Biomedical Ultrasound: Fundamentals of Imaging and Micromachined Transducers

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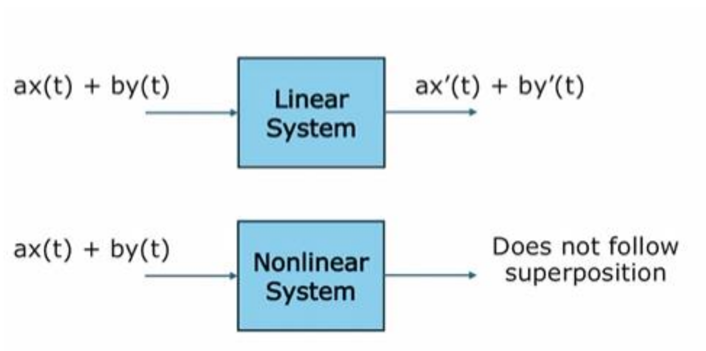
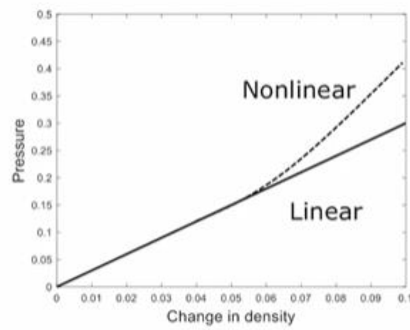
Lecture: 39

Nonlinear acoustics and imaging

Hello and welcome to the lecture on nonlinear acoustics and imaging. Let us discuss linear versus nonlinear systems. So linearity is a property of a system or a medium in which waves are propagating, for example, in which the principle of superposition is satisfied. So for a nonlinear medium, the shape and amplitude of a signal at a location is not proportional to that at the input. So here is a schematic of a linear system. Let's assume that if this system has the input as x(t), the output is x'(t), and if the input is y(t), the output is y'(t). In that case, if I sum the scaled versions of the input, the output will also be a scaled version. Now this property is not satisfied by a nonlinear system. So now nonlinear systems are more challenging to analyze.



You may be familiar that linear systems can be analyzed using principles such as convolution, especially when they are time invariant or shift invariant, but that property does not apply for nonlinear systems. So now what is a nonlinear medium? A medium can behave as linear or non-linear based on the applied acoustic pressure. Here we are talking in terms of acoustics. Now here is a plot where we are showing the change in density in the medium as a function of pressure. And what you see the figure here, beyond a certain threshold the curve becomes non-linear.



Nonlinear characteristics of water

- The change in density deviates from the linear behavior beyond a certain pressure threshold

So this is not surprising because almost all systems behave non-linearly beyond certain inputs. So if the input increases beyond a certain threshold, typically the system starts behaving non-linearly. You may have bought cheap speakers which sound pretty good at low volumes, but when you increase the volume, you start getting the distortion, which is the non-linearity. So similarly here, at low pressures, we see this linear behavior, but beyond it, we start seeing non-linearity.

So now what is a non-linear medium? We define a parameter called β or the coefficient of nonlinearity which denotes the strength of nonlinearity in the medium, and a measure of how nonlinear the medium is.

Now how do we get this β? So if we consider the equation of state, in the previous lectures you have heard Prof. Karla Mercado-Shekhar talk about the equation of state in the context of the derivation of the wave equation. So you will recall that the equation of state relates the changes in density in response to changes in pressure. So as the wave propagates, there are changes in pressure. How does the density of the medium change in response to those changes in pressure? Now, if you take this equation of state and you write it as a power series, where the first term is going to be the linear term, then you will have the second order term, third order term, higher order terms, then these constants A and B are the coefficients of the linear or the first order term and the second order term, which is the harmonic term. Now we can ignore higher order terms for now and if we take a ratio of these and we add this constant 1 to it, then we define a new parameter β which actually incorporates both B and A.

Nonlinear medium

- The parameter β (coefficient of nonlinearity) denotes strength of nonlinearity
- Power series expansion of "equation of state" – how density of changes in response to pressure changes – A and B are coefficients of the linear and second order terms

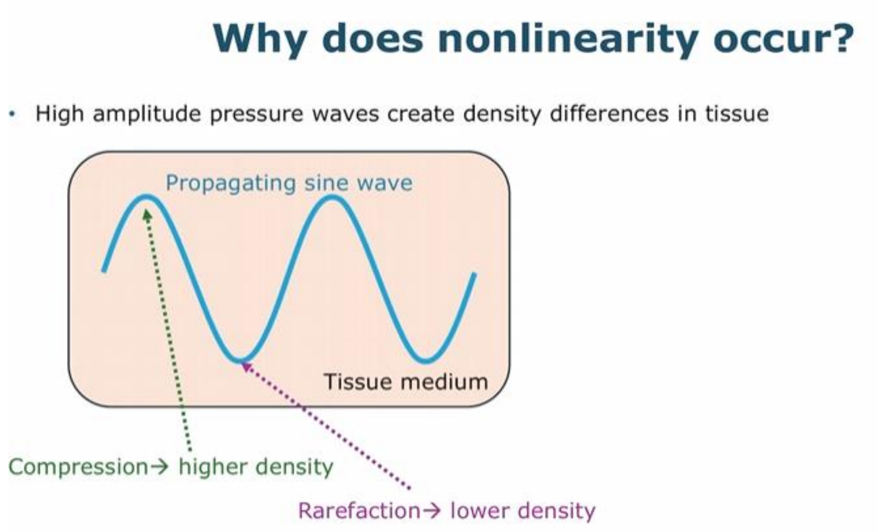
$$\beta = 1 + \frac{B}{2A}$$

Higher the nonlinearity in the medium, the higher will be the harmonic component relative to the linear component. So this is a metric of how nonlinear the medium is going to be. Now here are the β values for some different media which are relevant to us. For example fat, liver, heart, blood, breast tissue. And what you see here is that the β value is very high for fat. So we can expect fat to demonstrate higher non-linearity. Now it is not quite as simple as that. We will discuss later through a parameter called Goldberg number. Because there is another parameter or the attenuation. which is also important.

- β depends on pressure, density, and speed of sound in medium

Type of Medium	β value
Water	3.7
Liver	3.8
Heart	3.9
Blood	4.0
Breast	6
Fat	6.5

Nonetheless, let's proceed. So, first of all, why does this nonlinearity occur? What is the source of this nonlinearity coming from the medium? Wouldn't it be nice if we were just to send the wave and it came out as a scaled version of the input? Well, it turns out that typically in linear acoustics, we assume that the perturbation caused by the wave propagation in the medium is really small so that the medium properties are not really changing much. Any changes in density, for example, can be ignored. However, when we have high amplitude waves or even finite amplitude waves, what you can expect is that there will be density differences in tissue as the wave propagates. Because we have this compression phase and then we have a rarefaction phase.



So here is an example where you have the compression phase where the wave is actually going to compress the medium. And we have the rarefaction phase following it. So when the medium is compressed, the density increases and when the medium is rarefied, the density decreases. So now if you recall, typically we say that the longitudinal speed of sound, can be defined as:

$$c = \sqrt{\frac{B}{\rho}}$$

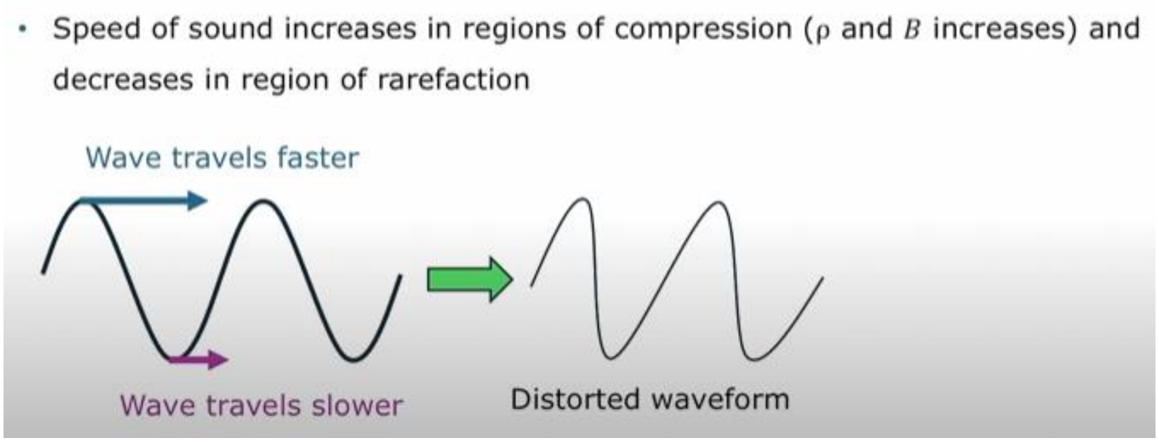
Where, B is the bulk modulus and ρ is the density.

