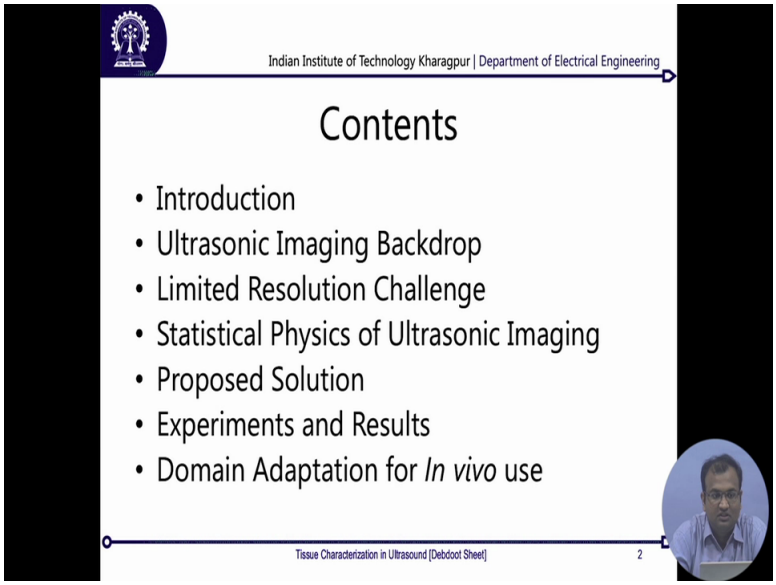
Introduction to Medical Imaging and Analysis Softwares
Professor Debdoot Sheet
Department of Electrical Engineering
Indian Institute of Technology Kharagpur
Module 4
Lecture No 19
Tissue Characterization in Ultrasound

(Refer Slide Time: 0:45)



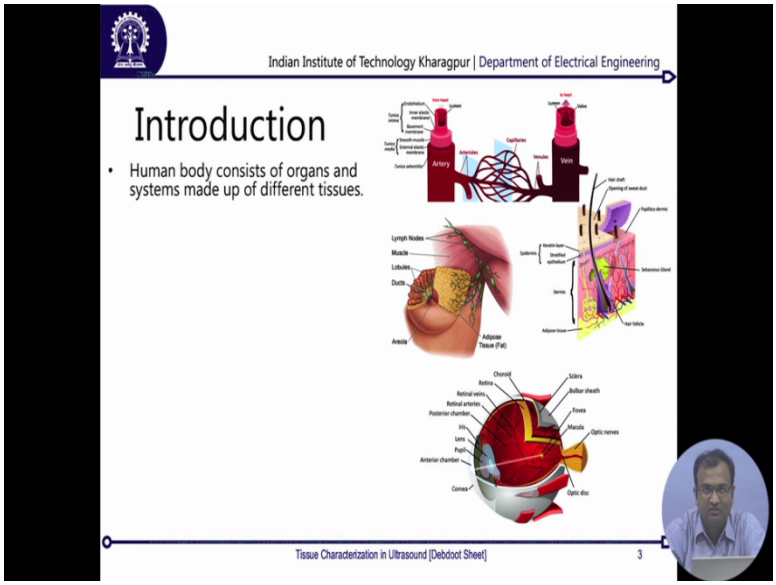
Welcome to today's topic and we have yet another interesting one on the application areas and this is on Characterization of Tissues in Ultrasound. And I would be specifically speaking about intravascular ultrasound and the whole nature about characterizing soft tissues within intravascular ultrasound. So let us get down to how it is organized, so I will be starting down with an introduction and then following down onto brief overview and backdrop of the ultrasonic imaging within intravascular ultrasound specifically. Since we have already studied ultrasonic imaging and how it is done, so you all are pretty much well aware of the physics of the instrumentation of imaging as well as some properties of how ultrasounds behave within biological soft tissues as well.

So we take up from there and then go into the signal analytics model and understands how signals behave and what are the amplitude behaviors, what are the distribution density functions for them and eventually from there we will end up getting into one of the major challenges with soft tissue imaging which is called as limit resolution challenge and the reason why limited resolution comes over here, as to it is not just increasing the number of transducers which would transduce elements which would help you get rid of the problem of limited resolution but why it will not lead to that one.

From there I would enter into something called as the statistical mechanics or the statistical physics of ultrasonic imaging, which will explain over the different stochastic models which describes how ultrasound signals can be interpreted which come down from different tissues and whether there are any tissues specificities available for these different kind of ultrasound amplitude values which you get down and reflect it from the tissue.

So using all of this we have a solution which I would be discussing about how you can leverage these kinds of never techniques in order to do tissue characterization. So with that I would move over to some experiments and results of what we have achieved in the recent past and then obviously again I would be drawing onto domain adaptation for In vivo use of all of these methods because whatever we had done on experiments till then was based on cadaveric data or in vitro acquired data. And from the last discussions which we had over the course of time and from the previous lectures you are pretty much well aware of that the actual final goal for medical image analysis is to make it useful for in vivo data and until you are making it working on in vivo data, your solutions are not coming into practical use.

