

Biomedical Ultrasound: Fundamentals of Imaging and Micromachined Transducers

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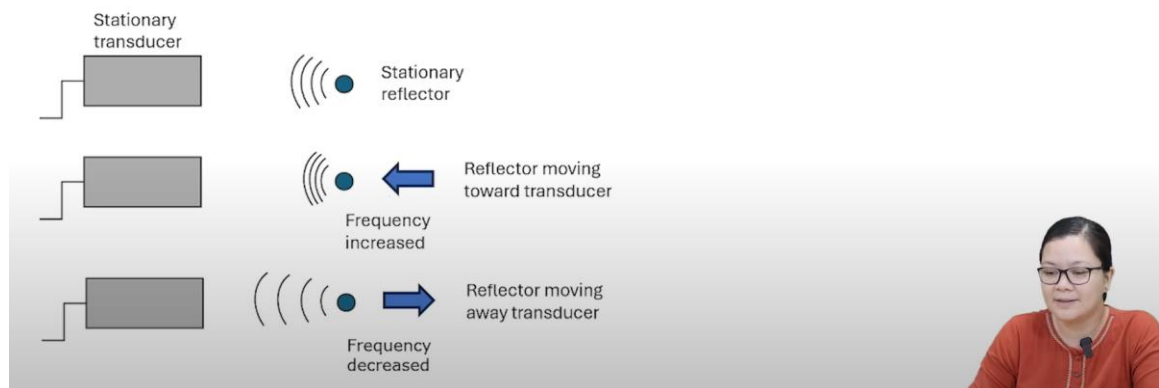
Lecture: 45

Recap of week 9

Hello, today we'll do a recap of what we had discussed in this week. We first started out with talking about Doppler ultrasound, and this is a method to measure blood flow in blood vessels. Doppler ultrasound has been used to diagnose blood clots, heart valve defects, as well as blocked artery or vessel narrowing called stenosis. So, what is being shown here is what a typical Doppler display looks like in a scanner, where you have color Doppler overlaid onto B-mode image, as well as the spectral Doppler that's being shown here that looks into the blood flow velocities. So, we'll do a recap on these parts in subsequent slides. So, we talked about different types of Doppler, continuous mode, post mode, both color and power Doppler.

Let's review what the Doppler effect is. So Doppler effect is a change in frequency of sound emitting from a moving source, and that's being perceived by an observer. So Doppler ultrasound is based on a Doppler shift of these ultrasound frequencies. And so, for instance, right here, you have a stationary transducer.

- Change in frequency of sound emitted from a moving source, which is perceived by an observer
- Doppler ultrasound is based on this Doppler shift of ultrasound frequency caused by a moving reflector/scatterer in blood vessels (e.g., red blood cells)



Send a signal. That reflector that's not moving will send the frequency that's the same back. Typically, the scatterers or the reflectors in the blood vessels are your red blood

cells. And that's what's being detected. So, if you have a case where the reflector or the red blood cells are moving towards the transducer, then the frequency will increase.

And if the reflector is moving away from the transducer, then the frequency is being decreased. Here's just an expression of the Doppler frequency shift, which we discussed. the function of the incident beam, the blood flow velocity, the sound speed, as well as this Doppler angle right here. If you reorganize this expression, then you can calculate the blood velocity based on this Doppler shift frequency right here. We've also discussed how the Doppler angle can affect the Doppler frequency.

So, we know that in that Doppler shift equation, the Doppler shift frequency is proportional to the cosine of this Doppler angle right here.

- Doppler frequency shift, f_D

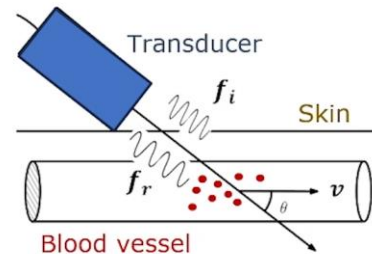
$$f_D = \frac{2 \times f_i \times v \times \cos(\theta)}{c}$$

f_i : frequency of incident beam

v : blood flow (red blood cell) velocity

c : speed of sound

θ : angle between direction of incident beam and blood flow (Doppler angle)

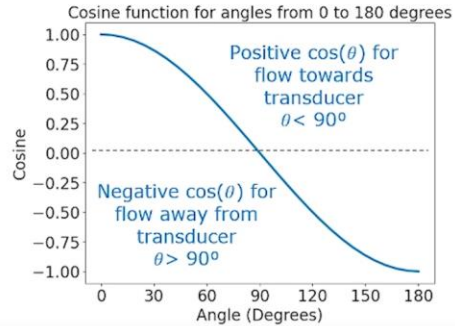
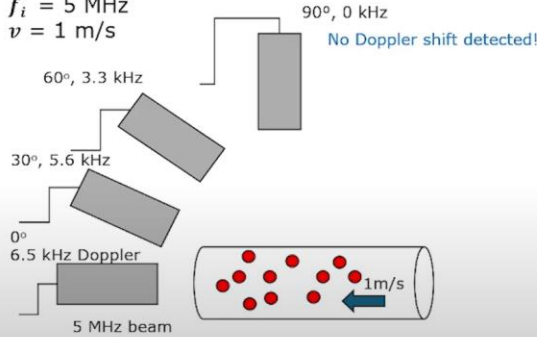


And when we looked at this scenario right here where the blood is moving from right to left at one meter per second, and your speed of sound is 1540, we're imaging using five megahertz right here. So that's the frequency of your transmitted or your incident beam. Depending on how you position the transducer, you will get a different Doppler frequency shift. So, if you angle the transducer with a zero-degree Doppler angle, then you will get a Doppler frequency of 6.5 kilohertz. And as you move away from that angle towards 90 degrees, then the Doppler frequency shift would decrease. So here at 90 degrees, there would be no Doppler shift detected. And that's because of that cosine function, cosine of that Doppler frequency. So here on the right, we talked about how the cosine function changes depending on the angle.