But it turns out, if you have this medium that is changing, then both the bulk modulus and density will become variable. They won't stay constant. So here is an approximation of the speed of sound for such a medium.

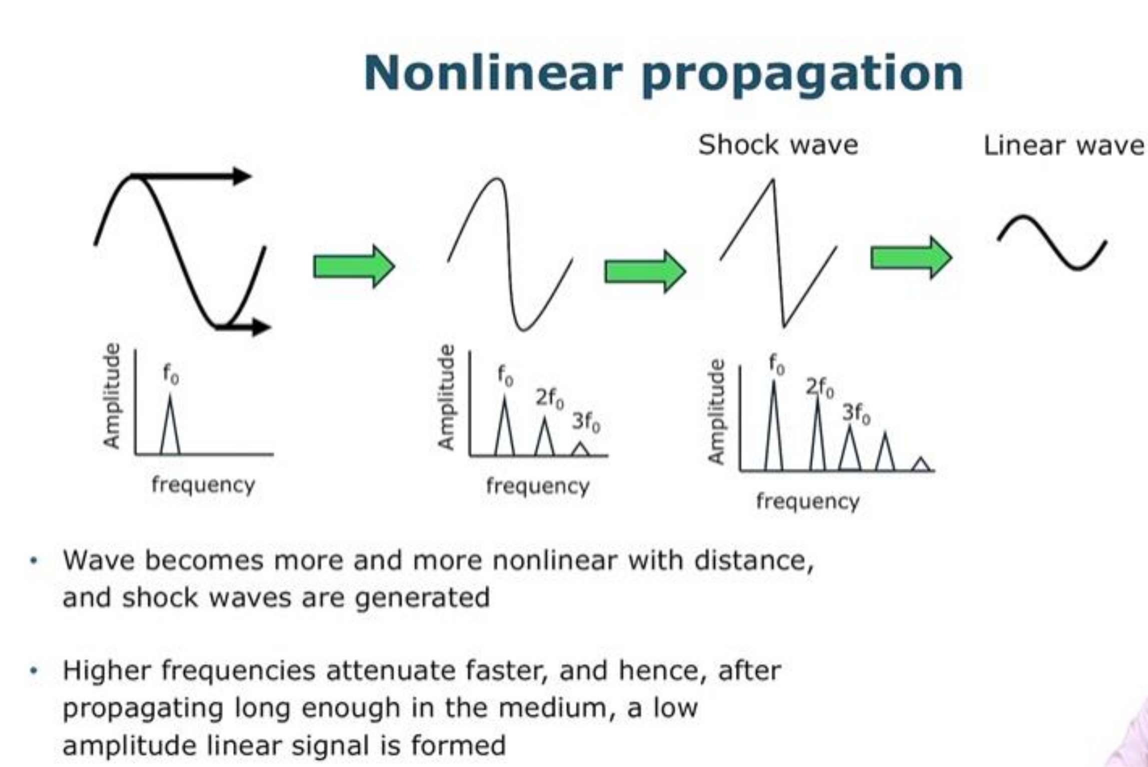
$$\frac{dz}{dt} = c_o + \beta u$$

c_o = speed of sound
u = particle velocity

The speed of sound doesn't remain constant, but it becomes a function of the particle velocity. So the velocity with which the particles in the medium are actually oscillating, that affects the overall speed of sound at that point. So now what this will do is, in regions where the density is higher, you will get increased speed of sound and in regions where it is lower or in rarefaction regions you will have a decreased speed of sound.



On the waveform above, the vectors denote the speed of sound, a shorter vector means lower speed of sound, and the longer vector denotes a higher speed of sound. So what do you expect? Because of this, the compression phase of the wave will actually start gaining over the rarefaction part of the wave. It will start moving forward and the rarefaction part will start getting left behind. So you start getting this distorted waveform.

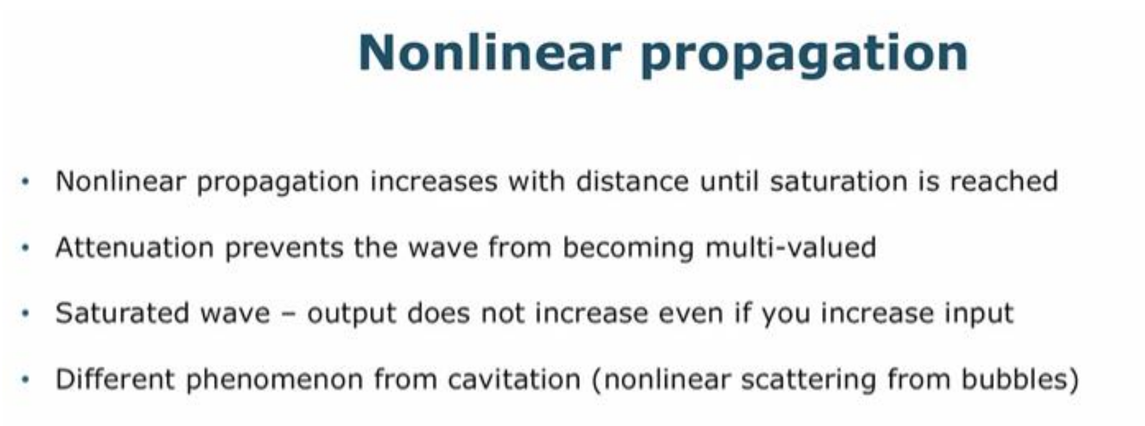


Now, in the extreme case, as the waveform starts getting distorted, you reach this waveform, which is called a shock wave. Shock, because there is a sudden change. You can see there is a very sharp transition. Typically, when we say a shock wave, that is what we mean, that there is a very drastic transition in the pressures.

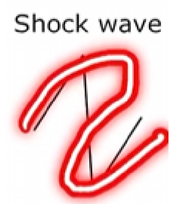
Now, as the wave starts getting distorted, let's look at the spectrum of the wave. What do you expect to happen? Initially, this is like a short sine burst, so the spectrum will be centered around a single frequency, f_0. But as the wave starts getting distorted, harmonics are getting added. So here are some harmonics, f_0, $2f_0$, $3f_0$. When it becomes a shock wave, a large number of harmonics will get added.

Theoretically, to get a shock wave, you would need infinite number of harmonics so that you will be able to create this kind of a shock wave. Now what happens after this wave propagates a very long distance? So these higher harmonics will start getting attenuated because we know that attenuation is proportional to frequency. So, like I said, the shock wave will become more and more non-linear with distance because as we move further, the wave starts getting more and more distorted. However, these higher frequencies now start attenuating very fast. So because of that, after a while, even if you provide more input, you are not going to get more output. And then the higher frequencies start attenuating. So if you move further and further, eventually all the higher frequency components die out and you get back a wave which loses its harmonic components.

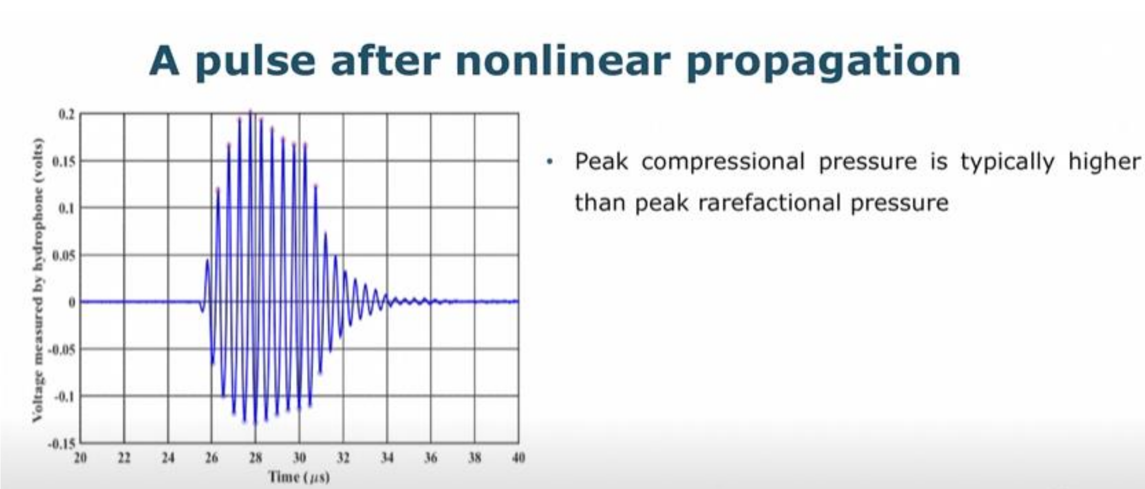
Now let's talk about this nonlinear propagation. Nonlinear propagation happens because the nonlinearity builds as the wave propagates further through the medium. So nonlinear propagation increases with distance till saturation is reached.



But once you have the saturation, the output is not going to increase even if you increase the input. Because any increase in energy that you are giving, the higher frequencies that are generated because of the nonlinear wave, or rather the distorted wave, will be very quickly absorbed. So that is what prevents the wave from becoming multivalued. Like for example, you may be wondering, what is preventing the wave from becoming like this?