(Refer Slide Time: 3:16)

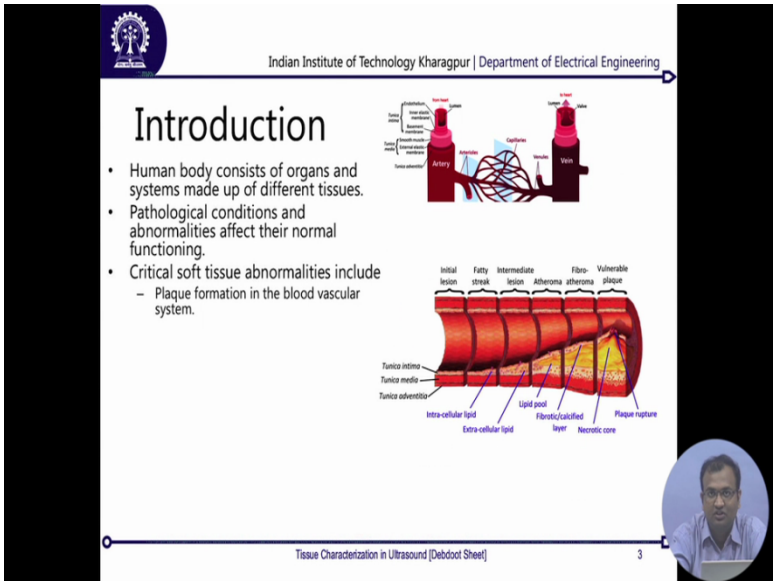


So let us start with a very basic introduction of what I meant by tissue characterization and what this whole idea is about. So basically if you look at the human body then you have a lots of organs and they are made out of different kinds of tissues and one of this kind of tissues is called as soft tissues, character is pretty much simple, so hard tissues are the ones like bones, your tooth, so these are the ones where which are really mechanically hard and soft tissues are like your skin, muscles adipose tissues.

So this is one which is mechanically quite soft and they just offer some sort of a protective coating on your body act as a shock observing buffer or is like skin is a thermoregulator which your body has. We are looking specifically at these soft tissues and since we are pretty much aware by now looking into the concepts of ultrasonic imaging that it is one of the best use is to do it for imaging of soft tissues and trying to find out soft tissue abnormalities and contrast between them rather than use it for hard tissue imaging where much more predominant use would actually be of computer tomography and X-ray modality based.

The other modality which is obviously use for soft tissue imaging is definitely magnetic resonance imaging, but we as taking down only to ultrasound as of now for its flexibility purpose. Now, if we go down together so what happens is with this soft tissue condition, sometimes in these soft tissues there would be some sort of an abnormality which in general is what we define as pathologies.

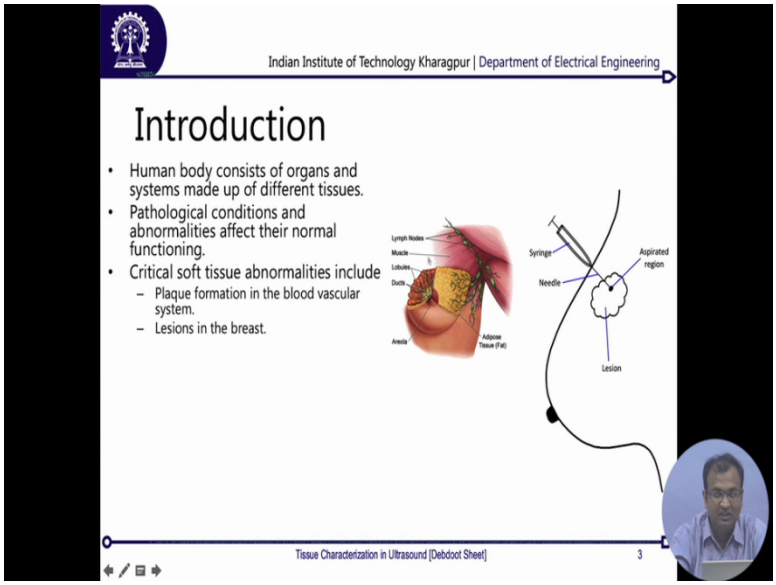
(Refer Slide Time: 4:41)



And some of them are really critical and so one of those critical ones is say a plaque formation within your blood vascular system, which is about so what happens in this case is that you have your blood vessels which sort of a pipe and then within that you will have cholesterol depositions, this is basically a physiological disease condition in which you have cholesterol which is just depositing on the walls over here. Now as imagine this one that there is a pipe and then there is some deposition going down over there, so eventually this pipe bore is going to get clogged and once that happens, then blood cannot flow down through the artery, so this kind of a condition is what is called as Atherosclerosis or even is called as