Doppler angle affects Doppler frequency

Doppler shift frequency, f_D , is proportional to cosine of Doppler angle, $\cos(\theta)$

$c = 1540 \text{ m/s}$
 $f_i = 5 \text{ MHz}$
 $v = 1 \text{ m/s}$

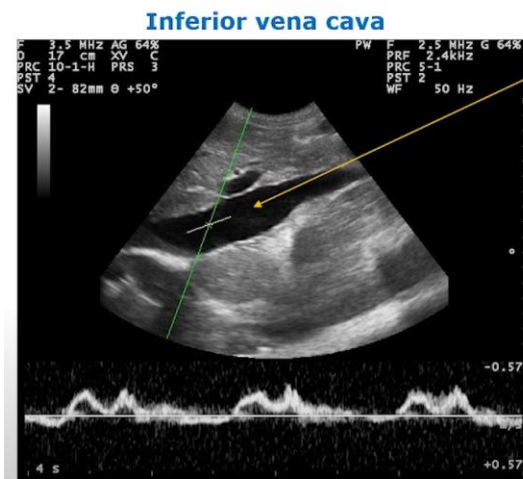


In practice, transducer beam oriented between Doppler angles of 30° and 60°



And typically, if you have angles that are less than 90 degrees, then that means you'll get a positive cosine theta. where the flow is towards the transducer you have a negative cosine theta or a higher and higher doppler angles more than 90 degrees then that indicates that the reflector is moving away from the transducer and typically we would like to orient the transducer beam such that they're between doppler angles of 30 to 60 to get the best response of your best estimation of what the Doppler frequency is. Here's just an example of what the Doppler display would look like. Also incorporating, trying to dial in what the Doppler angle would be. So, this green corresponds to the line that you were looking at.

Doppler ultrasound example



- Operator inputs the flow angle by adjusting **angle cursor** on B-mode image display
- Mistakes in specifying flow angle results in errors in velocity estimates
 - Small θ of $0-40^\circ$:
 - 5° error of leads to $<10\%$ velocity error
 - Large θ near 90° :
 - 5° error of leads to nearly 100% velocity error



And this white or yellow flat cursor here corresponds to the angle cursor. And typically, what the operator does is input this flow angle by arranging this angle cursor parallel to

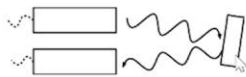
the direction of the vessel. And typically, this is being used to be able to compute the correct angle. That way, you can get the more accurate Doppler frequency shift. But as you can see, all of this is operator dependent, and there can be mistakes in specifying this flow angle.

So, there can be some errors in the velocity estimates as well. So, if you situate the angle with very small angles of around 0 to 40, any 5-degree error can lead to less than 10% velocity error, which is not so bad. But if you're looking at larger angles, almost nearing 90 degrees. Any 5% error can lead to almost 100% velocity error, error in the estimates of velocity. So, one needs to really take into account how they're placing this angle cursor in your Doppler image.

We also talked about continuous Doppler or continuous wave Doppler where you have two crystals here that are continuously transmitting as well as receiving the reflected signal from our scatterers. An advantage here is that you can accurately display the flow without aliasing. We also discussed what aliasing is. The disadvantage is that because you're continuously transmitting and receiving the signal, there's no time delay information that you won't be able to tell exactly at what step the signal is coming from. So, there could be some range ambiguity artifacts that can happen.

- **Continuous-wave Doppler:**

- Two crystals, continuous transmission and reception



- **Advantage:** Accurately display flow without aliasing
- **Disadvantage:** No time delay info - Range ambiguity

- **Pulsed-wave Doppler:**

- One crystal, produces short bursts of sound



- **Advantage:** Range resolution
- **Disadvantage:** Unable to measure high velocities (aliasing)



Now pulse wave, on the other hand, you look at one crystal and it goes through a pulse echo mode, produces short bursts of sound and receives the echo after the pulse, the transmitted pulse interacts with the tissue. The advantage of pulse wave Doppler is that you can estimate the range. using the time delay information. The range resolution is very good compared to continuous wave Doppler, but the disadvantage is you're unable to measure high velocities because it also depends on the frame rate, or the pulse repetition frequency of the signal and we'll discuss that again later and that's because of aliasing.

We also talked about Doppler spectral analysis in the previous slides, I showed you the Doppler spectrum.

Now, this spectral analysis shows us the distribution of Doppler frequencies within that vessel of interest. And it can depend on varying factors, such as the distribution of velocities in the vessel, the beam width of the transducer, and that can impact the size of the sample volume. So, if you're doing pulse Doppler. So here are just some scenarios of different flow conditions that can occur in a vessel. You have laminar flow that typically has this parabolic velocity profile where the blood cells that are moving at the center of the blood vessel, lumen, typically travel faster than the cells that are on the sides along the vessel wall.

- Number of different Doppler frequencies depends on:
 1. Distribution of velocities in vessel
 2. Transducer beam width
 3. Size of sample volume (if pulsed Doppler)
- **Spectral analysis:** Show distribution of Doppler frequencies



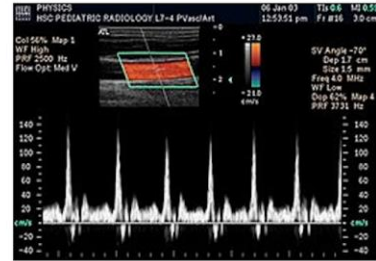
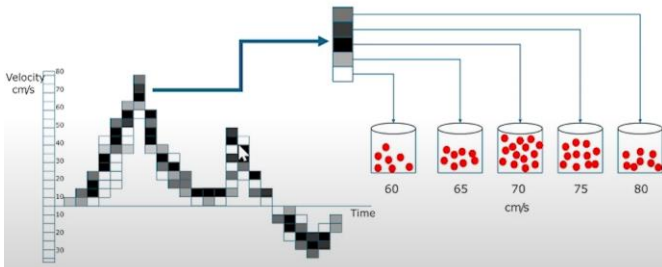
If you have larger arteries, then you can create this blunt profile right here. If there is an obstruction or a narrowing of the artery, then one can get turbulent flow in your Doppler images right here, where the flow becomes disturbed and there could be some streaming effects that can occur downstream. And that you can also detect via spectral Doppler. So, we'll talk about that a bit more. We talked about how we can get a spectral Doppler and that's basically the ultrasound signal is being analyzed into its frequency components and using a fast Fourier transform analyzer.

