Biomedical Ultrasound: Fundamentals of Imaging and Micromachined Transducers

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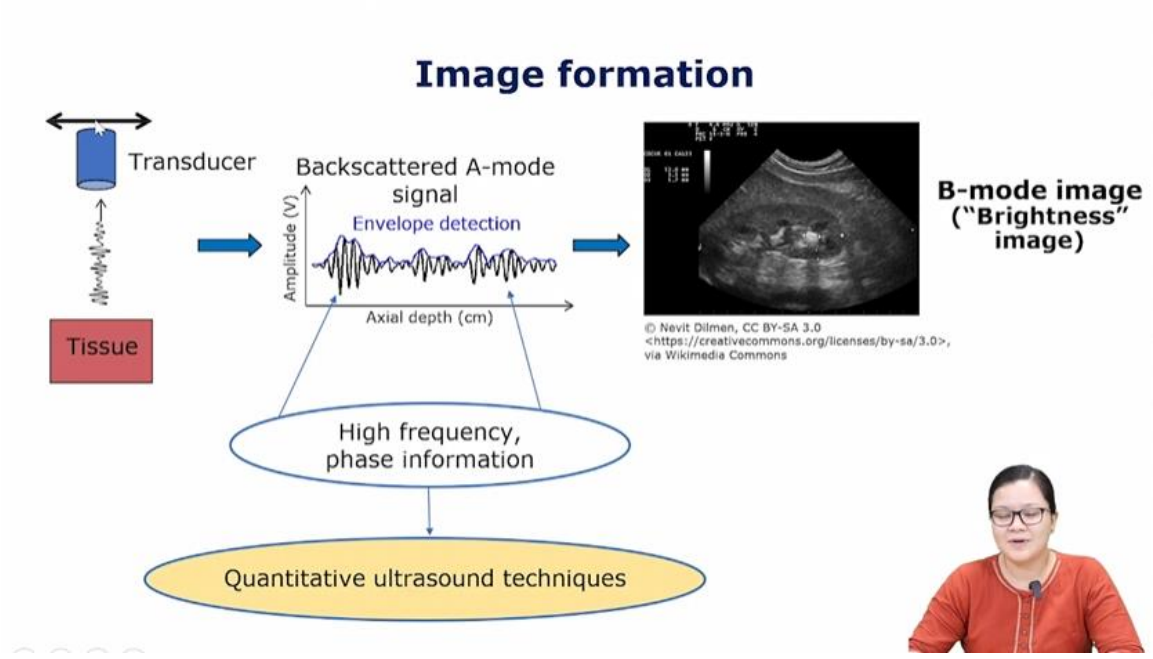
Lecture: 44

Quantitative Ultrasound

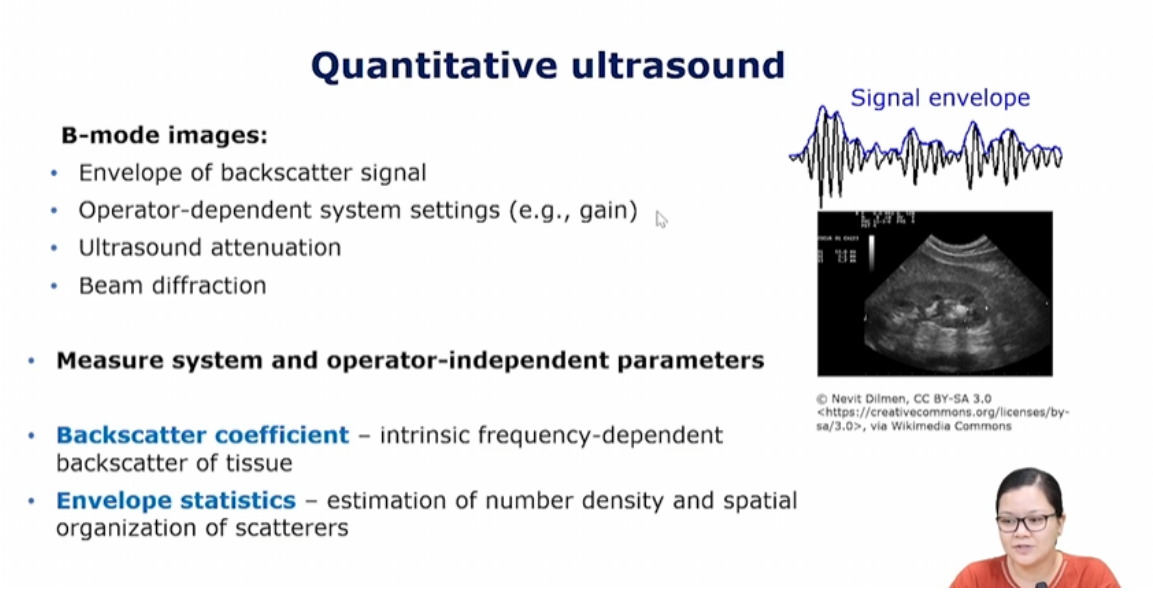
Hello, welcome to this lecture on quantitative ultrasound. Now let's remember how an ultrasound image is formed. First we have our transducer that sends an ultrasound signal to the tissue. The tissue interacts with the ultrasound and sends a backscattered signal echo back to the transducer. Now this transducer will then scan a two-dimensional region of interest and in each location that one is scanning, you can generate this backscattered A mode signal. Now this A mode signal is a function of the amplitude and the axial depth.



To be able to create our B mode or brightness mode image, we would compute the envelope of the backscattered signal by applying a Hilbert transform. And these A mode signals are stacked laterally along this imaging region of interest to create our B-mode image. Now you would have noticed that envelope detection does not take into account this high frequency phase information right here. So there's some information that is being lost when we are plotting the B-mode image.

Now there's a subfield in ultrasound that tries to utilize this high frequency phase information to be able to quantify the underlying tissue microstructure. And this is called **quantitative ultrasound technique**. Now the goal of quantitative ultrasound is to be able to measure system and operator independent parameters.

In the B-mode image, there are several parameters that are dependent on the operator, such as the system gain. You would have remembered the time gain compensation parameter that is being adjusted in a scanner. There's also some tissue effects such as ultrasound attenuation. You would have remembered that attenuation of the sound happens to tissue due to scattering as well as absorption of the ultrasound. Also, typically, focused beams are being used in imaging. Therefore, the beam is not uniform throughout the axial direction, and there can be some diffraction effects that also result in a loss of ultrasound signal. Now these system and operator independent parameters give us some indication of the underlying tissue microstructure.



There are two categories of quantitative ultrasound techniques, that are being developed that have been used to be able to categorize this tissue microstructure. So the first set of techniques are based on spectral-based analysis. And the one that we will discuss today is called the backscatter coefficient. And what is this? It measures the intrinsic frequency-dependent backscatter of tissue structures. The second set of techniques is called envelope statistics, and this allows us to estimate the number density and spatial organization of the scatterer based on the probability density function of the echo amplitude signals. So we'll go into these two categories of techniques more in detail.