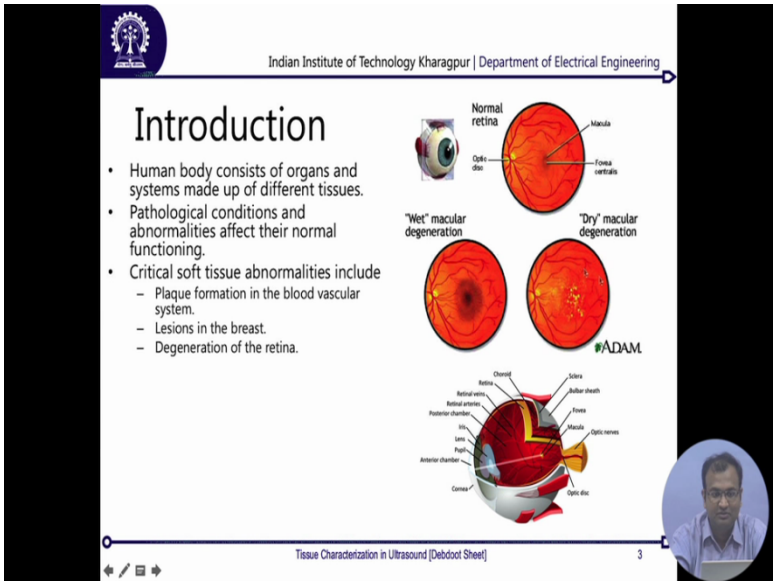
hardening of the artery. Now this is one of the problems which will happen down in case of soft tissues.

(Refer Slide Time: 5:27)



Now from there another problem is that in case of women with Breast there can be Lesions, which are not necessarily always Cancerous, but they are just Tumors or some sort of an abnormality over there, so these are again another kind of soft tissue abnormality which is quite predominant in the word.

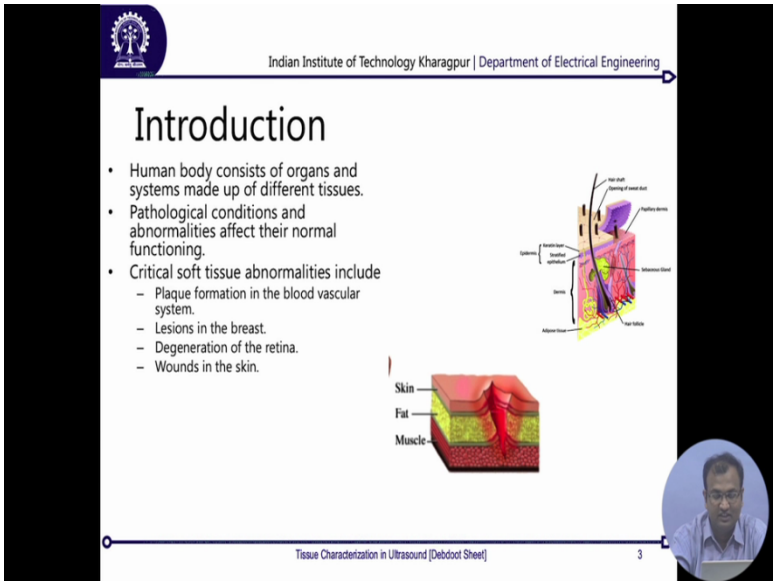
(Refer Slide Time: 5:44)



The other one is about retina, so since we have already done about our class on retinal image analysis so you are pretty much well aware of what that means, but these also are objects or

organs where you have lot of problems with soft tissues and you need to have some modality of handling soft tissue abnormalities very carefully.

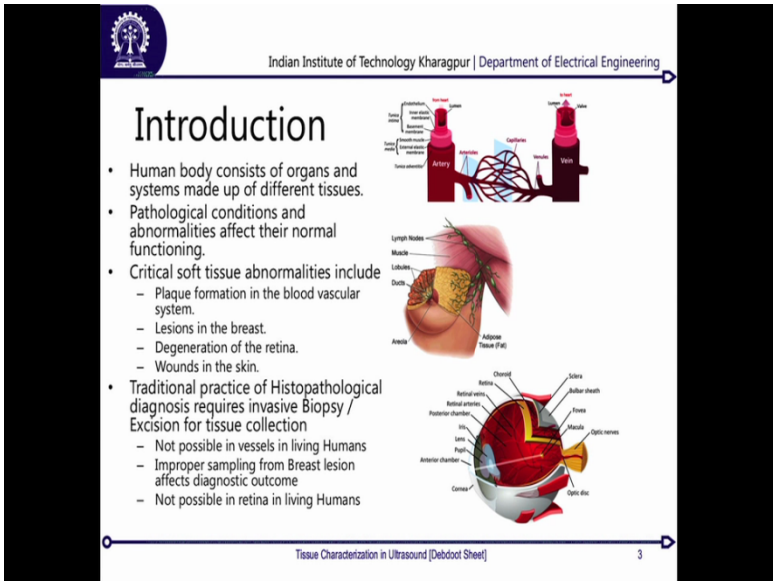
(Refer Slide Time: 6:03)



And the other one is definitely skin, one of the major areas and the major abnormality is actually wounds, so you can get bruises, cuts, or there can be burns and all of these lead to some sort of abnormality on the skin as well. Now, the traditional practice for understanding any sort of a soft tissue abnormality is to actually do a some sort of a Biopsy based investigation, so what is also called as a histological investigation. This is basically at invasive way in which what you do is you surgically or some way you remove a part of the tissue from your body. So there is a small cut made and the tissue is removed outside and then it is processed and then put on a glass light and put under a microscope for microscopic detailed observation.