So, the way spectral display looks is something like this, where you have in the Y axis, the velocity of the blood, and it bends depending on the distribution of blood flow inside the vessel right here. And so, this is what you would see. You don't really see one single line because typically in the color flow box that you're indicating or the Doppler box, your sample volume does not only include one set of velocities or one velocity value, typically has a distribution of velocities. So, what you will be looking at is the

distribution of these velocities at a single point in time. And what the Doppler spectra would look like for different flow conditions.

Spectral analysis

- Complex signal is analyzed into simple frequency components
- Fast Fourier transform analyzer

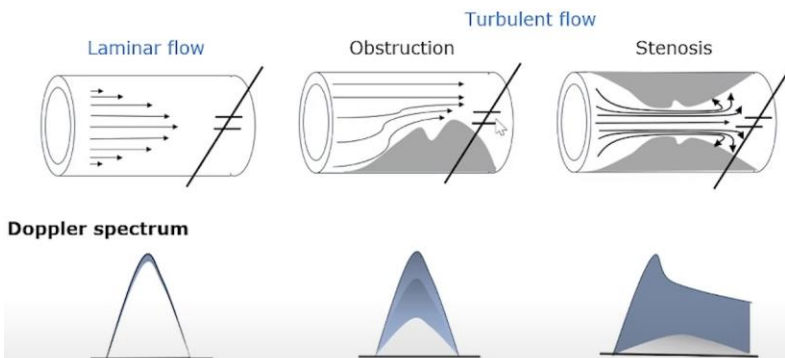


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So here we have laminar flow. If you have a small sample volume right here, then you would get a Doppler spectrum profile that looks like this, where typically the velocity hovers very close to each other. you have a turbulent flow such as an obstruction or a stenosis right here and you measure downstream of that obstruction or that stenosis then you can see a wide distribution of velocities which can be seen like right here and right here and this is as a function of time so this is how clinicians use the Doppler spectra to be able to gauge the health of a vessel It depends on the spectrum profile and how wide the distribution of the velocities are.

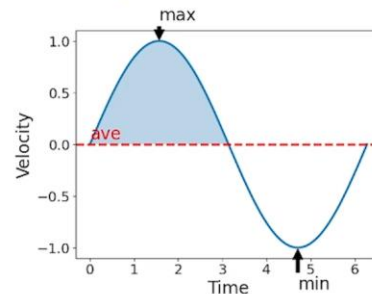
Doppler spectra for different flow conditions



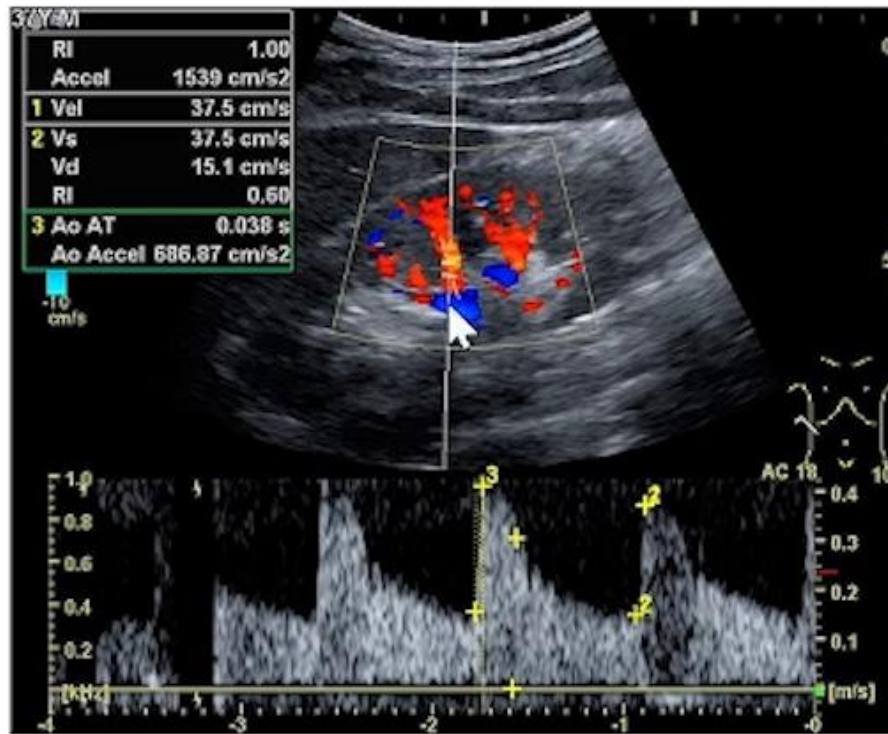
One can also quantify or get some quantitative parameters from the spectral profile. And we have pulsatility index, which we can calculate based on the max and min and the average flow during the cycle, as well as the resistivity index based on the max and min velocities within that spectral profile. And what it does, it can give you a relative resistance measure to flow of a certain vascular network in a tissue. So, if there is some obstruction downstream within an organ, let's say the organ is not getting enough blood, healthy blood, then there could be some we can use the spectral analysis to be able to gauge whether the good blood is flowing into that organ. Otherwise, if the resistivity index is high, then it means that there's not much blood flow going into that region. So, this is how clinicians would utilize these parameters to be able to gauge the health of an organ.