If that was the case, the wave would become multivalued. At a given time instant, there would be multiple values. That doesn't happen because beyond the shock wave formation, you cannot have higher frequency generation because those higher frequencies are very rapidly attenuated. So moving on, I just want to make one more point that this nonlinear propagation is a different phenomena qualitatively and quantitatively from nonlinear scattering of bubbles that we have studied in cavitation. So both are nonlinear effects, but cavitation is different from nonlinear propagation as we will see more. So here is an example of some data we captured in our lab. This is a pulse, relatively short pulse. This pulse has propagated a certain distance.



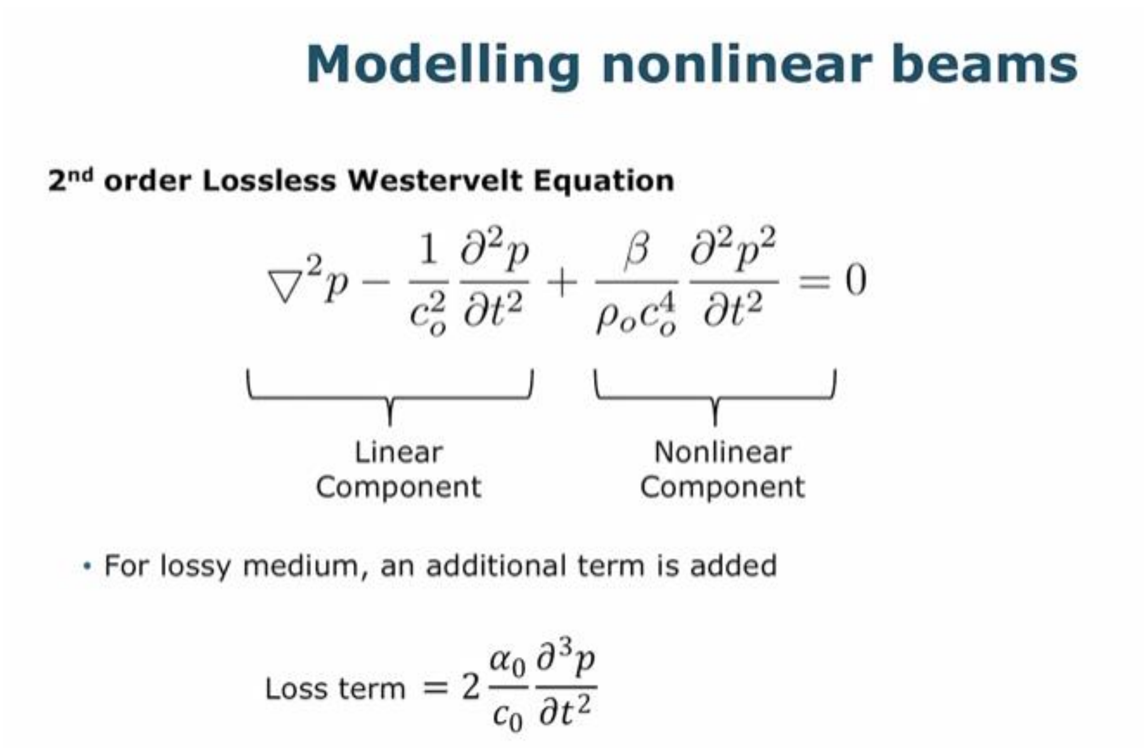
And now initially this pulse was shaped like a sine wave. But now you see, if I look at the peak positive or the peak compressional pressure, then you will see that this is 0.2 units. But if you look at the rarefactional phase, it is not even 0.15. So as you can see, there is asymmetry in the wave. The peak compressional pressure or peak compressional amplitude is more than the peak rare fractional amplitude. And this is somewhat characteristic of nonlinear propagation.

Now, in diagnostic ultrasound, you don't get very extreme nonlinear propagation, shock waves, etc. But when it comes to therapeutic ultrasound, you get shock waves and there are applications such as histotripsy, lithotripsy, where you get shock waves. But this is a moderately nonlinear wave and this is more relevant to diagnostic ultrasound.

Now how do we analyze this nonlinearity? We can do modelling to do it. There are several models so that we can figure out what these beams do. So one model is called the second order Westervelt equation. Here we are talking about the lossless Westervelt equation.

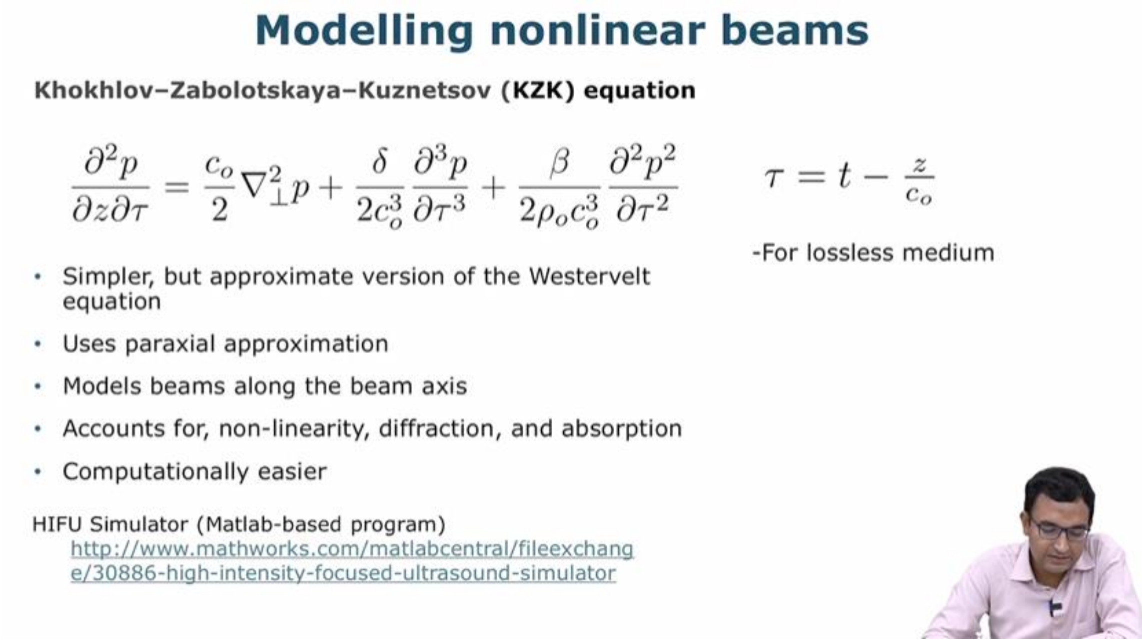
Here, p is the instantaneous pressure. c_o comes from the equation we have previously written,

$$\frac{dz}{dt} = c_0 + \beta u$$



And ρ_0 is the equilibrium density because the density is changing. You are getting compressions, you are getting rarefactions, but the mean density is going to be ρ_0. So this can be modified if you have an additional term related to viscous absorption. The α_0 term relates to the absorption or the attenuation coefficient.

Like I had said, typically absorption is the primary part of the attenuation. Therefore, sometimes it's harder to measure absorption and easier to measure attenuation. Sometimes we go with the attenuation coefficient and we call it absorption coefficient because they're approximately similar. Now this Westervelt equation is harder to solve, computationally more intensive. So there is a simplification which uses an approximation and this equation is called the Khokhlov-Zabolotskaya-Kuznetsov or the KZK equation.



It was formulated by a group of Soviet scientists. And this equation is simpler to solve and it accounts for non-linearity, diffraction and absorption. It largely is accurate along the axis of the beam, assumes a circular transducer. It's not very accurate beyond the axis. And there is a package called HIFU simulator, HIFU standing for high-intensity focused ultrasound, which is a MATLAB-based program. You can download it. It's freely available, and you can use it to simulate these kind of nonlinear beams.

So now let's talk about Goldberg number, which I mentioned in the beginning of the lecture. So first let's define this parameter called normalized distance nonlinearity parameter or σ.

$$\sigma = \beta \varepsilon k z$$

z is the distance that you are traveling, ε is the acoustic Mach number. So you may have heard of Mach 1, Mach 2, Mach 3. So Mach relates to the speed relative to the speed of sound. So you may have heard of a fighter jet going at Mach 1 or Mach 2. So, here this Mach number relates to the speed of the particle relative to the wave speed.