Now the challenge which comes out of all of this is that it is a very invasive procedure and you cannot always do these kind of invasive procedures in living human beings on their vessel because this would mean that you have to in order investigate whether there is an abnormality on a vessel you are basically going to cut down a small part of the vessel and pull it out. Now that is not feasible practically, so you cannot do a histological investigation on vessels.

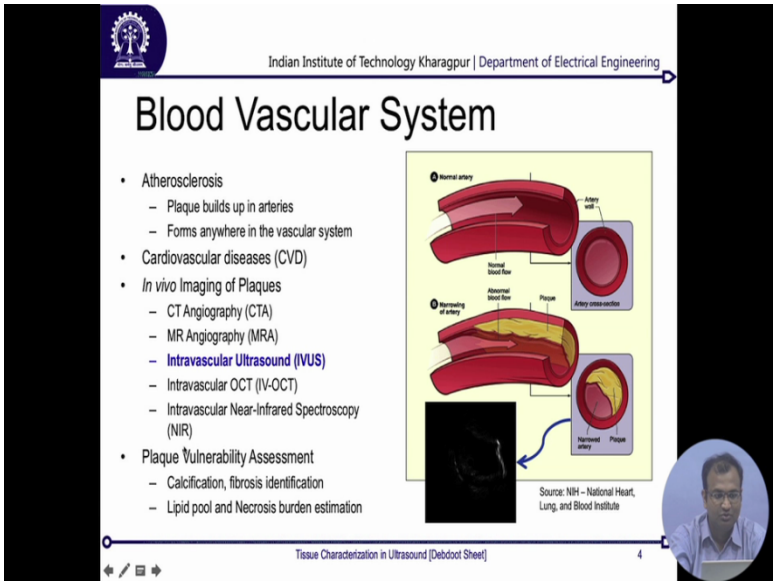
(Refer Slide Time: 7:16)



Similarly for Breast although it is done, Breast biopsy is quite common but it is a very painful process as such. And if we can find out some way of getting rid of it that would obviously much more appreciable. You can definitely not do it on the retina because the movement you try to probe the retina by this invasive method you are going to damage the retina. In any ways I mean either way either in order to investigate whether you have a perfect disease or not, you are going to damage the retina, anyways if you are not even investigating it would naturally damage after a few years, so it is not technically feasible to do it.

And similarly for wounds, I mean if we would generally like to investigate clinically as to whether the wound is healing and that would mean that there are multiple layers of skin and whether each of these layers of skin are growing out in a perfect way. But the problem is the movement you want to do that so say this is the skin and I want to look into these layers I am going to chunk out a part of tissue over there. So that means that in order to understand whether a wound is healing, I am going to inflict another wound over there and pull out the tissue and do it. So these are the major technical challenges why you can sometimes not use Biopsy within a clinical environment setting. And this whole tissue characterization thing is what comes into play for investigating a histological equivalent in condition when you cannot do a Biopsy.

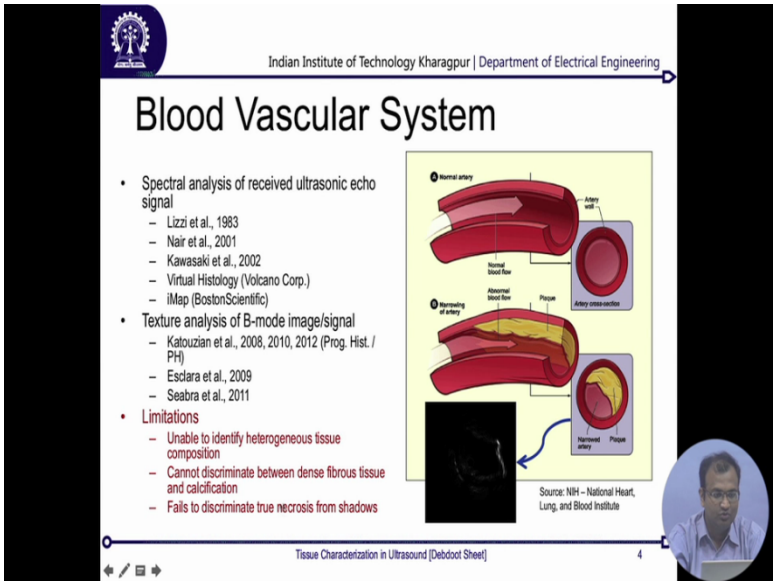
(Refer Slide Time: 8:28)



So if you want to look into a blood vascular system, so a basic details of it is generally when there whenever there is a plaque formation or Atherosclerosis, this is going on this is what would happen over there and they lead to something which is called as Cardiovascular disease and there are lot of techniques for in vivo imaging of these ones. So there is CT Angiography, MR Angiography which are basically for localization and one of these detail investigation methods is was called as Intravascular Ultrasound.