Spectral analysis: Quantitative parameters

- Provide data on the relative resistance to flow of vascular network
- Pulsatility index: $PI = \frac{max-min}{ave}$
 - max → peak systolic
 - min → minimum diastolic velocities during the cardiac cycle
 - ave → average flow during the cycle
- Resistivity index: $RI = \frac{max-min}{max}$



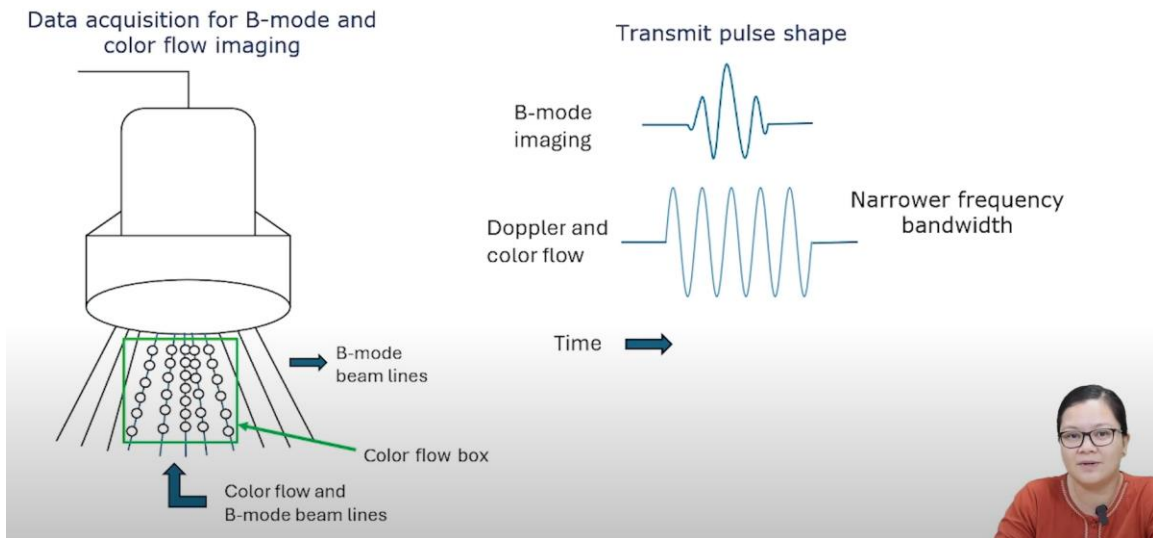
We also talked about color flow doppler imaging here. And this is nice because it gives you a two-dimensional view, a color-coded view of the direction of the blood flow as well as the amplitude of the blood velocity. And the nice thing is also it's typically plotted over the B-mode image, so you can look at the anatomy of the tissue as well. So, the way data is acquired for both color Doppler and beam mode is you have your array transducer here sending out beam lines. And a couple of those beam lines at the center are being dedicated to color flow Doppler.



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And this is set up this way to also make sure that there's a real time frame rate. So, one can select a color flow box here. And within that beam line, there are color flow pulse packets where that's being looked into to gauge what the flow profile is as a function of the depth. If we compare the beam mode imaging pulse to the Doppler in color flow, you can see that the beam mode transmit pulse is typically two to three cycles, very short pulses. But for Doppler pulses, typically several cycles are being used, and that's to create a narrow frequency bandwidth to be able to accurately calculate that Doppler shift frequency.

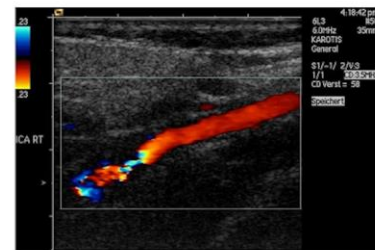
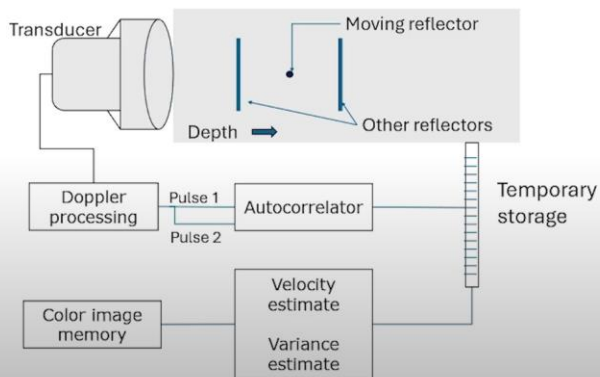
Data acquisition



So, with their color flow imaging system, you can estimate the velocity of the flow, also looking into the variance in the velocity estimates. Now, if you have turbulent flow, for instance, in this image here, you have a color flow image of an artery with a stenotic region here. There's some obstruction here that's causing these different color changes in the Doppler color map right here. And that's because of the flow. Now, if one looks into a region of interest here where the turbulence is, look into the range of velocity values and compute the variance will be much higher compared to a region of interest with smoother flow right here.

Color flow imaging system

- Velocity estimates
- Variance estimates for detecting presence of turbulent flow
- Mapping color to velocity estimates and flow direction



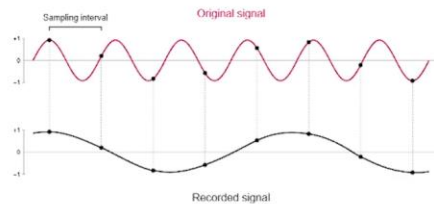
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So, these variance estimates are useful for gauging the presence of turbulent flow within regions of interest in the vessel. We also talked about different hues in the color display of the color Doppler. So typically, a red hue means flow moving towards the transducer, blue moving away. In this image right here, you can see that there are some vessels that are moving blood towards the transducers and some vessels that are moving blood away from the transducer. Depending on the brightness or the intensity of that hue, that will give you an indication of flow rate.