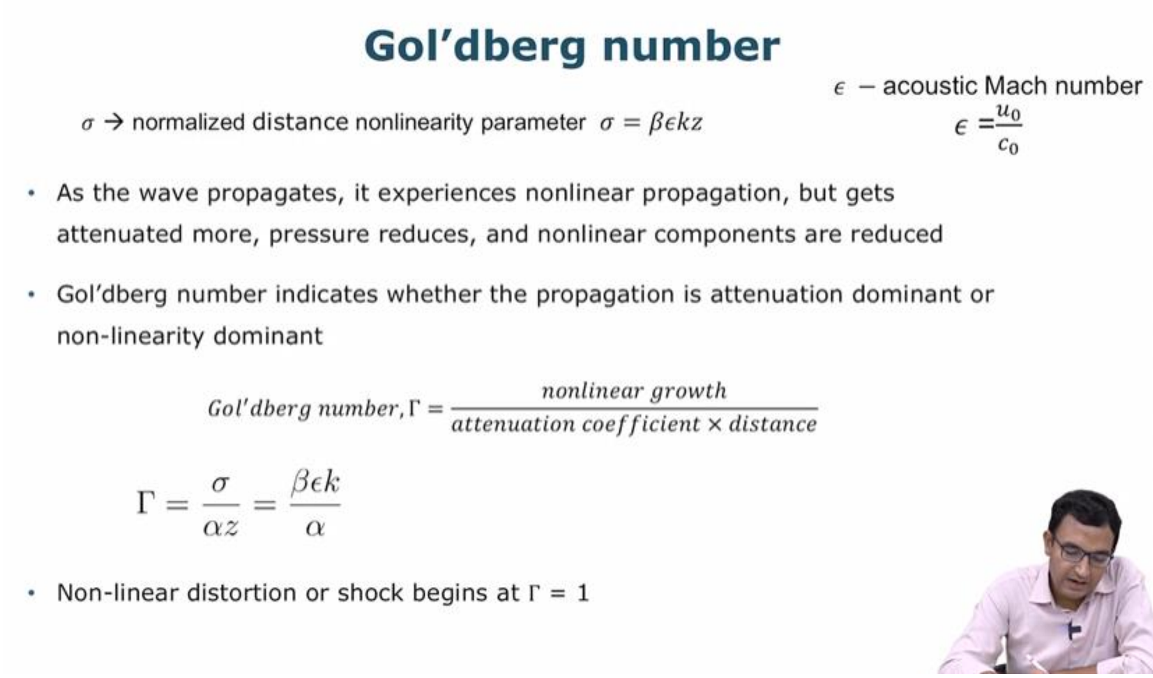
$$\varepsilon = \frac{u_0}{c_0}$$

And higher Mach number is going to lead to higher non-linearity.

So, β, as you saw in the previous slides,

$$\beta = 1 + B/2A$$

And, k is the wave number.



So as the wave propagates, it experiences nonlinear propagation but after a point it starts getting attenuated, the pressure reduces and since nonlinearity is proportional to the pressure then the wave will reach a stage which is called old age in which the harmonic components are mostly attenuated and the wave starts looking sinusoidal again. But there is another aspect to it. A medium may have a strong propensity to be non-linear as dictated by the non-linearity parameter, but the medium may also have very high attenuation. So these are two competing effects. The non-linearity metric is suggesting that a lot of harmonics will be generated but the attenuation is suggesting that they will also be attenuated rapidly. So these two competing parameters will decide how distorted a wave gets. If you have, say, moderate non-linearity but very high attenuation, the wave is not going to distort much because attenuation is going to very quickly dissipate the high harmonics.

So, to understand whether or not a medium will show significant nonlinearity. A parameter called Goldberg's number was created

$$Gol'dberg\ number, \Gamma = \frac{nonlinearity\ growth\ term}{attenuation\ coefficient\ *distance}$$

$$\Gamma = \frac{\sigma}{\alpha z} = \frac{\beta \varepsilon k}{\alpha}$$

When this Goldberg number becomes 1 then you start getting shock or nonlinear distortion. So here are some Goldberg numbers of certain tissues in the body and these were tabulated at 5 MHz frequencies and for 5 MPa amplitude of the ultrasound wave.

- Nonlinearity is much easily generated in water

Type of Medium	Gol'dberg number
Breast	<14
Liver	<14
Muscle	<14
Blood	14
Water	266

So what you see here is for breast tissue, Goldberg number is less than 14, for liver, it is less than 14, blood it's about 14. But for water, it's 266. So this is very interesting because water is not a very attenuating medium. So even though the nonlinearity is not that high, because it is not an attenuating medium, effectively the amount of distortion that the wave sees is much more in water than compared to all these other tissues.

So now let's start thinking about the properties of these non-linear beams. So if a wave distorts, what kind of an ultrasound beam results and how we can exploit it for our benefit. So, it turns out that if you look at the beam, you can decompose the beam into the fundamental frequency f_0 at which the transmission was made and you can also filter out f_0 and you will be left with the higher harmonics or let's say you could look at the second harmonic of the beam or the third harmonic. For these harmonic signals, it turns out the wavelength is less because of higher frequency, and the speed of sound remains the same. If you apply that, you will see that, if frequency doubles, lambda becomes half. And we also discussed that as you focus the beam, the lateral resolution is limited by the wavelength.

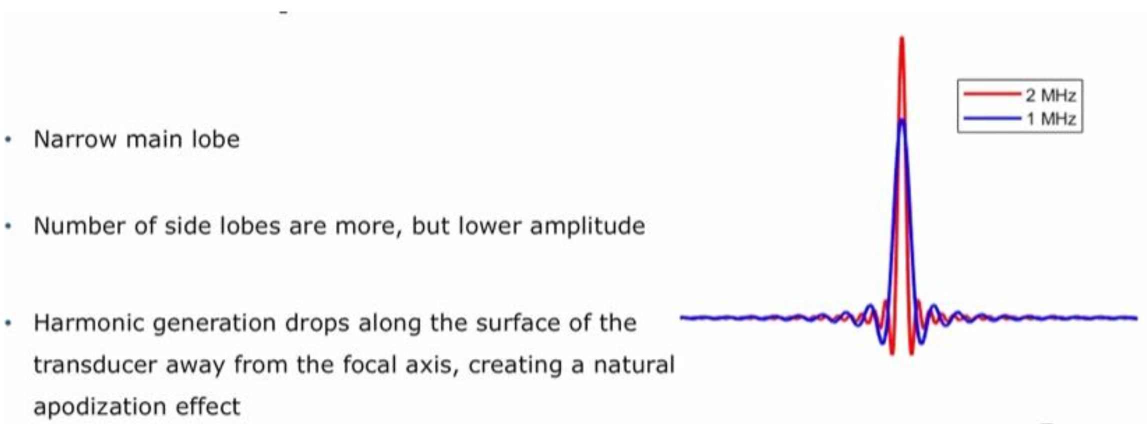
But now the wavelength itself is reducing, so the beam becomes narrower and narrower. As the beam becomes narrower, the main lobe width reduces. And because of which, if you do imaging, you can get better resolution. More on that later. But here's the formula for beam width. If you remember, this is a simplified formula, just after the Fresnel region.

$$Beamwidth = \frac{axial\ diatance * \lambda}{Aperture\ diameter}$$

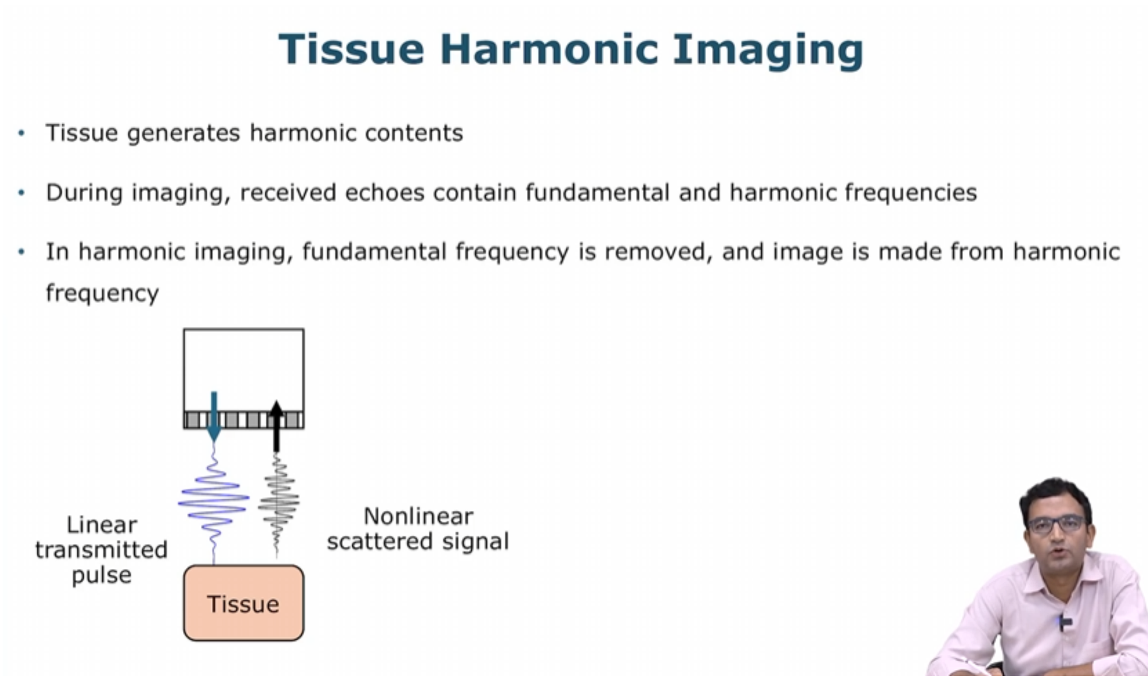
Properties of nonlinear beams

- For harmonic signals of higher frequencies ($\lambda \rightarrow \lambda/n$), beam width narrows
- An improvement in main lobe width by a factor of 1/n