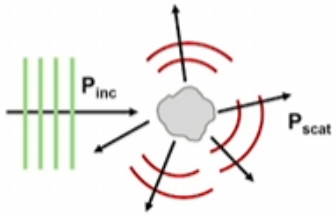
Let's first refresh scattering. So in a previous lecture, we had talked about scattering. Scattering is any redirection or disturbance of an incident ultrasound wave. We talked about how reflection is a special case of scattering, and it's being used to visualize

structures in ultrasound imaging. So here's just to remind you of what the total acoustic field is composed of. It's composed of the incident pressure wave as well as the scattered wave that is being scattered by the structure in the tissue.

Scattering

- Any redirection or disturbance of an incident ultrasound wave
- Reflection is a special case of scattering
- We visualize structures in ultrasound imaging based on scattered signal
- Total acoustic field:

$$p_{total}(\boldsymbol{r}, t) = p_{inc}(\boldsymbol{r}, t) + p_{scat}(\boldsymbol{r}, t)$$



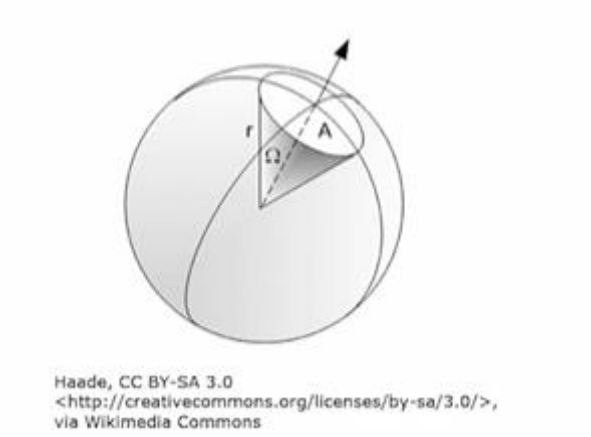
We also talked about the backscatter coefficient in brief detail, and that is also known as the differential scattering cross-section. It's the power scattered per unit solid angle in 180-degree direction, and that's divided by the incident wave intensity.

Backscatter coefficient

- Differential scattering cross section = power scattered per unit solid angle in the 180º direction, divided by the incident wave intensity
- Backscatter coefficient (BSC):

$$BSC = \left[\frac{(backscattered\ power)}{(solid\ angle) \times (incident\ intensity) \times (scattering\ volume)}\right]$$

So this is just the schematic of what a solid angle is. And the backscatter coefficient is just the amount of power that's being sent across this solid angle. And this is just a very general expression of the backscatter coefficient, which is also a function of the incident intensity as well as the scattering volume.



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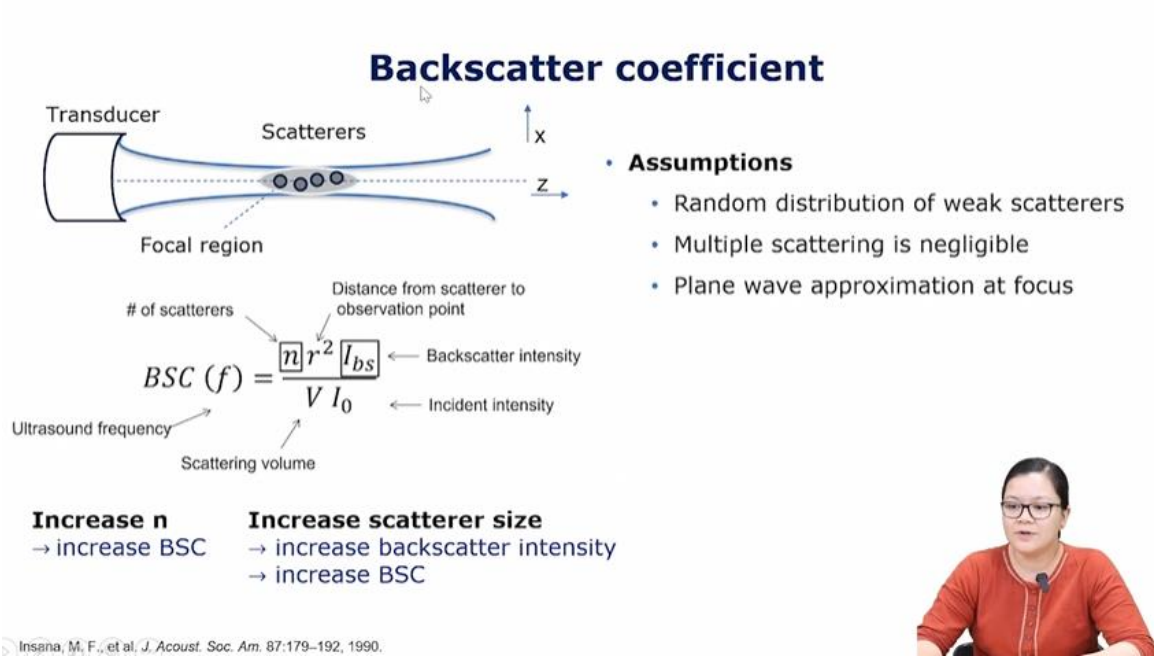
Now several theories have been derived to be able to compute this backscatter coefficient. So there is one theory that's described by Insana in 1990 which defines the backscatter coefficient of this form.



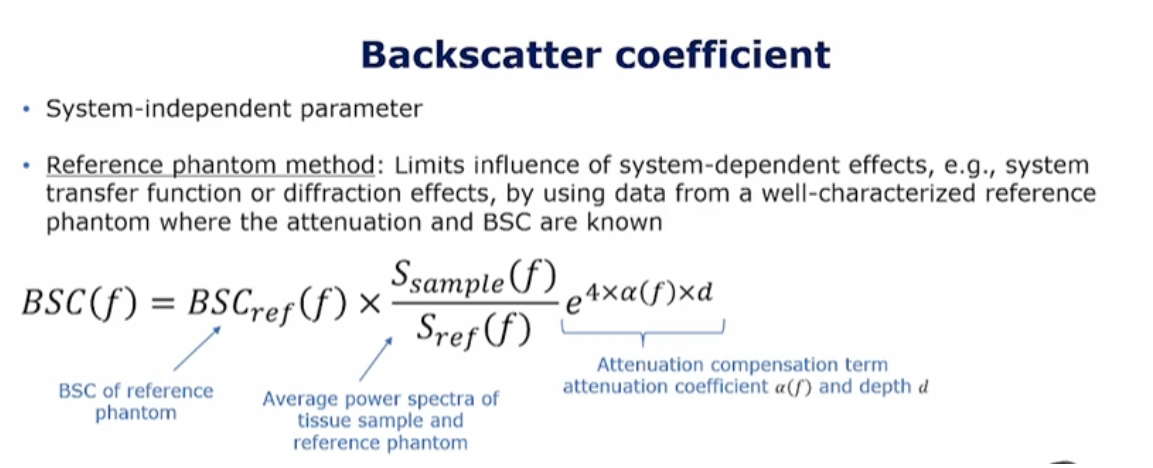
So if you look at the tissue space, you have your transducer and the scatterers are right within the tissue. The transducer beam is typically focused and what I'm presenting here is of a single element transducer so you have your focal region and you have scatterers within your focal region within your tissue and there are several assumptions that are being made. First you assume a random distribution of weak scatterers meaning that there are no strong scatterers such as bone or air tissue interface that are present inside the tissue. Also we assume that multiple scattering is negligible as well as there's a plane wave approximation at the focus. So here is the general expression of the backscatter coefficient.