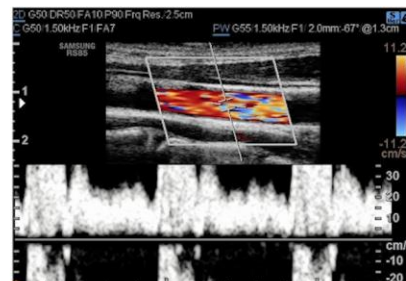
So, from dull to bright red means that the flow is going faster and it's reaching bright red. Now both the pulse Doppler as well as color Doppler are affected by aliasing because they're dependent on the pulse repetition frequency of the imaging.

And insufficient sampling of the signals can result in aliasing artifacts where there could be some lower frequency components that get registered into the spectrum. So, factors that can cause aliasing are really high blood velocities. If the system is unable to capture all that does go at high velocities, then there could be some aliasing. Also, increasing depth of region of interest can cause some range ambiguity.

- Insufficient sampling rate results in artifactual lower-frequency components in the spectrum



Laurens R. Krol, CC0, via Wikimedia Commons, https://commons.wikimedia.org/wiki/File:Signal_aliasing_demonstration.svg



Case courtesy of Bällint Botz, Radiopaedia.org, rID: 64786

- Factors that can cause aliasing:
 - Higher blood velocities
 - Increasing depth of region of interest, causing range ambiguity
 - Inappropriate Doppler angle
 - Large sampling volume



If there's an inappropriate in setting the Doppler angle, that can also cause aliasing. And if there's a large sample volume. So, you want to keep the sample volume small enough to be able to look at accurately measuring the velocity at that region of interest, but also large enough to be able to get a good view of that entire vessel. But if it's too large, then there could be a large distribution of velocities, some really high and some really low, which can also cause some aliasing. So, here's just an example of the wrap around artifact that one can see in a spectral Doppler.

Here you can see that high flow velocities are wrapping around in the lower frequency components right here. And in a color Doppler, you can see that different colors, red and blue, are also in the region of interest. Just because this aliasing artifact could cause this also wraparound in the Doppler display. We also talked about how to avoid aliasing. And you're familiar with the Nyquist sampling rate.

So, in Doppler ultrasound, what we must keep in mind is that the pulse repetition frequency has to be at least twice that of the Doppler shift frequency.