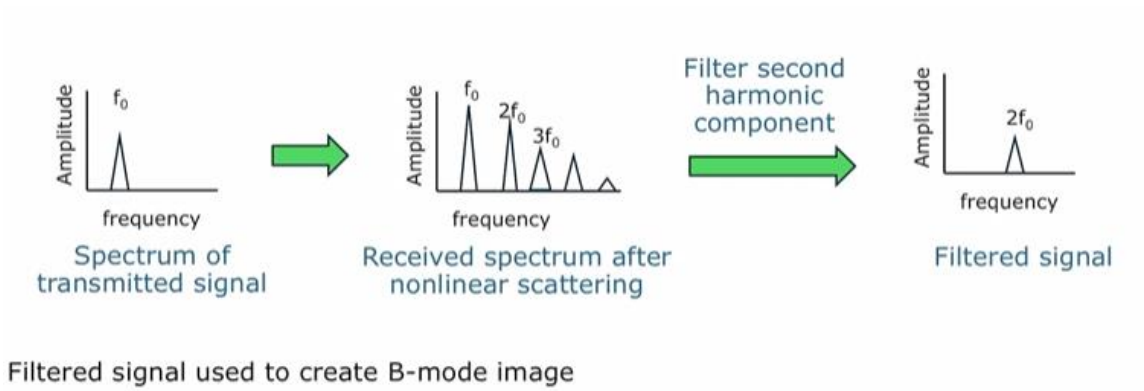
So reduced lambda is actually going to give you a narrower beam width. If you have a thinner beam or a narrower beam, you will get better lateral resolution. Now, if you have narrower beams, that means the main lobe of the beam is narrower. But as you know, if you have a finite size transducer, you are also going to generate some side lobes. So it turns out that as you go higher and higher in frequencies, the side lobes are more. but they are much lower in amplitude and also since these beams are pressure dependent, wherever you have high pressure, that is where these higher harmonics are generated. So the side lobes are weak in pressure and they don't really generate much signal. Therefore, these beams have relatively weak side lobe levels, which is great for imaging because it actually creates a natural apodization effect. We discussed earlier that in apodization we provide weights to the transducer array so that you have a smooth pattern of particle velocity variation along the surface of the transducer array. But here that is happening naturally because the side lobes are getting suppressed anyways.



So now how can we exploit it? There is something called tissue harmonic imaging which is used very frequently in cardiac and some deeper abdominal imaging. So tissue generates harmonic components and when you receive the echoes, as long as your transducer is sensitive to this harmonic component, let's assume the transducer bandwidth allows you to measure some harmonics as well along with the fundamental. So both the fundamental and the harmonic is being captured. Now we can do some processing and we can eliminate the fundamental frequencies so that only the harmonic frequency remains. So now the image that we can create with these harmonic frequencies is called harmonic image. For example, a second harmonic image.

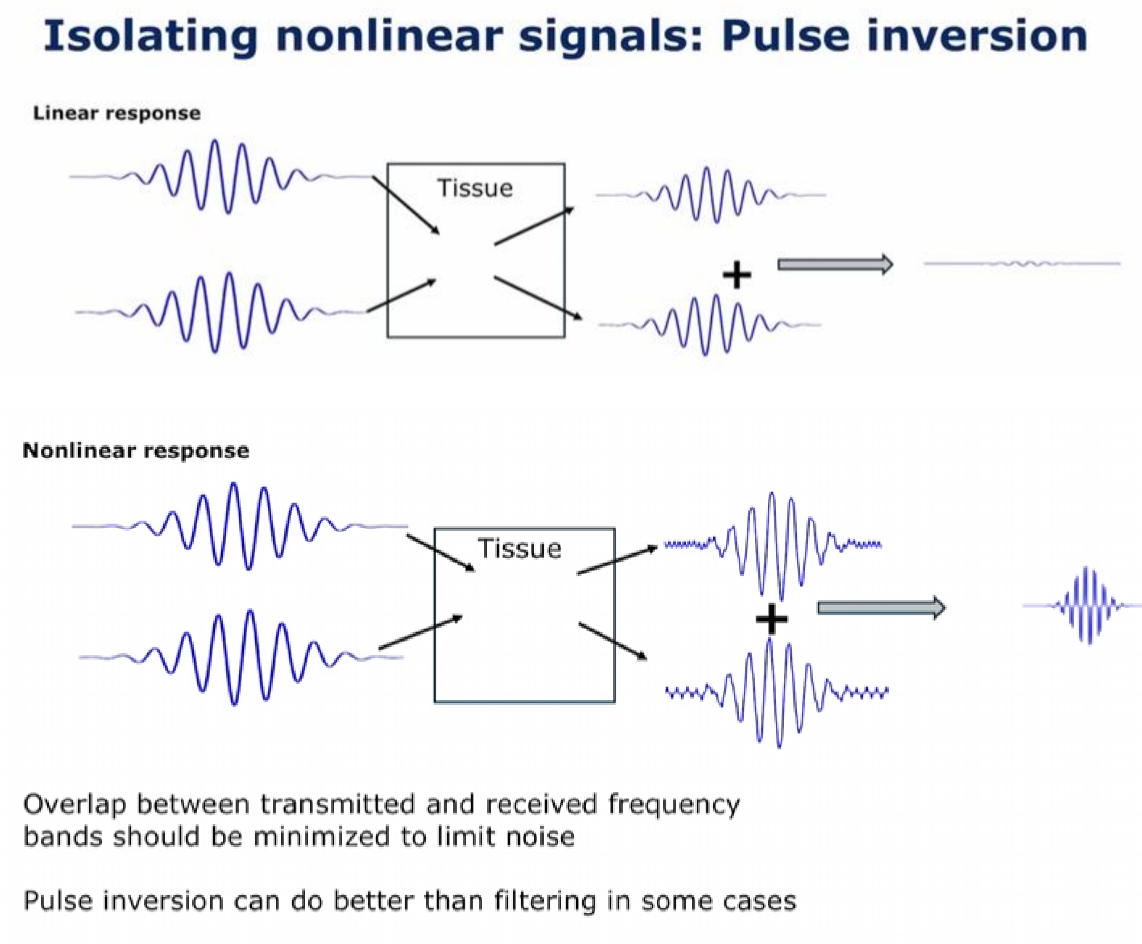


So what's the benefit? So it turns out that these images will have better lateral resolution because of higher frequency, and at the same time lower side lobe levels. Here, the process is shown schematically.



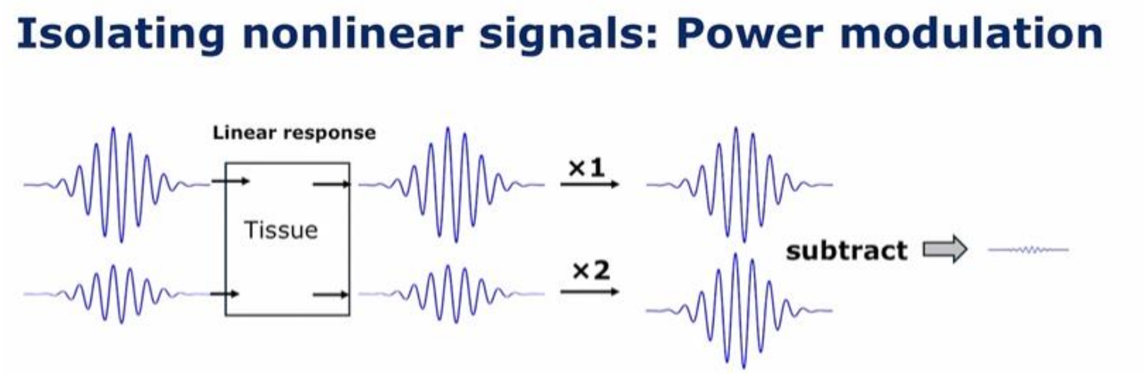
Initially you fire at a particular frequency. It's not going to be with a very high Q factor transducer so it has a range of frequencies. Now as the wave propagates in the medium, you start getting harmonics. Let us say of this harmonics, the strongest component is $2f_0$. So I am going to filter the $2f_0$ component and I am going to now have a harmonic beam and I am going to make an image out of this. So now how do I isolate this harmonic signal? One way is to use a filter, but there are other ways as well. Sometimes it's hard with filtering because you may need a very high order filter to separate these fundamental and harmonics because there may be some spectral overlap, because we use relatively broadband signals. And that is where the filtering will not do a great job.