$$BSC(f) = \frac{nr^2 I_{bs}}{V I_0}$$

It's a function of the ultrasound frequency. Also, what goes into it is the number of scatterers, the distance from the scatterer to the observation point, r (squared), the backscattered intensity, the scattering volume, as well as the incident ultrasound intensity.

So what you would have noticed from this equation is that as you increase n, the number of scatterers, there's an increase in the backscatter coefficient. Also, if you're increasing the scatterer size, that in turn increases backscatter intensity, and an increase in the backscatter intensity increases the backscatter coefficient. So what the backscatter coefficient can tell us is that, if there's any changes in the number of scatterers in a tissue as well as any changes in the size of the scatterers within the tissue.

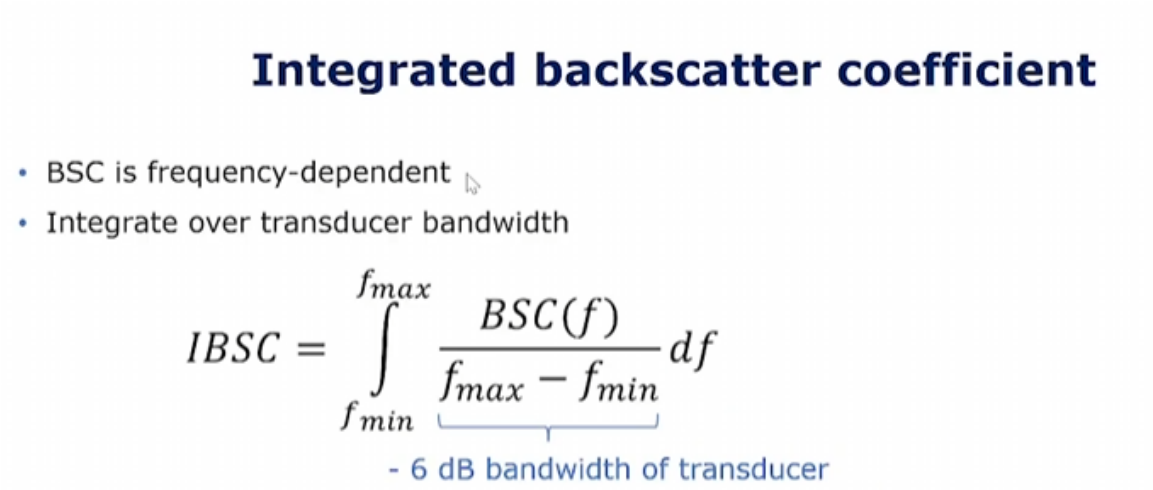
Now, the backscatter coefficient is a system-independent parameter. But how do you make it system-independent? So there are two techniques. One is the planar reflector technique, and the one that I'm presenting here today is the reference phantom method.



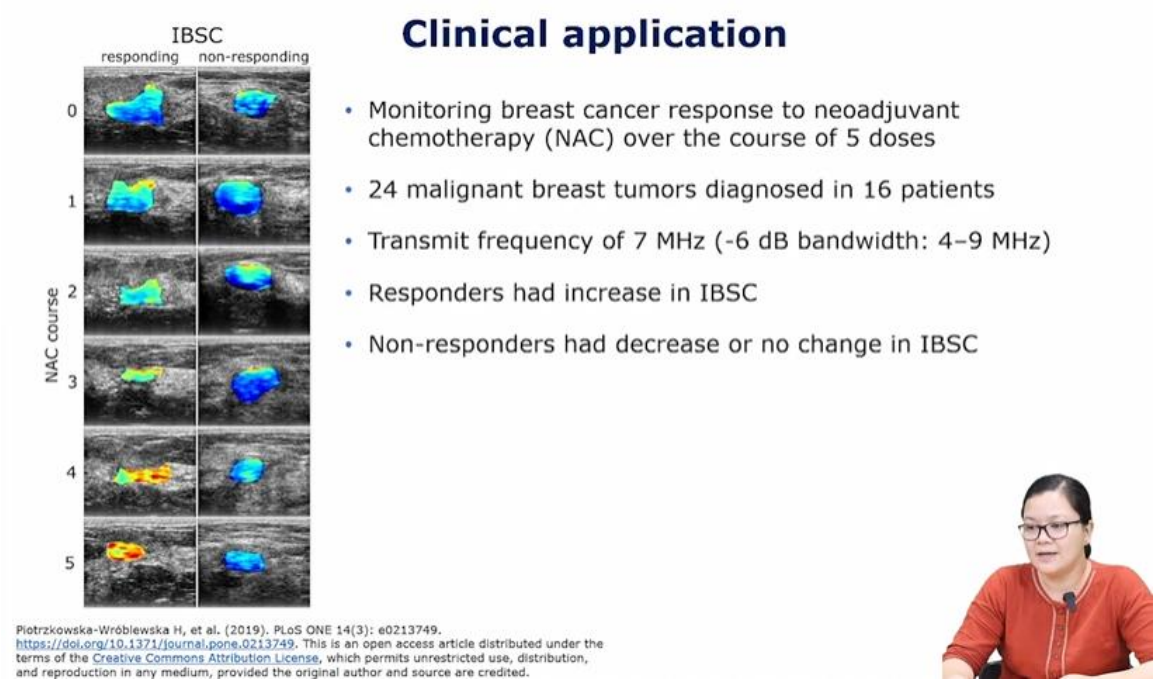
And what the reference phantom method does is it limits the influence of these system-dependent effects, such as the transfer function of the system or any diffraction effects due to the beam. And that utilizes a well-characterized reference phantom where we know what the attenuation and the backscatter coefficients are. So here's just a general expression of how you can calculate a backscatter coefficient of the sample based on the backscatter coefficient of the reference phantom as well as the power spectra of the tissue sample and the average power spectra of the reference phantom. There's also an attenuation compensation term here that compensates for the acoustic attenuation through the depth of the tissue and that utilizes the attenuation coefficient of the sample. The way you can get this attenuation coefficient parameter, is by experimental techniques, which we had discussed previously. So the term α in the expression is the attenuation coefficient of the tissue sample. And d is the depth at which you are interested in imaging, which is

the axial depth. Now we can calculate backscatter coefficient and its frequency dependent.