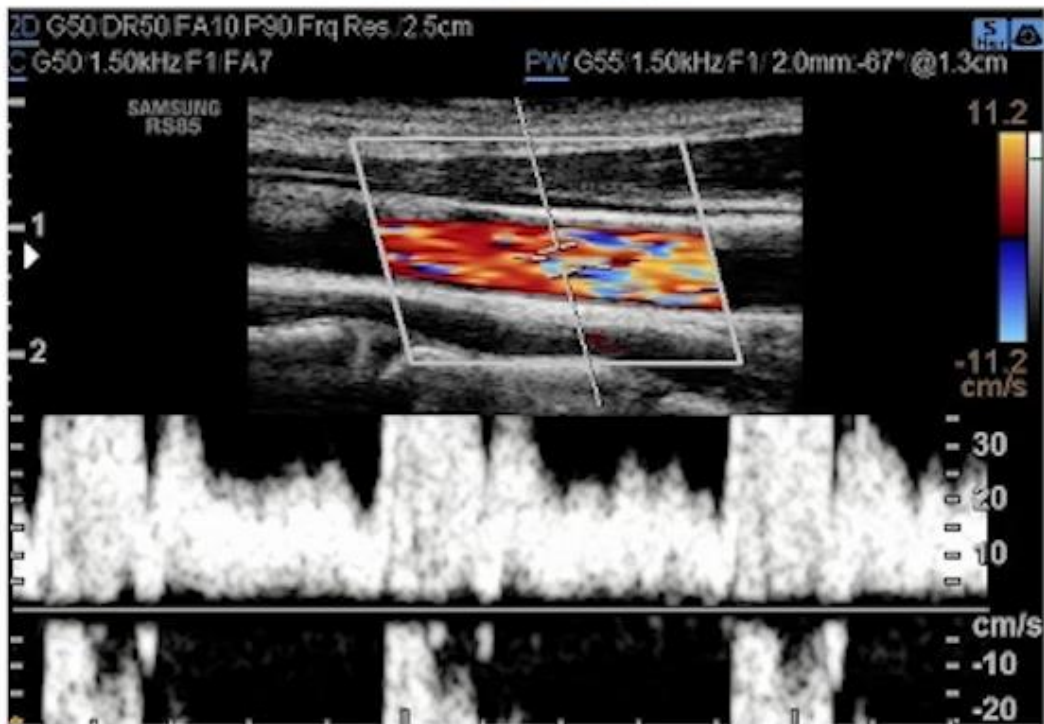
$$PRF \geq 2f_D$$

$$PRF_{max} = 2f_D = \frac{4f_o v_{max}}{c}$$

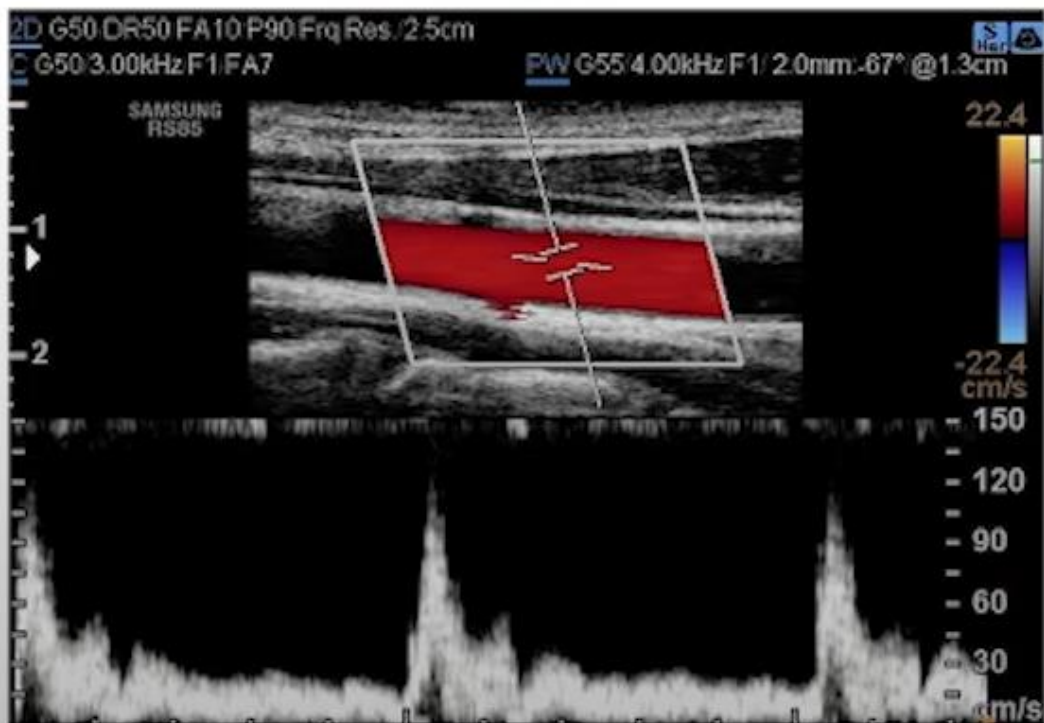
$$v_{max} = \frac{cPRF_{max}}{4f_o} = \frac{c^2}{8f_o d}$$

And then to avoid aliasing, we keep in mind what the maximum velocity is. And that way we can set up the highest PRF we need to set the scanner to be able to capture those high velocities. So, we talked about one such example right here. One way to remove or eliminate aliasing is to increase the pulse repetition frequency.

PRF: 1.5 kHz



PRF: 3 kHz



Case courtesy of Bálint Botz, Radiopaedia.org, rID: 64786

So here I showed an example of color Doppler as well as a spectral Doppler display here with a pulse repetition frequency of 1.5 kilohertz now if you double that pulse repetition frequency then you can see that there's no more wraparound artifacts the high flow velocities can be detected here and in color Doppler you can see a smooth profile of blood flow right here and here this is a nice image of a video showing how if you increase the pulse repetition frequency, you can see that transition of this aliasing artifact here. Once we increase further, as the blood is flowing, you can see that that coloring aliasing artifact has now disappeared. So, this is one such way you can remove aliasing.

We also talked about the power Doppler ultrasound. Now the image that is being color coded is not based on the flow, blood flow, or the velocity, but based on the intensity of the flow. So, it's not dependent on the Doppler frequency as well. Therefore, there's no signal aliasing. Not also dependent on the Doppler angle. And the nice thing is that it can enable detection of very small vessels with slow flow.

So, here's just an example of the power Doppler image of a kidney, where now you can see even small vasculature that are within the kidney containing the nephrons. When we compare between power and color Doppler, if there is a difference in the frequency of the Doppler signal, color Doppler will be able to, you can see in a color Doppler image that the pixel value will be different, but in a power Doppler, the pixel values will be the same because again, power Doppler does not depend on the frequency. If you have the same frequency but different amplitudes of the Doppler signal, color Doppler will show that the pixels will be the same, but power Doppler will show differences in the pixel values.

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Comparison between power and color Doppler

Different frequency, same amplitude			Same frequency, different amplitude		
Doppler signal	Color Doppler image pixel	Power Doppler image pixel	Doppler signal	Color Doppler image pixel	Power Doppler image pixel
	Pixel value varies with Doppler frequency and flow velocity	Same		Same	Pixel value varies with signal strength

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So, the last lecture we looked at was quantitative ultrasound. And here, the goal of quantitative ultrasound is to be able to measure system-independent and operator-independent parameters that can give you some quantification of the underlying tissue microstructures.

So, we talked about two classes of quantitative ultrasound. The first is the spectral based type of technique. We talked about the backscatter coefficient. And then the second is the envelope statistics type technique. And we'll just review what was discussed in that lecture.

So, let's start with the backscatter coefficient. What we have is our transducer here sending the ultrasound beam into a scattering region that is within the focal zone of the transducer. And then we get echoes back. Now the backscatter corresponds to the scatter that is being directly sent back to the transducer. If we assume that we have a random distribution of scatters, plane wave approximation at the focus, and multiple scattering is negligible, then we can get a backscatter coefficient equation like this now backscatter coefficient is a function of the number of scatterers and the backscatter intensity as you can see here if we increase the number of scatterers in a tissue then there will be an increase in the backscatter coefficient if you increase the size of the scatterers then that leads to an increase in the backscatter intensity because larger scatterers you know they would backscatter and more ultrasound and that leads to an increase in the backscatter coefficient now as you can see in this expression that backscatter coefficient is frequency dependent and to be able to have one value to assess the tissue, then what's being done is to integrate the backscatter coefficient over the transducer bandwidth.