So there are these methods which we have discussed in contrast enhanced imaging previously. One method of pulse inversion in which if you send two pulses in succession and then they propagate in tissue and after some time you sum these pulses, the only thing is these pulses were initially inverted in phase. So if you sum up the input, you get the answer as zero. But now, because of the principle of superposition, if you sum up the output, the answer is also going to be zero. So by doing this, we can eliminate any fundamental (linear) components and the non-linear components will remain which is shown in this schematic.

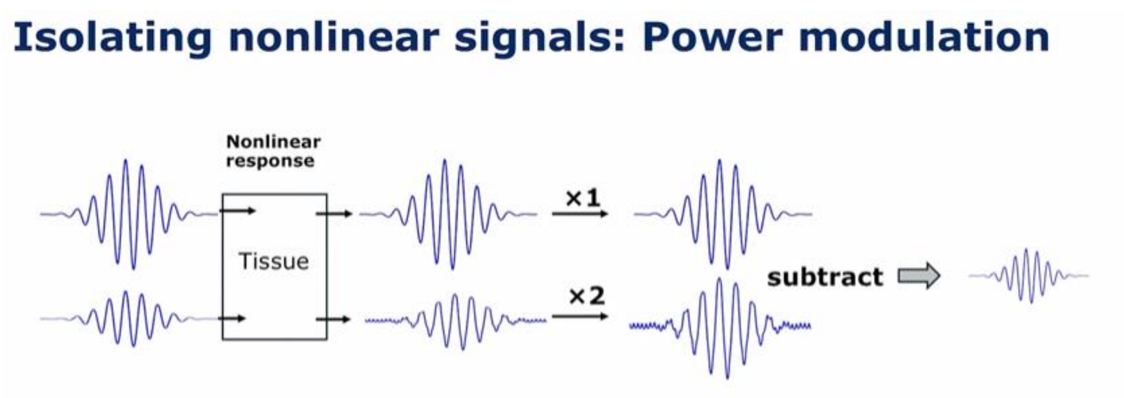


Like I said, there should be minimum overlap between the transmit and receive frequency to limit noise and to limit clutter. So in some cases, pulse inversion does better than filtering. When there is some overlap, then filters don't do a great job, but pulse inversion does a good job.

So now let's talk about power modulation in more detail. So here, if you have the input, that has a relationship that the amplitude of the first input is twice that of the second. So now if I scale the second waveform by a factor of two and subtract from the first waveform, I am going to get an answer of zero. Now, as this is a linear system, even in the output, this relationship will hold. And therefore, if I scale the second output by two and subtract from the first output, under linear systems, I am going to get almost zero output. Theoretically it will be zero, but practically because of some motion, etc., you are not going to get exact cancellation. So because of physiological motion, for example, some time is elapsed between the capturing of these pulses, and therefore there may not be exact cancellation, but more or less the signal is suppressed.

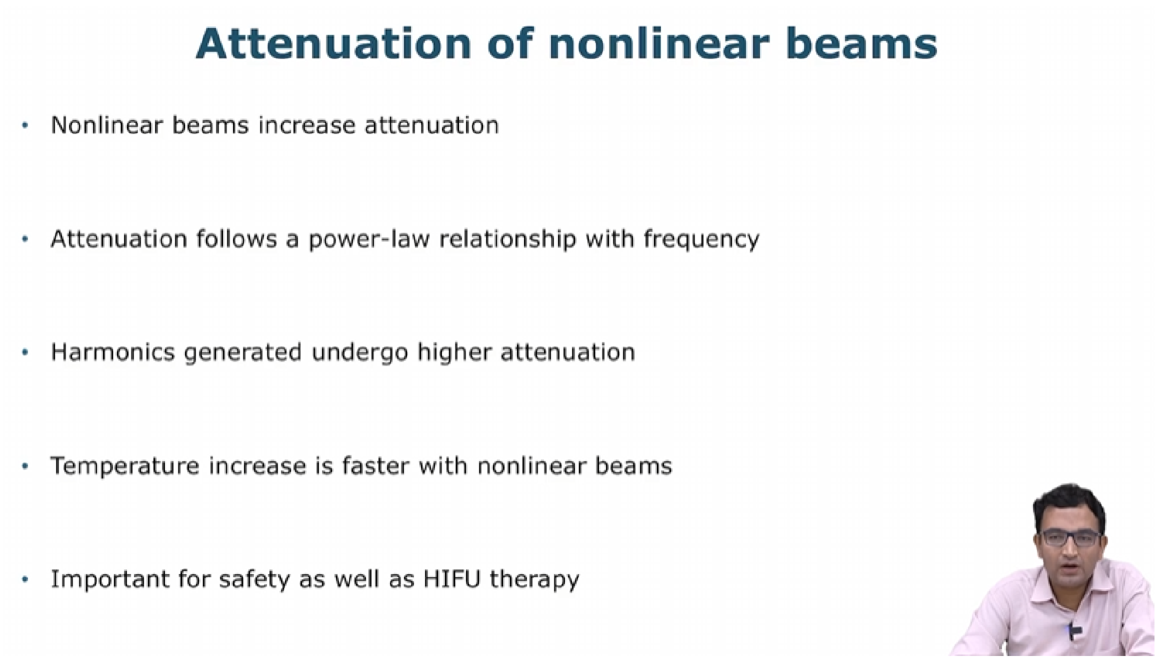


If you consider a non-linear medium, so tissue is a non-linear medium under this framework where we are dealing with finite amplitude waves. So now this scaling property is not going to work. So even after you scale the output by 2 and subtract, there will be a residual non-linear signal.



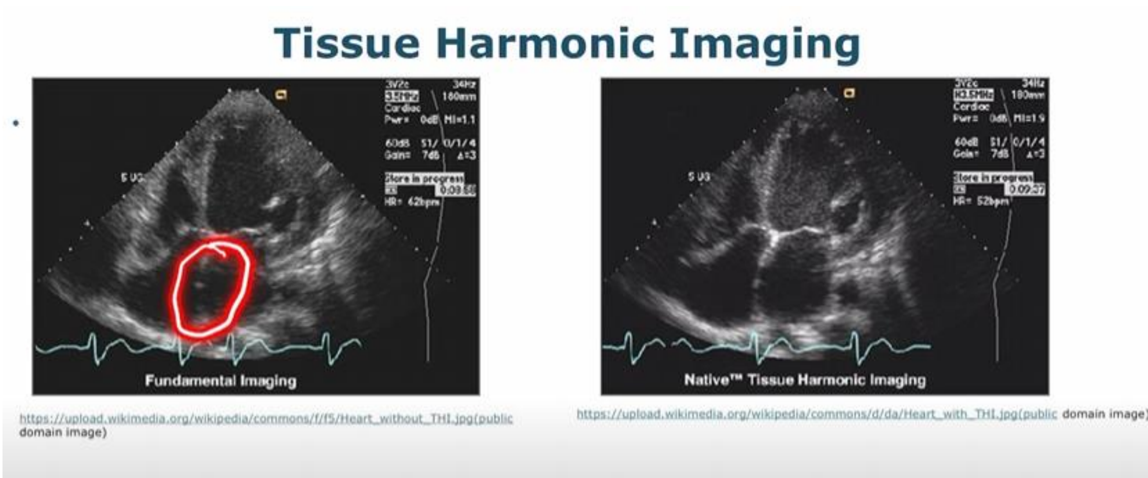
And this is essentially the harmonic signal that you are capturing. So these are clever methods of isolating the non-linear signal.

Now let us talk about attenuation of nonlinear beams. Like I mentioned, higher frequency is attenuated faster. Because if you remember, attenuation follows a power law relationship with frequency. So higher the frequency, higher the attenuation. And these harmonics will undergo higher attenuation. But what is the physical consequence? The physical consequence is, the absorption is higher now because of these higher frequency components, and that will lead to a temperature increase.