So what is typically done is that ultrasound probe is put within over here which rotate 360 degree totally and then it produces this sort of a polar scanned out image and then on this image you can look down for cross sections, but then for an untrained eye this would basically appear as just a black or some white spots over there and not of much major sense. So the whole of intravascular ultrasound tissue characterization is what deals with instead of showing this kind of an image, can we show something which is almost like this or equivalent to a histological image so that is a basic problems treatment which we do. Now this is very useful because we would like to assess Plaque Vulnerability in terms of very preciously identifying whether there is a calcification versus there is some sort of fibrosis over there.

(Refer Slide Time: 10:04)



And the other one is we would like to investigate a Lipid pool versus Necrosis burden and what is the condition of the Necrosis. So these are the major clinical indicators which need to be investigated from intravascular ultrasound as well for when investigating out these vascular structures. Now, there have been quite a lot of contributions in the past and some of them include papers to commercial products as well and one of them is called as a Spectral analysis method. So what it does is whatever received ultrasound signal is there so say you have a 20 megahertz probe, which is imaging your artery so you set down a 20 megahertz signal and then whatever you are receiving, you use a white band receiver for receiving it.

So obviously you are getting your fundamental frequency at 20 megahertz, but when it interacts with tissues and due to motion and all of this, so there would be a spectral spread, right over there. So now we also try to although the emitted one was a very narrow mind 20 megahertz precise emission but the received one is a white band, so it is centered almost at 20 megahertz but then the bandwidth is much higher. So those kinds of analysis is what is called as Spectral analysis, so that was started somewhere in 1983s by Lizzi and it continued going on and we have two commercially available products called as Virtual Histology from Volcano and iMap from Boston Scientific which make use of this kind of methods in order to characterize tissues.

Now, from that a bit later on in time, so somewhere around 2010, so we had these methods which were making use of texture analysis in ultrasound signals and images in order to find out what kind of tissues they belong to and there was a quite amount of good success coming

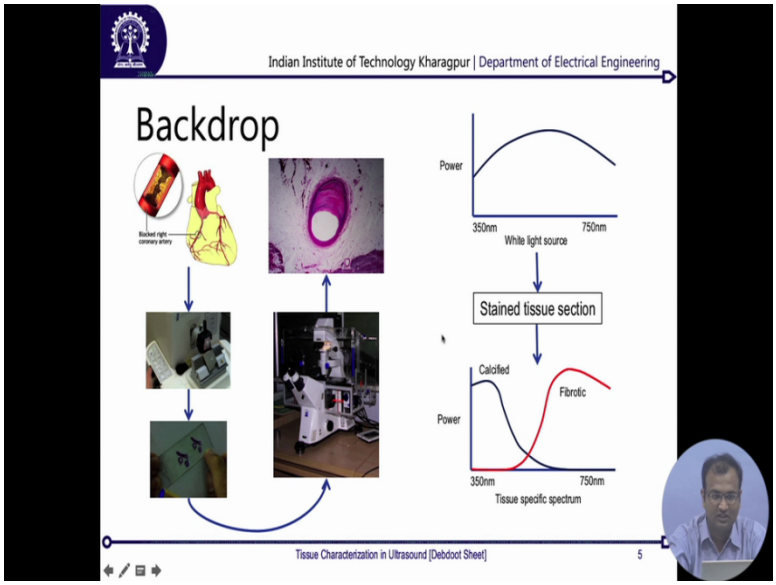
down. But the major thing is that these all of these methods are still limited because they do not identify what is a heterogeneous tissue composition.

So what that means typically is that our body you never have a pure tissue which means that if I say that there is fatty tissue over there, so there would be some fibrositis as well, there would be some epithelial cells over there as well, so it is never a pure fatty tissue which is over there. So you need to somehow identify what is the coexistence or the relative co-occurrence of these mixed heterogeneous tissues and that none of them is possible with all of this prior methods which we have.

The next one is that all of these methods failed to discriminate between dense fibrous tissue and calcification, because both of them exhibit a very steady speckle behavior as you see over there, so just none of them have been able to do that in the past. And then all of these too definitely fail to discriminate between a true necrosis from shadows and what that means is that over here you would see that whenever there is a calcification, so since that is a sharp reflection happening over there so most of the acoustic signal is just reflected form this part and then beyond it since you do not have any signal which is penetrating neither is able to come back, so you would see a perfect shadow coming down, so that is a perfect black region.

A similar kind of region is also exhibited by a Necrotic pool somewhere over here. And what that means is over there the content is so homogeneous that there are no scattering particles present over there and since nothing can be scattered out so you do not get a speckle intensity coming down over there. Now how do you discriminate between a shadow and a true necrotic region, this is another challenge which has not been solved any of them, because visually they look pretty much similar to each other. So with these challenges is what I would be discussing one of the basically a series of papers, but a major contribution from one of the papers.