But typically, if you want to generate an image of backscatter coefficient, you would need one number that is representative of that tissue region of interest. So what is done is that the integrated backscatter coefficient is calculated using the following form here, where you have your frequency-dependent backscatter coefficient, and you integrate that over the transducer bandwidth. Now, this is a negative 6 dB bandwidth of the transducer, which is typically used. And by doing so, we get one number, the integrated backscatter coefficient, for that particular region of interest.



Now, here is one clinical application that shows you how the integrated backscatter coefficient can be used. So in this study right here, what the researchers were doing is that, they were monitoring the breast cancer response to a neoadjuvant chemotherapy, or NAC, and that's over the course of five doses. So they looked at 24 malignant breast tumors that are diagnosed from 16 patients, and the imaging frequency was 7 MHz with this 6 dB bandwidth. And here we show the integrated backscatter coefficient images that are color-coded and are overlaid into the B-mode images.



So in the Y direction we have the doses that were given to the patient. So the first, second, third, fourth, and fifth doses of the chemotherapy. And then the first column corresponds to the responders. And whatever is color mapped here is based on where the region of the tumor is. And the second column is based on the non-responders.

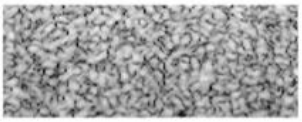
So here, blue indicates a lower integrated backscatter coefficient and red indicates the highest integrated backscatter coefficient. As you can see, for the responders, as the patients were treated with the dose of chemotherapy, there was an increase in integrated backscatter coefficient over the course of five doses. So you see more red that's appearing here. Whereas for the patients who are not responding to the treatment, you can see that there is a decrease in the IBC, and observe that here, or even no change in the integrated backscatter coefficient. So this is just showing you one example where the integrated backscatter coefficient would be able to assess changes in the underlying tissue microstructure. And these results were also confirmed with histology images of these tissues that were taken from the patients.

Now the second set of technique, which I'll talk about in detail, is called envelope statistics. Now this looks into the statistics of the speckle pattern in ultrasound images. So as you can see here, this is an example of what speckle looks like in an ultrasound image. And that's due to the interference effects of the waves that are being generated from tissues.

Envelope statistics

- Statistics of speckle pattern in ultrasound images
- Envelope amplitude of backscattered echo RF signals
- Contains information about underlying tissue microstructure

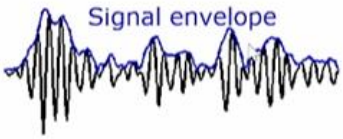
Speckle from ultrasonic scattering



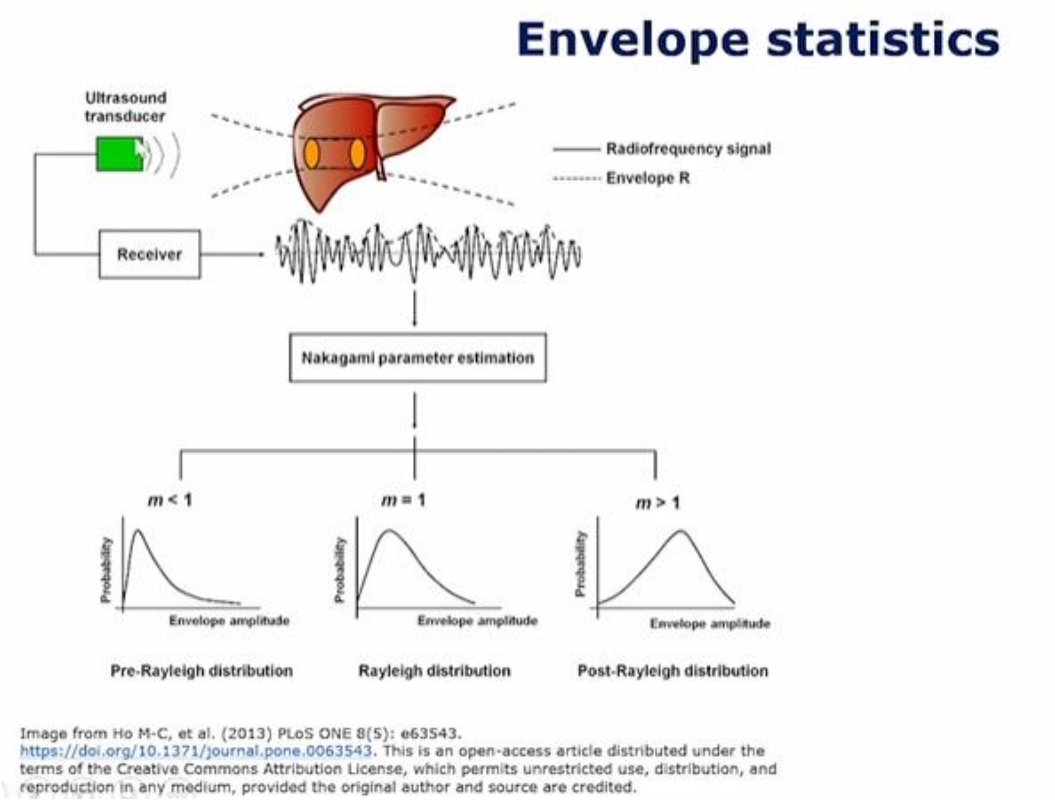
So we look into the envelope amplitude of the backscattered echo signal here, these envelope amplitudes also contain some information about the tissue structure. And there are several statistical models that were used to be able to bin these signal envelope amplitudes and try to model it based on several distributions. For instance, Rayleigh distribution, Ricean distribution, K distribution, Homodyned K distribution, and the Nakagami distribution. So we'll take a look at these different distributions and how it relates to the tissue microstructure.