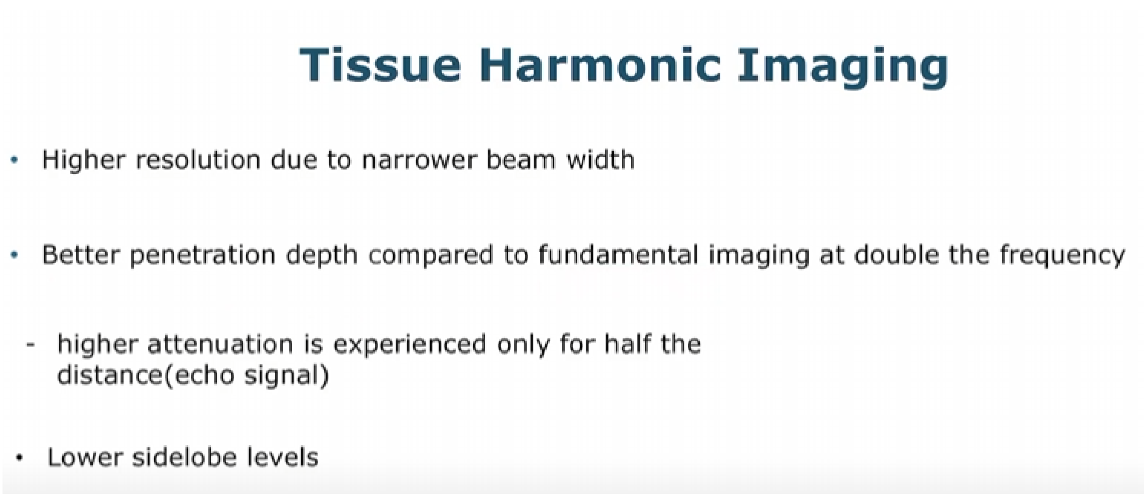
So when we are dealing with nonlinear beams, there can be high temperature increase. So this is important from the safety point of view, but also it is useful when we talk about high intensity focused ultrasound surgery, because these high frequency beams have a very high absorption and that leads to a very rapid temperature increase, which leads to the destruction of targeted tissue by thermal necrosis.

So here is an example of tissue harmonic imaging. If you see, there are some features here in this fundamental image which was taken at f_0 and it is more clearly visible in the harmonic image (on the right). The boundaries are better visible in the harmonic image as well. Some parts are invisible in the fundamental image, which are better visible and the image in general looks sharper in the harmonic image.

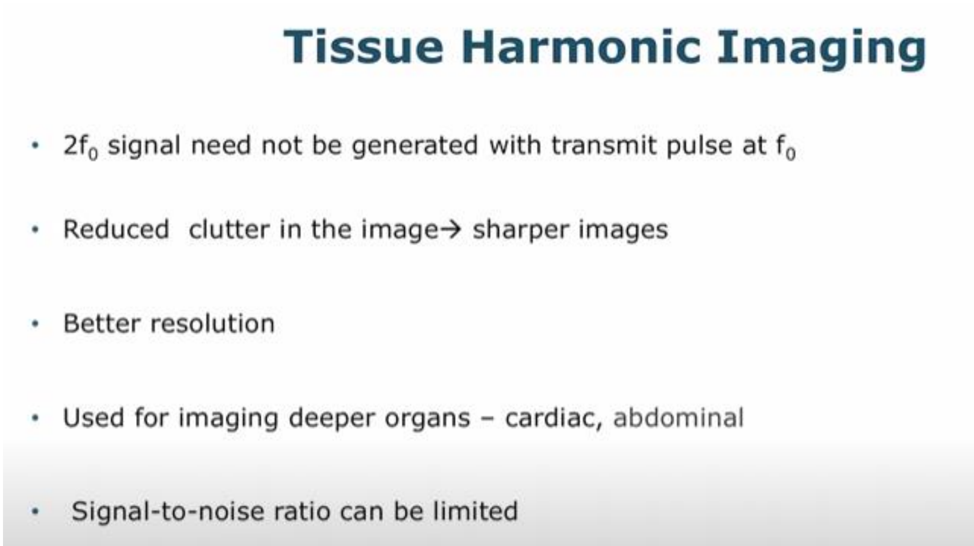


So in tissue harmonic imaging we get higher resolution due to a narrower beam width or the higher frequency that is generated. So a natural question might be why not just use a frequency in the first place, and why do we need to rely on this tissue harmonic imaging to generate frequencies which are higher. It turns out that tissue harmonic imaging has better penetration depth compared to fundamental imaging at double the frequency.

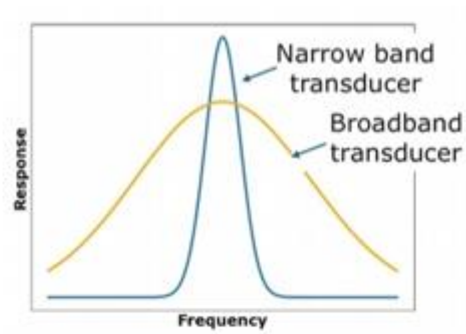
Imagine that a $2f_0$ beam was used to image, it will face higher attenuation in the transmit phase, as well as on the path back to the transducer. But if we transmit using $f_{0,}$ the non linearity is only being developed as it propagates, and it faces higher attenuation only o the path back, and hence there will be lower attenuation in harmonic imaging compared to if I simply use $2f_0$ frequencies. So higher attenuation is experienced only for half the distance for the echo signal. While going you don't experience that much attenuation because the non-linear signal is still being developed. It is growing as the distance increases. Also, like I said, you will have more side lobes with harmonic imaging, but lower side lobes because the side lobes are weak. And when we are imaging at higher frequencies, if it was just $2f_0$, it would have more but lower side lobes. But when we generate this $2f_0$ frequency with non-linearity or non-linear propagation, then because the side lobe pressure is very weak, you don't really generate very strong side lobes. So there's an additional advantage right there.

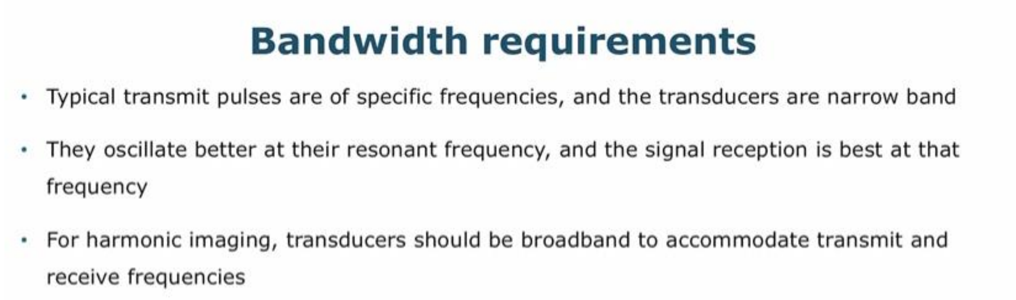


So like I said, we are getting this $2f_0$ signal. Now you may ask why $2f_0$, why not $3f_0$, $4f_0$? Well, it turns out there is some bandwidth limitations which we will discuss in a later slide. So $2f_0$ or harmonic imaging is the most popular. Now if you have lower side lobes, you are going to get reduced clutter, you will get sharper images, you will get better resolution because of narrower beams and you will get better contrast because of lower side lobe levels. So like I mentioned earlier, this is used for cardiac and abdominal and other deeper organs. The only challenge here is the harmonic signal typically is weaker than the fundamental signal; several dB down, relative to the fundamental signal. So the signal to noise ratio can be a challenge. But nowadays with sensitive electronics, we trade off the signal to noise ratio to get better contrast, better resolution and still improve imaging performance.

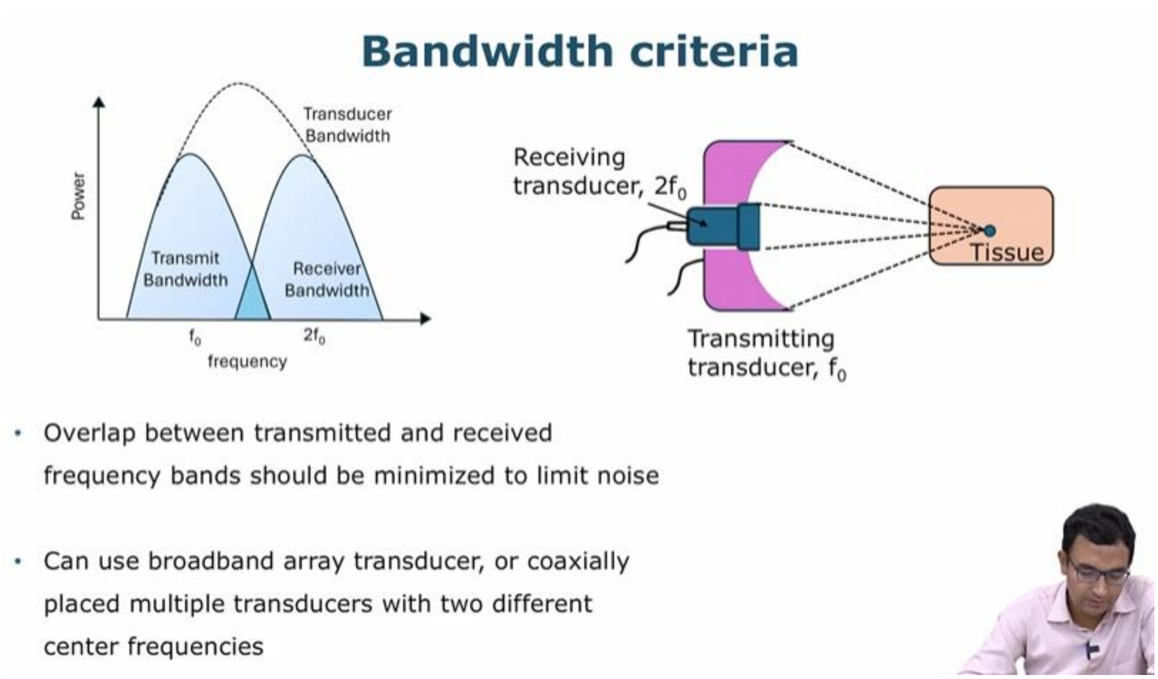


So now let's discuss what kind of transducers are needed for tissue harmonic imaging. You would need transducers that are sensitive to both the transmit frequency as well as receive frequency. So for example, if I am sending the signal at f_0 and now the receive signal is at $2f_0$, then my transducer has to be sensitive at f_0 as well as $2f_0$. So if it is a very narrow band transducer, such as the one shown here and it is centered at $f_{0,}$ then $2f_0$ will be beyond the bandwidth of this transducer. So it cannot be used. But if I have somewhat broadband transducer, I can fire at f_0 on the lower edge of the bandwidth, and then on the higher edge of the bandwidth, I can capture $2f_0$. So this is how there is a more stronger constraint in terms of bandwidth requirements when you are going to do tissue harmonic imaging.