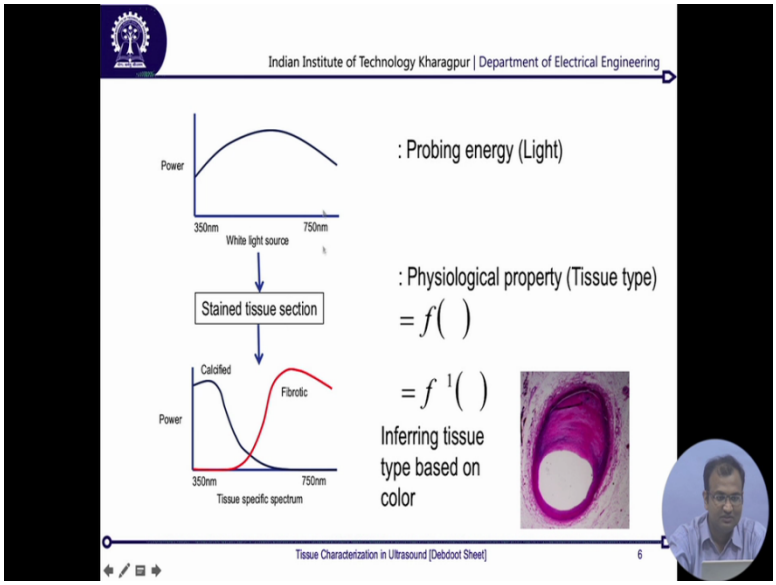
(Refer Slide Time: 13:08)



So the backdrop starts something like this that as I was explaining you the histological prospective. So what I would try to do is if I want to investigate a plaque within an artery in a actual histological sense, then I would have to plaque out this artery and then do some sort of a block preparation over there, so take out that piece of artery then do a biochemical processing to dry it and fix it so that hardens and then you put it inside a block of vax to harden it even more. And then you do thin slicing of it, say consider slicing of bread over here it will be slicing of tissue and we use a machine called as microtome to do that and then you mount them onto a glass slide and then stain them and after that you would be looking into microscope and then you see something of this kind over there.

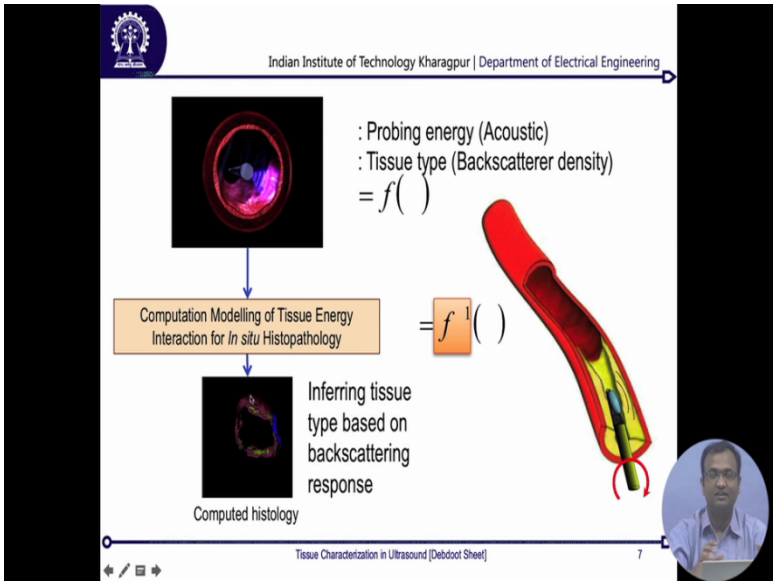
Now in terms if you look in the engineering prospective of a transfer function, then what comes out is that on this microscope we are going to eliminate with white light as we have learnt in a microscopic lectures. So you illuminate this mass of tissue over here which is mounted on the slide with white light and then what you get down on the response is something like this, so for each pixel is some sort of a transfer curve over there, now based on the intensity whether you are looking at blue and what is the intensity of red, you will be able to tell what is the relative density of these two kinds of tissues over there, whether it is calcified or fibrotic and this is typically for a H&E stained tissue which we are looking at.

(Refer Slide Time: 14:31)



Now in sense what it translates down to is that there is some sort of a probing energy which goes through it and there is some sort of a physiological property which is say f of that particular object over there. Now, what we want to do in tissue characterization is we want to find out what is this f inverse over here, which would give me as to what is the relative distribution of the tissues by looking into the total histological image over there.