45 Recap of week 9

Backscatter coefficient

Assumptions

- Random distribution of weak scatterers
- Multiple scattering is negligible
- Plane wave approximation at focus

Reference phantom method

Transducer

Scatterers

Focal region

Distance from scatterer to observation point

of scatterers

Backscatter intensity

Incident intensity

Ultrasound frequency

Scattering volume

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

Increase n

→ increase BSC

Increase scatterer size

→ increase backscatter intensity

→ increase BSC

Insana, M. F., et al. / J. Acoust. Soc. Am. 87:179-192, 1990

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So, what we get is this integrated backscatter coefficient parameter right here.

$$IBSC = \int_{f_{min}}^{f_{max}} \frac{BSC(f)}{f_{max} - f_{min}} df$$

And what I showed is an example where you can use the integrated backscatter coefficient was used to monitor the response to chemotherapy in breast cancer patients who received over five doses, over the course of five doses. So here, malignant breast tumors were looked at and the image, they imaged at a seven-megahertz frequency. In these images, you can see the backscatter coefficient that is in the color map here overlaid onto the grayscale B-mode images. And as you would have observed in the responding patients right here, so responding patients means those who were able to respond well to the chemotherapy. You can see that as you increase the number of doses, the IBC of those tumors appear more red. So that means that there's an increase in the integrated backscatter coefficient. In contrast, if you look at the patients that were not responding to the treatment, so the tumors were not responding to the treatment, then you can see that there's a slight decrease in the integrated backscatter coefficient, or there's no change in the integrated backscatter coefficient. So, this is one example of how this type of parameter can be used to determine whether there are any changes in the tissues based on a type of therapy.

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Clinical application

- Monitoring breast cancer response to neoadjuvant chemotherapy (NAC) over the course of 5 doses
- 24 malignant breast tumors diagnosed in 16 patients
- Transmit frequency of 7 MHz (-6 dB bandwidth: 4–9 MHz)
- Responders had increase in IBSC
- Non-responders had decrease or no change in IBSC

Piotrkowska-Wróblewska H, et al. (2019). PLoS ONE 14(3): e0213749. <https://doi.org/10.1371/journal.pone.0213749>. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

23:14 / 33:25

The second class of quantitative ultrasound techniques that we looked at is called envelope statistics. And here I'm just showing an example of what the workflow would be like, where you're interrogating a tissue at a particular region of interest right here. within the focal zone of your transducer. And then you receive the signal. And what is being done in envelope statistics is that you would compute the envelope of this A mode signal, your RF signal.

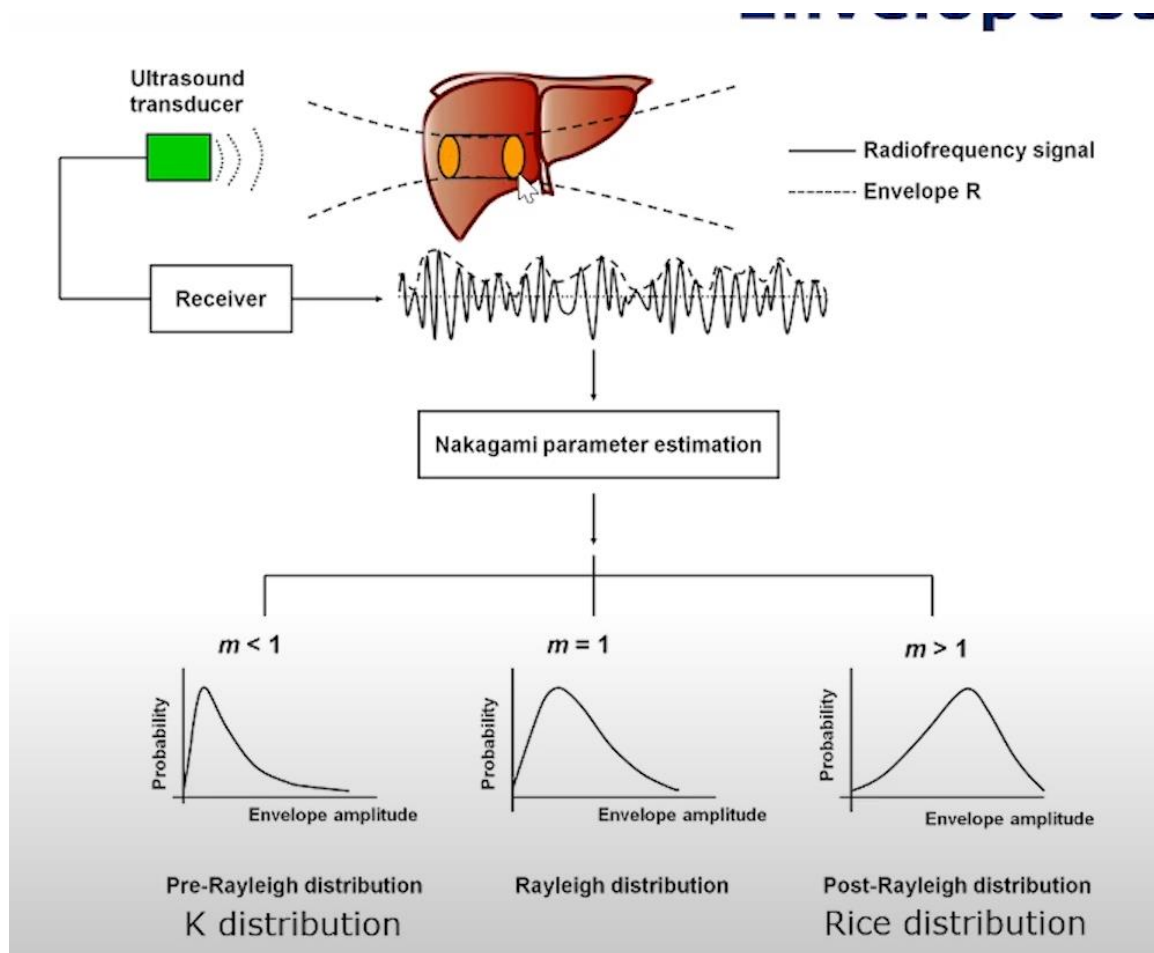
And based on the probability distribution function of the envelopes, you can extract some parameters that are modeled out of different statistical distributions. So, what we had discussed are these five statistical models. The Rayleigh distribution is one that corresponds to a fully developed speckle, meaning that you have a large number of randomly distributed scatterers. So, there's no coherent signal component here. And what it measures is basically a fully developed speckle with an SNR of 1.91. So, this is the simplest form. Now if you have a coherent component added to that Rayleigh distribution, a coherent component can be caused by periodic distribution of scatterers within the tissue. So, the scatterers would be placed less than a wavelength apart. And in this case, in the coherent signals, the phase would matter. And so, adding a coherent signal would result in an echo amplitude distribution that will model a Rician distribution. So, this Rician distribution models tissues that have a periodic distribution, spatial distribution of scatterers, as well as some random spatial distribution of scatterers.