- Statistical models investigated in medical ultrasound:

i. Rayleigh distribution
ii. Rician distribution
iii. K distribution
iv. Homodyned-K distribution
v. Nakagami distribution

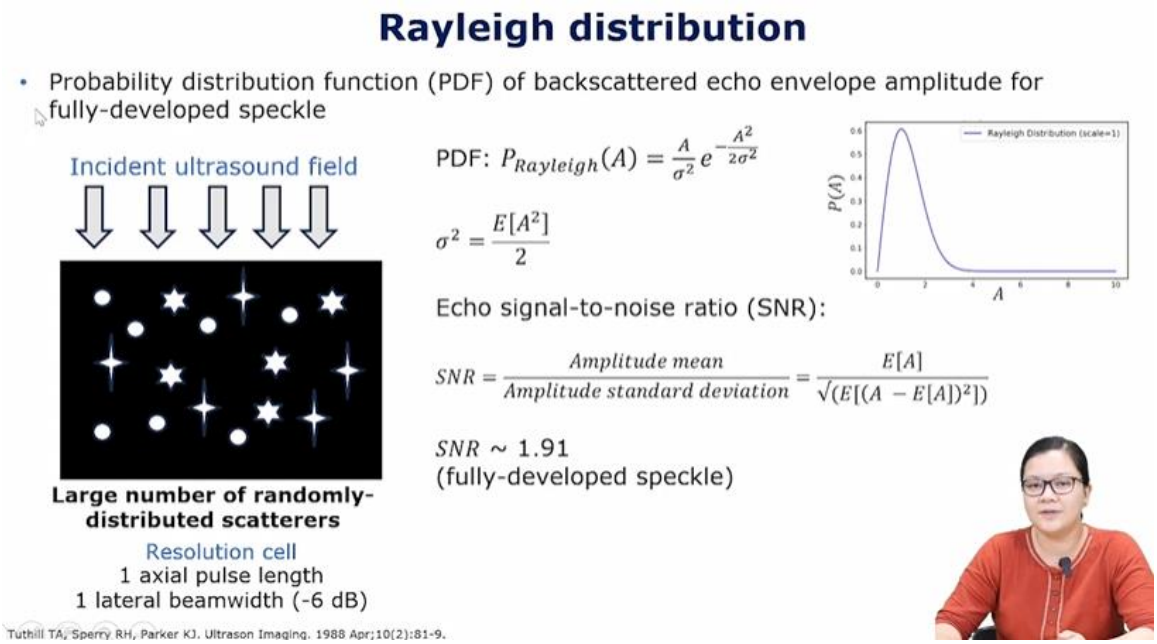


Here is a schematic of the workflow, of what is being done in envelope statistics. So we have our ultrasound transducer, looking into a sample volume that's typically within the focal region of the transducer. And then we receive the echo signals, and the envelope is being computed. And based on the probability density function or distribution function of the envelope, you can model that based on several of these distributions.



So this is just one of the distributions that I had talked about in the previous slide, the Nakagami distribution. And depending on the Nakagami parameter,(we'll discuss this more in detail in subsequent slides) it will show you how the probability distribution function of the echo envelope amplitude changes.

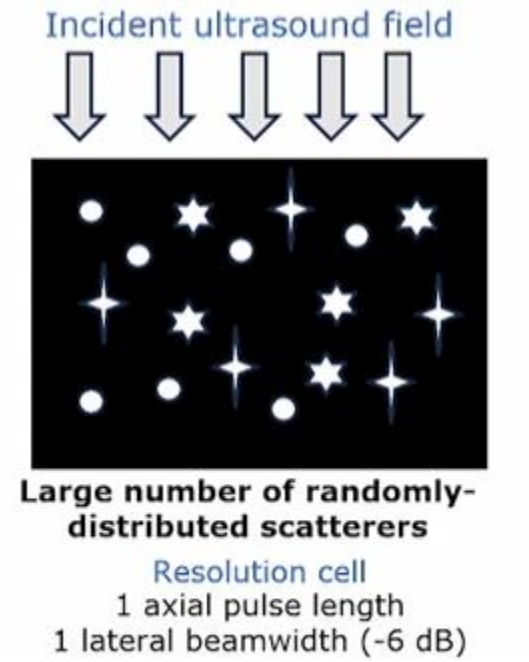
So let's first talk about the simplest type of distribution. It's called the Rayleigh distribution. Now the Rayleigh distribution is a probability distribution function or PDF of the backscattered echo envelope amplitude for a fully developed speckle.



We had briefly talked about what fully developed speckle is. How one approaches it in an ultrasound image is that, if you have a large number of scatterers, then the scattering distribution from those are independent of amplitude and phase. So that's a fully developed speckle. So this is what the probability distribution function of a Rayleigh model looks like, a Rayleigh distribution here. It has a Gaussian type shape. And this is what the probability distribution function looks like of an echo amplitude A.

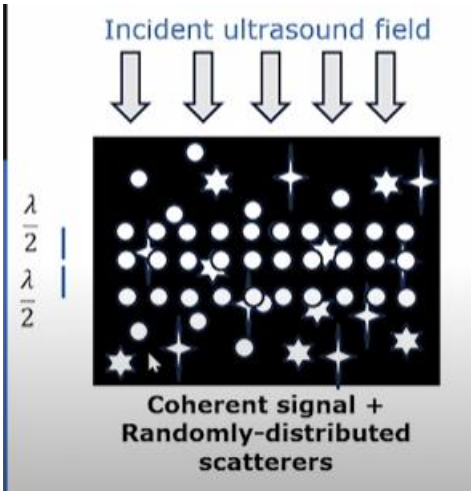
And typically, when one tries to determine whether the speckle pattern is a fully developed speckle, then one calculates the signal to noise ratio (SNR) of the echo. The SNR is computed by the amplitude mean over the amplitude standard deviation. And SNR that approaches 1.91 is typically regarded as a fully developed speckle.

So this is what these distributions of randomly distributed scatterers would look like in space. So if you have a Rayleigh distribution within a resolution cell, now this resolution cell is typically a function of an axial pulse length or a lateral beam width, so a three-dimensional cell.



And within this resolution cell, you have these scatterers that are high in number as well as randomly distributed. So this type of distribution of status is called a Rayleigh distribution.

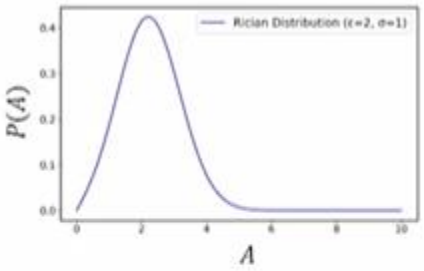
The next type of distribution is called Ricean distribution, and it extends the Rayleigh probability distribution function to include coherent signals. We talked about coherent and incoherent signals previously. So this provides estimate of the strengths of the coherent signal. So in the spatial domain, you have randomly distributed scatterers and including a coherent component where you have scatterers that are arranged in some periodic function and are spaced away from each other by less than a wavelength. So you can see here these circle scatterers correspond to scatterers that can produce a coherent signal.



