the B-mode image. So here's just an example where I show that in the B-mode image, the clinician is trying to measure the size of the lesion. In the strain elastogram image, you can see that there could be some differences in the size of the lesion as well.



These measures are being used today. However, one should note that these strain measurements only look at the local differences in the strain within one strain image. So it's very challenging to be able to compare these types of metrics from one patient to the other. So when interpreting strain images, it should be done under caution.

I will also introduce another elasticity score that is widely used in breast cancer diagnosis. This is the Tsukuba score, which looks into the pattern of the strain elastography images. And depending on that pattern, it will categorize the tissue as benign or malignant.



So you can see this is a five-point scale, and depending on the pattern, the clinician can either score it as benign or malignant and in the intermediate stages as well.

I hope this gives you a good overview of the physical principles that are being utilized in elastography. We talked about the different modulus, bulk, Young's and shear modulus, especially the Poisson's ratio as well, and how these are interrelated depending on the assumptions that we have. We also talked about the relationships between the sound wave speeds and the modulus of soft tissues. So for instance, if you can measure the shear wave speed, then one can also measure the shear modulus, depending on certain assumptions, of course. We also went through a list of ultrasound elastography methods. And in particular, we delved deeper into strain elastography, how it's being developed, and what are the clinical applications of this technique.

Summary

- Physical principles in elastography
- Sound wave speeds and moduli of soft tissues
- Ultrasound elastography methods
- Strain elastography
- Clinical applications

So in a subsequent lecture, we'll talk more about the shear wave imaging techniques. That's all for today. I will see you in the next lecture.