Now, the K distribution, if you have clusters of scatterers within a tissue, then the K distribution has a clustering parameter that will incorporate that into the statistical model.

And so, these three, Rician, Rayleigh, and K-distribution model different scenarios of the spatial distribution of scatterers as well as the number of scatterers where the K-distribution looks into, you know, modeling that the number of scatterers per resolution cell is very, very small. Whereas Rayleigh distribution, the number of scatterers is very large. So, these three distributions model different types based on the scattering distribution, spatial distribution, as well as the number of scatterers. Now the final two, Homodyne-K distribution and the Nakagami distribution, they look into generalizing all of these, putting all the distributions together by tweak of one of their parameters.

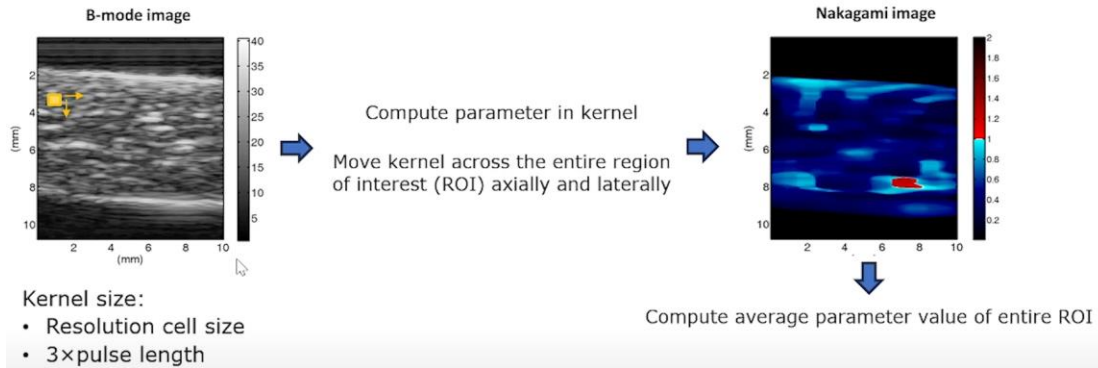
So, the homodyned K distribution and Nakagami are quite versatile. However, from homodyned K, there is no closed form expression for it. So typically, it's expressed in an integral form. And that can be quite computationally expensive and complicated to implement. But there have been researchers who have developed methods to be able to map homodyned K distribution parameters.

The last one was Nakagami distribution. And what is being shown on the left schematic here is just an example implementation of that. So, the Nakagami distribution parameter, m , is being displayed here. where if m equals 1, then you get a probability distribution function of the envelope amplitude that is similar to a Rayleigh distribution. Now if m is less than 1, then the probability distribution function becomes a pre-Rayleigh or a K-distribution. And if m is greater than 1, then the probability distribution function approaches that of a Rice, Rician distribution right here.



So, what these Nakagami distributions can do is basically, depending on the m parameter, it can model these previous three statistical distributions right here. And to be able to estimate a value that corresponds to the tissue structure, one usually creates a parametric image. So, each distribution has several parameters that can model the spatial distribution of the scatterers as well as the number of scatterers. So, here's just an example for a Nakagami image where you first start with a B-mode image and select a kernel of a particular size. Typically, that kernel is now in the order of three pulse lengths and that kernel, the data within that kernel is being used to compute the parameter. After computing the parameter, it then gets registered into a pixel in a Nakagami image.

And so that kernel is then moved at a different lateral and a different axial location. And so, at each spatial location, another Nakagami parameter is being estimated. And that value gets registered into a pixel in the Nakagami image. So, this is what a complete Nakagami image looks like.



And this is based off the m parameter. Now, one can also compute the average parameter value of the entire region of interest and report that. So that is also being done in the literature. And we also discussed one clinical application here, we were looking into the statistics, Nakagami statistics of human liver tissues. And in this study, what was done is that the sonographer would place a transducer right above the abdomen to image deliver. And then the B-mode image would be displayed, and different kernels would be moved across the region of interest, axillary and laterally, to be able to image this Nakagami parameter right here.

And on the right, we showed the envelope distributions. where the green bars correspond to the actual distribution values of the envelope amplitudes and the yellow curve that you can see here corresponds to the fitting of a certain model. So, in this case, the Rayleigh distribution tried to fit onto the probability distribution function. And on this study, what was being done, they were changing the frequency of the transmit frequency of the transducer here from 2 to 3.5 megahertz. And they wanted to assess how the Nakagami parameter changes as a function of frequency.

And what is being shown based on this envelope distributions right here, you see that as you increase the frequency of the transducer, then the distribution of the echo amplitudes deviates away from the Rayleigh distribution. So more on the pre-Rayleigh distribution. And so, one can also use this type of Nakagami images to compare between different tissues or compare between diseased and normal cases of the tissue as well as monitoring therapeutic response. So, this week we talked about Doppler effect, continuous Doppler, pulsed Doppler, color flow, power Doppler. So, these different Doppler modes are used to assess the blood flow velocities in a tissue and as well as map the vasculature of a tissue.

We also talked about quantitative ultrasound, two classes of quantitative ultrasound, such as the backscatter coefficient, which is a spectral-based technique, and envelope statistics, which are used to assess the spatial distribution of scatterers as well as the number of scatterers. So, these quantitative ultrasound techniques are being investigated for various

clinical applications. more progress is being made towards this field. So, hope you enjoyed these topics that we discussed this week and look forward to seeing you next week.

Thank you.