So for harmonic imaging, transducers should be broadband to accommodate both the transmit and receive frequencies. In some cases, two different elements are used, one for transmit, one for receive. One is sensitive at f_0, which is used for transmit, and the other one is sensitive for $2f_0$, which is used for receive. So like I said in the previous slide, there is a more stringent bandwidth criteria. You have to have a transmit bandwidth which is contained in the transducer bandwidth as well as the receive bandwidth should also be contained in the transducer bandwidth. And there's some overlap here, which is inevitable, but that is usually taken care of by techniques such as pulse inversion or power modulation.



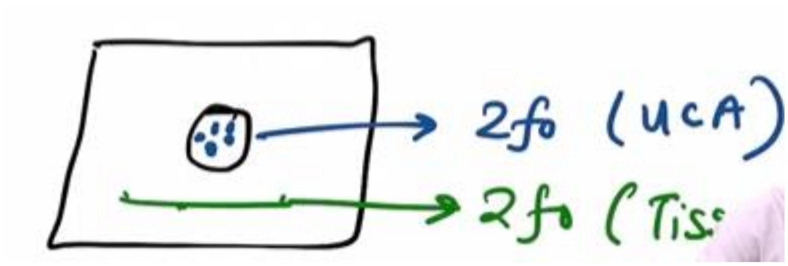
They are able to still separate the linear and nonlinear frequency components. So typically, we use a broadband array transducer or in some cases, researchers have reported coaxially placed multiple transducers where the one element serves for transmit and the other element serves for receiving the signal which is shown in the schematic above. So you are sending the signal with f_0 using this outer element and the inner element is receiving the signal at $2f_0$. So these crystals are designed to be sensitive to f_0 and $2f_0$ respectively.

Now, contrast agents have been discussed in a prior lecture. And so, like we have discussed, contrast agents exhibit significant nonlinear behavior due to a different mechanism because of their volumetric oscillations in which they oscillate nonlinearly. Here we are talking about the nonlinearity caused by nonlinear propagation.

Contrast-enhanced harmonic imaging

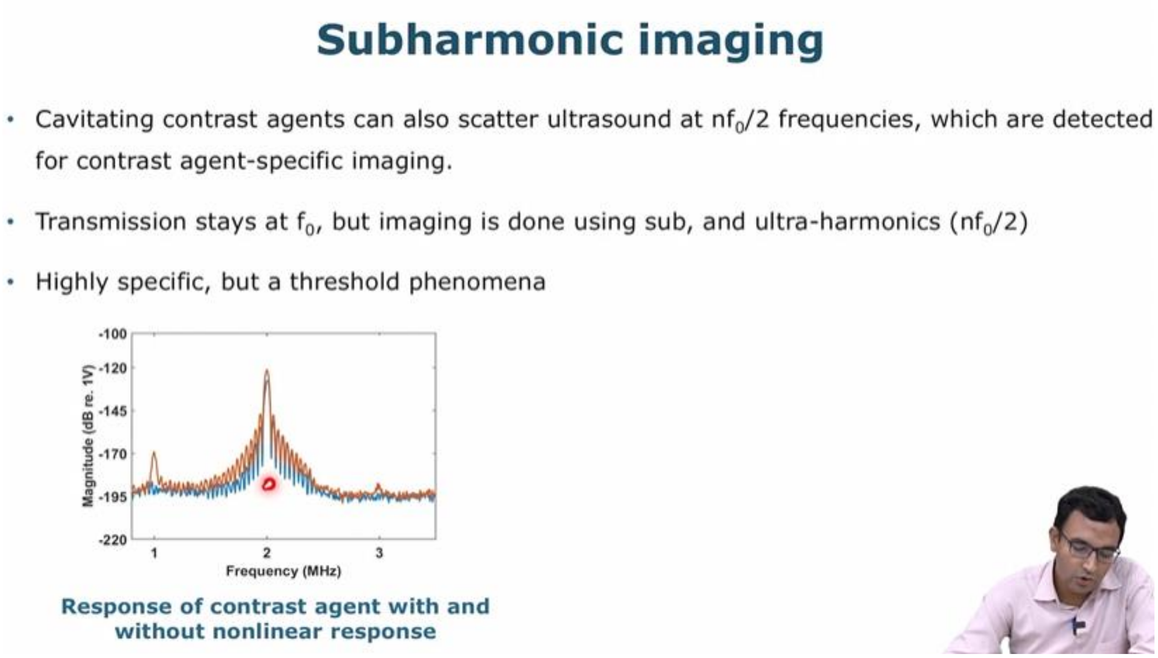
- Ultrasound contrast agents exhibit non-linear behavior
- Cavitating contrast agents scatter ultrasound at nf_0 frequencies, which are detected for contrast agent-specific imaging
- Imaging at $2f_0$ is called *second harmonic imaging*
- At higher pressures, second harmonic imaging can be confounded by tissue harmonics
- At lower pressures, second harmonic imaging improves contrast relative to fundamental imaging

So, cavitating contrast agents also scatter ultrasound at frequencies that are harmonics. and this is what is called stable cavitation and they are detected for contrast specific imaging. So there is a mode which is called second harmonic imaging in which $2f_0$ is used. But now consider if you have some tissue where there is some blood vessel and it has contrast agents.



The contrast agent will give you harmonic signal at $2f_0$. But you have a tissue which is also acting as a non-linear medium and it is also giving you signal at $2f_0$. So now the harmonic from the contrast agent will become confounded because of the harmonic from tissue.

So if I use higher pressures for imaging, I will get significant tissue harmonic because of which I will not be able to get good imaging performance in detecting these bubbles because the background signal will also be present. So in other ways, the $2f_0$ frequency is not going to be very specific to the bubbles. So at low pressures, when the tissue harmonic is weak and the bubble oscillations show moderate nonlinearity, you can still get an improvement with these bubbles. But at higher pressures, you are not going to get an improvement because of strong tissue harmonic generation. So researchers have looked at another mode called the subharmonic imaging in which you don't look at f_0 frequency or $2f_0$ frequency but $f_0/2$ frequency.



You preferentially isolate and visualize these subharmonic frequencies and it turns out that subharmonic signal is not generated in tissue harmonic imaging. Because in the mechanism through which tissue harmonics are generated, primarily harmonics are generated and not subharmonics. Therefore, if the transmission is done at f_0, but the image is created using either subharmonic at $f_0/2$ or $nf_0/2$, with higher order n's generating what you call as ultra harmonics. Then these frequencies are specific to bubbles. They are not generated significantly through non-linear propagation. So now you can still have your tissue with bubbles.

The bubbles are giving out sub harmonics or ultra harmonics and the tissue is not. So therefore you can very clearly separate the bubble region from the tissue region. So that is the benefit of subharmonic imaging. But the main challenge with subharmonic imaging is that it is a threshold phenomena. You have to exceed a certain pressure threshold. Only then you start getting these subharmonics. And sometimes when you are doing subharmonic imaging, there is also a chance of bubble disruption because of the higher pressures that are needed for subharmonic imaging.

So to conclude this lecture, let us just summarize what we have learned. We learned about sources of nonlinearity in ultrasound and cavitation being one and nonlinear propagation is the other. We also learned about the absorption of nonlinear beams, how the higher frequencies generated by these beams will be absorbed more. This can lead to temperature elevation. We discussed how nonlinear beams can improve the performance because of better resolution of these beams, also because of lower side lobes which leads to lower clutter and better contrast. We discussed the hardware and signal processing considerations, especially related to transducer bandwidth and how we can separate out these harmonic signals by suppressing the fundamental signal. And lastly, we contrasted how non-linear acoustics is different from contrast agents. So with this, I think we will conclude this lecture and I will see you in the next lecture. Thank you.