(Refer Slide Time: 14:59)

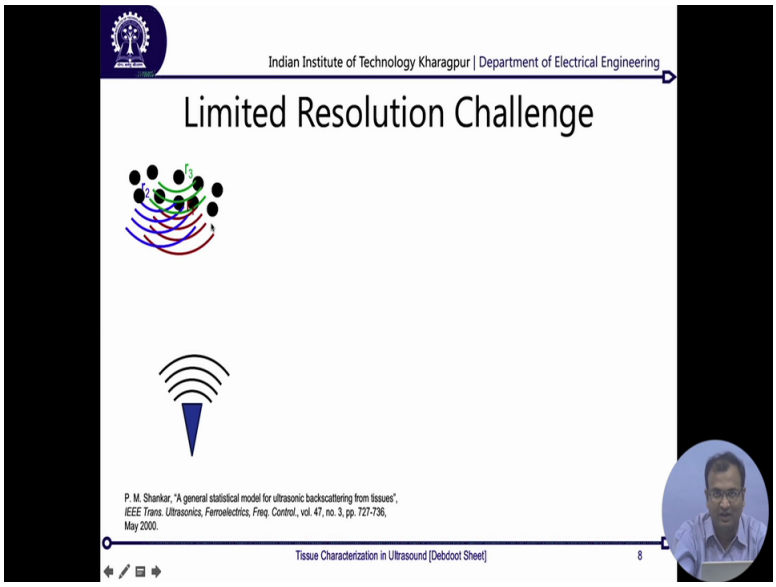


Now if we take this one and then translate it directly onto our ultrasound space what that ends up giving is, say I have this scanning ultrasound probe over here which circularly rotates and then it ends a pulse, it receives back the same pulse over there. So I have a series of signals coming down and now on that stack of signals I need to do some sort of a mathematical

model, which is going to end up giving me this sort of a model which will just be giving me relative density of these different tissues in different colors.

So over here my forward function will be this Acoustic energy and this tissue backscatterer density over there. Now, I need to find out some way of inverting this whole function such that on this inversion I am able to get this sort of a map coming down. So this is in a sense what tissue characterization is mathematically defined as and that is what we try to solve.

(Refer Slide Time: 15:55)



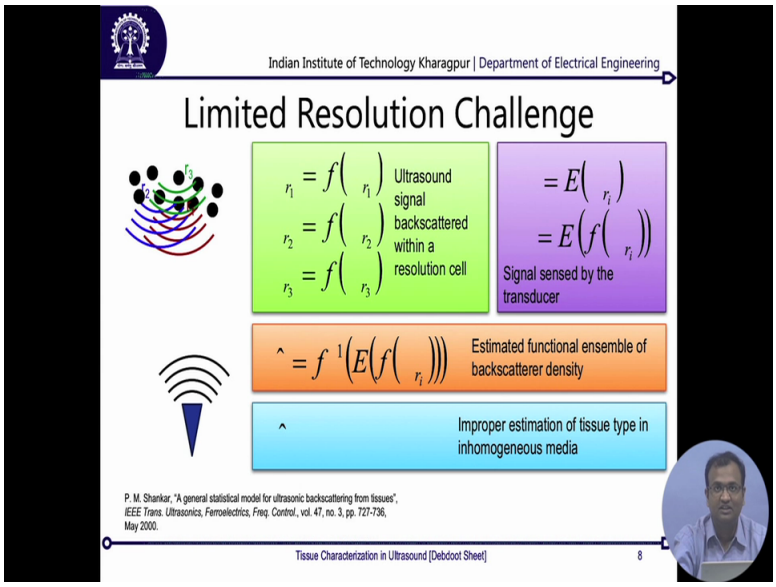
But the problem is that it is not so easy to do it, thus you will never get down pure tissues and the reason is within this limited resolution challenge. So what would happen is, say I have a ultrasound transducer and it is emitting a pulse, now as it emits and it strikes down this mass of tissues over there, so you would be getting this multiple scatters, now the whole concept of scatters is that it is generally on theory that the cytoplasm to nuclear boundary, so the nucleus within your cells they are the ones which are quite hard and strong and very dense and they reflect back the ultrasound waves.

Now if the tissue these all these nuclei are quite densely packed very close to each other, then all of them are going to emit down and what you get down at the transducer is not the response of one of these cells, but it is a combine response of all the cells present over here. And as such when you are getting down this once, so what will happen is that your resolution is limited to this group of cells and no more to a single cell, so even if I am increasing the number of transducer that is not going to play any significant role over there, because even by increasing the number of transducer I am still going to get for each transducer just there will

be a group of cells which will be sending it back. And until I do some much more signal analytics on top of it, I will never be able to identify directly I will never be able to identify each single cell.

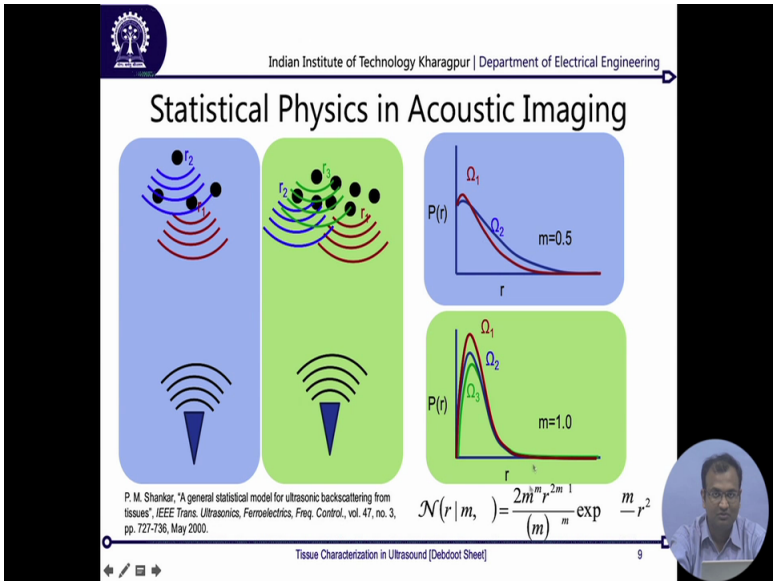
And for that reason that the minimum homogeneous structure within your body which has to be identified is actually one cell. So a cell can be of one particular tissue type, but otherwise that within a small volume there can be mix group of cells coming down. And what the best what you can identify always through some sort of a analytics is what is the relative density of each of them.