And in this case, the phase of the backscattered signal matters. So the Rician distribution can be mathematically presented like this, where you see a similar organization as the Rayleigh distribution, but now it has this coherent signal component also, ε, and an extra term here that incorporates that coherent signal component.

$$P_{Rician}(A|\epsilon,\sigma) = \frac{A}{\sigma^2} e^{-\frac{A^2+\epsilon^2}{2\sigma^2}} I_o\left(\frac{\epsilon A}{\sigma^2}\right)$$

$$\sigma^2 = \frac{E[A^2]}{2}$$

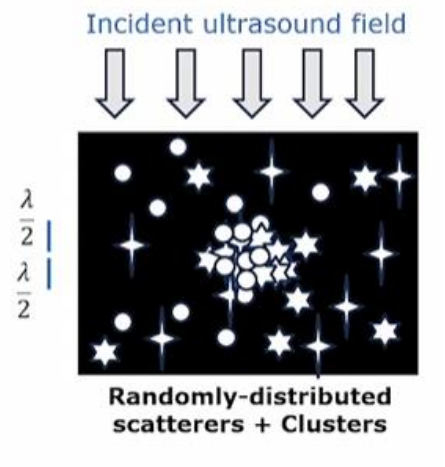


$I_o \rightarrow$ modified Bessel function of first kind of order 0

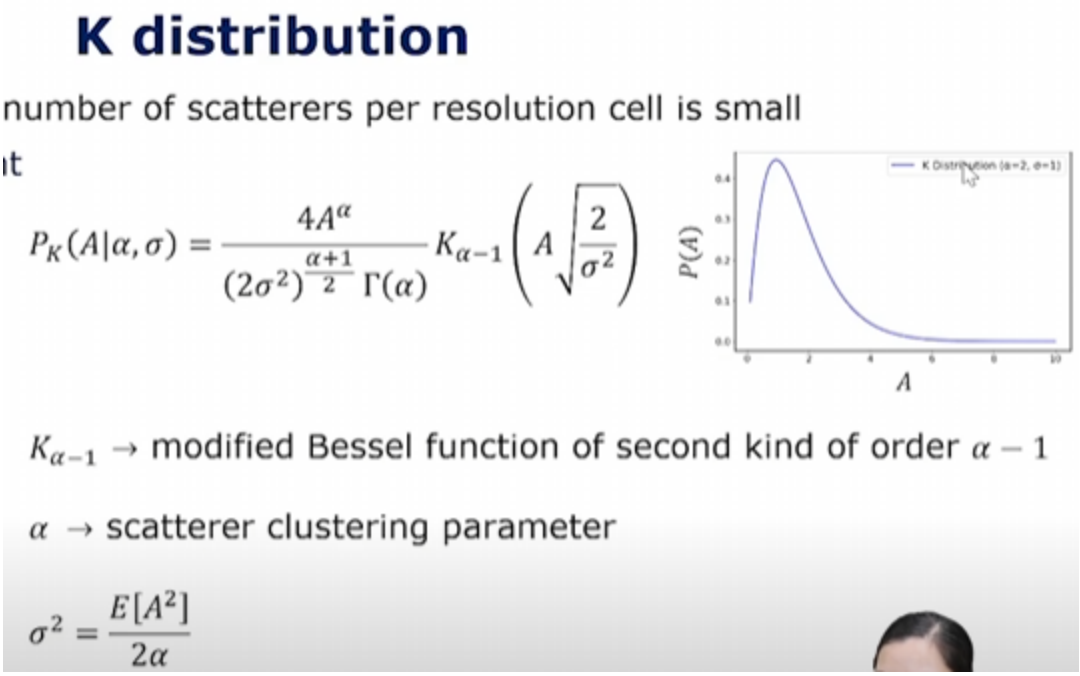
$\epsilon \rightarrow$ coherent signal component

So you can also see the probability distribution function, and what it looks like for an echo amplitude. So it's a bit more shifted to the right side with higher echo amplitudes due to the contribution of the coherent signal component.

The next case is the K-distribution. So this is a generalization of the Rayleigh distribution, where in this case, the number of scatters per resolution cell is relatively small. Typically, a rule of thumb for a fully developed speckle is that there are at least 10 scatterers in a resolution cell. For a K distribution, the number of scatterers is much less than 10. So in this case, you see that the spatial distribution of the scatterers are like this. And typically, what K distribution characterizes are also echoes coming from a cluster of scatterers.

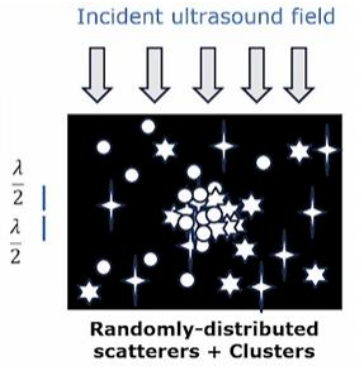


So this is what the mathematical form of the K-distribution looks like.

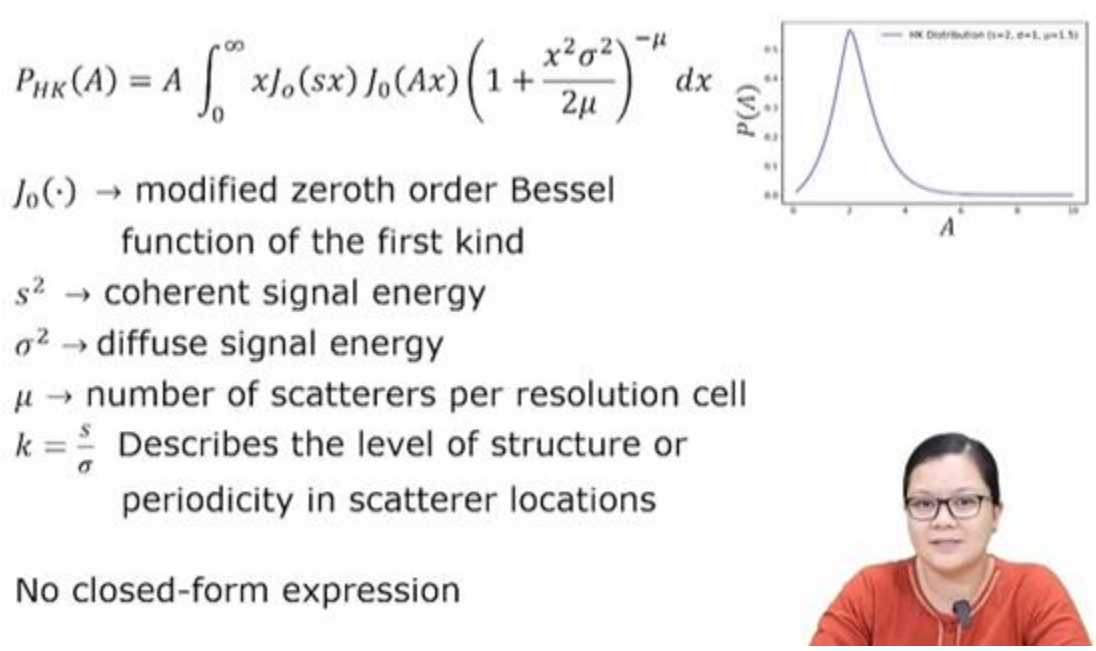


This is what it looks like if you plot the probability distribution function of the echo signal amplitude. And what is added in the K-distribution term is the scattering clustering parameter. Now this is what characterizes the clustering forms within the tissue structure. There's a scattering cluster term parameter which is also included in the expression.

So the Homodyned K distribution is the next generation distribution that combines all the characteristics of the Rayleigh, Rician, and the K distribution parameters. So this is a general case that involves incorporating all these spatial distribution aspects from those previous three distributions. So it's a general case. It's a variable effective density of random scatterers, and it does not have to include the coherent signal. So it can or cannot include the coherent signal. And the incoherent signal component is also taken into account. So this is quite a versatile type of distribution. that will be able to characterize clustering as well as high number of scatterers and whether there's some organization structure or randomness in the scatterer distribution.



So here is a general term for the homodyned K distribution. And this is how it looks if you plot it as against the probability distribution function of the echo amplitude.



And depending on the parameters in the above image, the homodyned K distribution is being used to look at various clinical cases. However, there's no closed form expression for this. So it's typically described as an integral form, which makes it quite computationally expensive. And so this is a more complicated type of distribution to compute, relative to the others. But nonetheless, it includes all these spatial characteristics of the other distributions.

And finally, the other type of distribution, the Nakagami distribution. It also models the backscattering conditions from Rayleigh, Ricean, as well as the K distribution. So it looks at different scattering as well. So here's just the probably distribution function expression for the Nakagami. And you can see here that it's a function of two parameters, m and Ω.

Nakagami distribution

- Models all backscattering conditions

$$P(A) = \frac{2m^m A^{2m-1}}{\Gamma(m)\Omega^m} e^{(-\frac{m}{\Omega}A^2)}$$

$\Gamma(\cdot)$ is the gamma function

- **Parameter estimation:**

$$m = \frac{[E(A^2)]^2}{E[A^2 - E(A^2)]^2}$$ Degree of heterogeneity

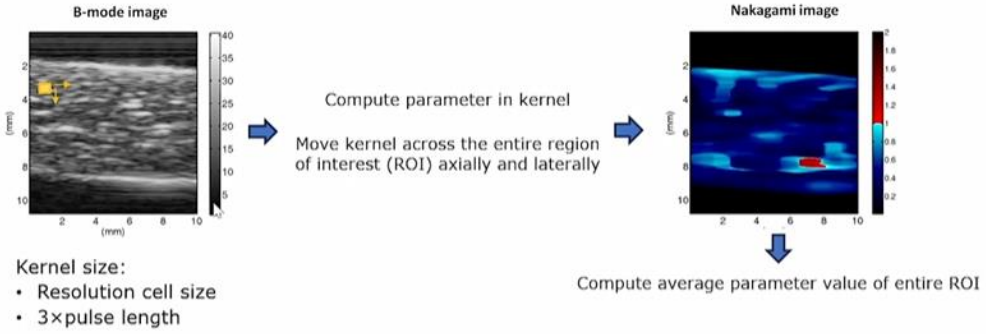
$m \approx 1$: Rayleigh distribution
$m > 1$: Rice distribution
$m < 1$: K distribution

$\Omega = E(A^2)$ Average energy of the backscattered envelope

So the m and Ω parameters can be estimated by the expression above, which is based on the moment. Now, m can tell you the degree of heterogeneity of the tissue scattering distribution. And typically, what you can do is that, if m approaches 1, then the probability distribution function of the echo amplitudes approaches those of the Rayleigh distribution. If m is much, much greater than 1, then the probability distribution function approaches that of a Ricean distribution. And if m is less than 1, then the probability distribution function approaches that of a K distribution. So you can see how varying the m parameter can also give you some indication of the different scatter distribution or organization within the tissues.

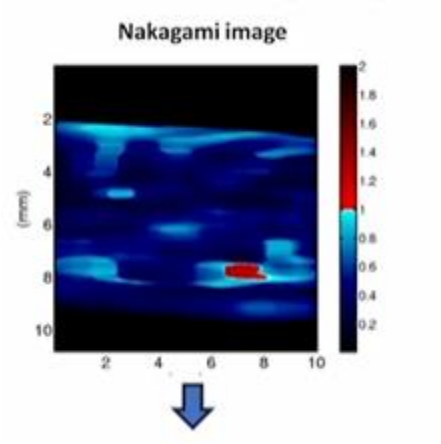
What one typically does to compute the Nakagami parameters, or any other envelope statistical parameter for the matter is that, you create a parametric image. So how that is being calculated is, first you have your B mode image and then you select a small region of interest or a small kernel.

Envelope statistics: Parametric imaging



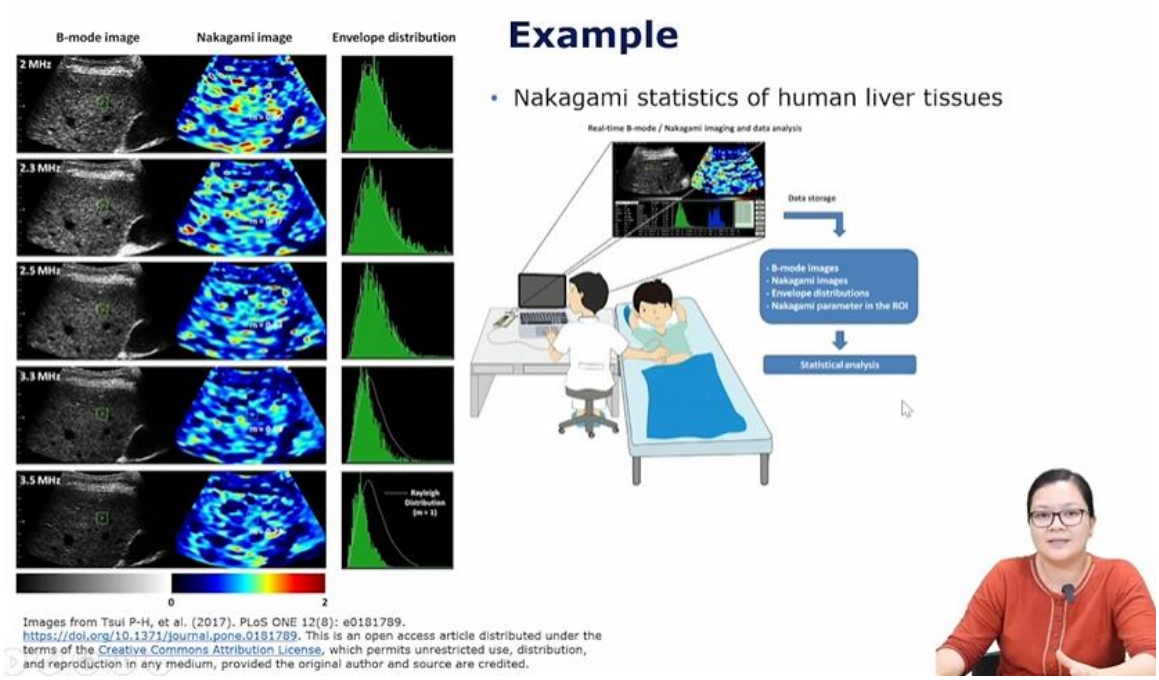
You have a bigger region of interest corresponding to the entire tissue region that you want to look at. But if you want to create an image of a parameter distribution within that larger region of interest, you divide it into smaller kernels marked in yellow in the B mode image above. So typically this kernel size is on the order of the resolution cell size or three times the pulse length. So three times the pulse length is typically what is now being reported in literature. And what one does is for each of this kernel, you take the backscattered echo amplitudes, plot the probability distribution function of that echo amplitude, and then you try to fit it to a model, like for instance the Nakagami parameter model, and then you would extract an m parameter.

So you would compute each parameter in that kernel, then you would move the kernel across laterally and axially within that larger region of interest. And as you are moving the kernel, you're going to a different spatial location in the image. So then you would calculate another parameter value at this different spatial location. So you're generating different pixels associated with that parameter in your image. So what you would get is something that looks like this.

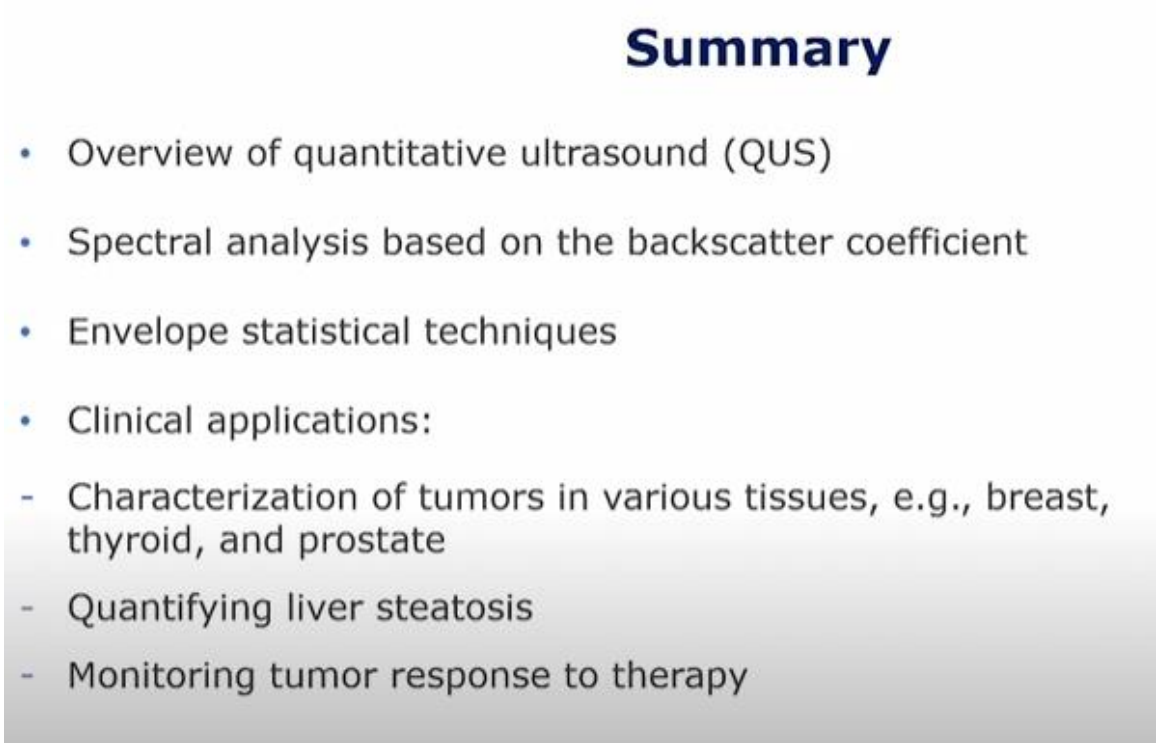


Now this is based on the Nakagami parameter m. And you can see that it's based on a color scale values. And within this larger region of interest, there are differences in the m parameter, meaning that location in the image with a red region, , the m parameter is corresponding to a different structure in the tissue. And what one can typically do is you can compute the average parameter value of an entire ROI and report that. So typically the images are shown as well as the average value.

So here is an example of a Nakagami statistics of human liver tissues. So what was done in this study is that you have a researcher/ sonographer who is imaging the liver of a volunteer and then what you can do is one has captured the B-mode image and some post-processing to generate the Nakagami image right here. And at a particular location in that Nakagami image, here is what the envelope distribution would look like. This is the probability distribution function that is also denoted by this light curve right here.



So what this study did is, depending on the frequency of the ultrasound that is being used, they wanted to assess whether this would affect the Nakagami statistics. And what they had found is that as you increase in frequency, the statistical distribution goes away from the Rayleigh distribution parameter. So you can see in the bottom most envelope distribution, the Rayleigh distribution does not fit well with the actual envelope amplitude distribution, and that could be also because of higher the frequency, the smaller resolution cell you have, therefore there are less scatterers within that resolution cell. So there's several parameters of the scanning system that can also affect what your Nakagami distribution parameters are. But if one takes care of selecting a particular transducer frequency at the particular transducer focal region and try to use those parameters between different cases, then one can do a one-to-one comparison between the Nakagami parameters between those cases.



So in summary, I hope this gives you a good overview of quantitative ultrasound. It's an evolving subfield in ultrasound imaging, and it allows us to characterize different tissue structures. And we've talked about two categories of quantitative ultrasound techniques. The first is being a spectral analysis, which is based on the backscatter coefficient. The second is the envelope statistical techniques. We talked about homodyned K distribution and as well as like Nakagami distributions which are now more widely used in the literature and being investigated for various clinical applications. So several applications that are being done now are characterizing tumors in different tissues such as breast, thyroid, and prostate and there are many more that are being investigated. Also, these techniques are being used for quantifying liver steatosis, which is a buildup of fat in the liver. As well as these techniques are being used for monitoring tumor response to therapy. So the example that I gave you with the integrated backscatter coefficient is one such case where these quantitative ultrasound techniques are being used to guide the response to therapy. So this is looking into monitoring treatment response. So there's much work that's being done still in these types of techniques. And over time, more and more techniques will be validated in the clinical scenario. So I hope you enjoyed this lecture, and see you again in the next lecture. Thank you.