(Refer Slide Time: 17:26)



Now for that what we try to do is something like this, say that for each of them R1, R2 and R3, you have some signal coming down over there. Now at the end what happens is an estimation framework, so it just a consolidated effort which is sent back over here and your final objective is to do some sort of an inversion of this forward pass function. Now you have to invert it given that your forward pass is not from each individual cell, but is from ensemble and still you have to end up getting that one.

(Refer Slide Time: 18:17)



And through that one you will be able to get some sort of a estimation although initially it will be improper but eventually it would become proper. Now, in order to solve this sort of a say intractable problem we enter into a interesting fact over here. Now this interesting fact is that we make use of statistical physics of acoustic imaging. Now for that what we do is something like this, say that I have different tissues which are different kinds of cellular densities over there.

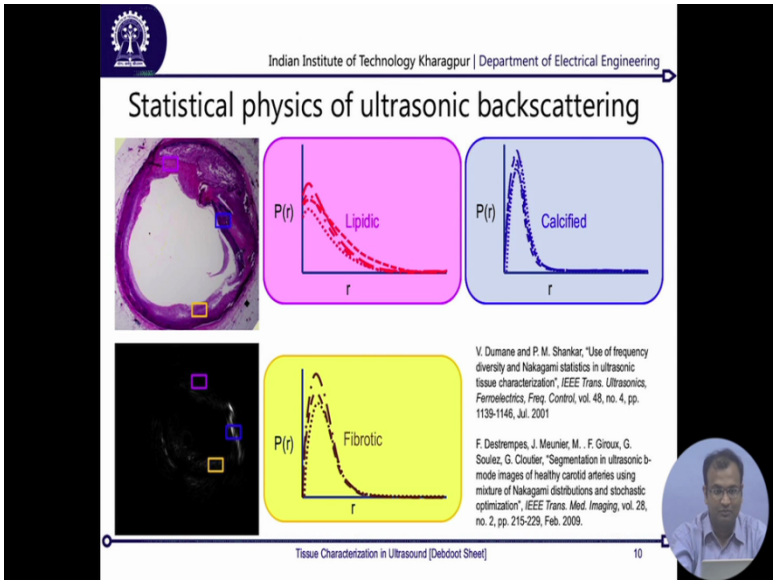
Now one thing which was observed is that as you pass a pulse of ultrasound and then it gets reflected back, so whatever signal you are getting down you can actually plot down that as a probability function so you keep on say for this example, it will be something like thousand times you keep on sending a pulse over there and for each pulse you keep on recording what is the intensity you have received. So it is the same transducers, same tissue region and you are sending number of multiple pulses.

And then you just plot down a histogram or a after that you can find out a probability density of each of these amplitudes. So the amplitude of this pulse is along this X axis which is called as r and then on the Y axis is the probability of getting that value of r. Now, as you keep on doing that one, what you would get down is some sort of a distinct curve. Now say I did it once for 1000, I got this kind of a curve in red. Now, again I did it for 1000 times I got this kind of a curve in blue, both of these curves are quite similar to each other this what you will find out. Now, next time for a different kind of tissue where the cells are much more densely

packed, so this may be say fibrous tissue where you have very thin fibrous (()) (19:32) and all of them are quite densely packed.

And then if you look at them what you would see is you also get a similar kind of curve if you are doing this experiment every time, but there is sharp difference between the curve over here and the curve over here. So for different kinds of tissues you are going to get a different kind of distribution curve and that distribution curve is what is denoted by a Nakagami distribution function as we have over here. Now this is what was theory proposed by Mohan Shankar in one of the early papers and we make use of this whole theory of Nakagami distribution of ultrasonic signals and then come down to our actual work. So that is where we start by defining the statistical physics of ultrasonic backscattering.

(Refer Slide Time: 20:18)|



Now what we did for our work is quite simple, so we had histologist because it was done in vitro, so that means that you have dead bodies or cadavers form which the heart was extracted out and the artery was pulled out and then there was circulating saline in a refrigerating environment and the ultrasound was acquired. So we could do it but then it was all a glass model and it was a in vitro data acquisition, so from that what we have is that this whole histology was registered with the ultrasound image which we have over here, such that every point on this ultrasound image corresponds to a point on the histology and we decided to look into different regions.

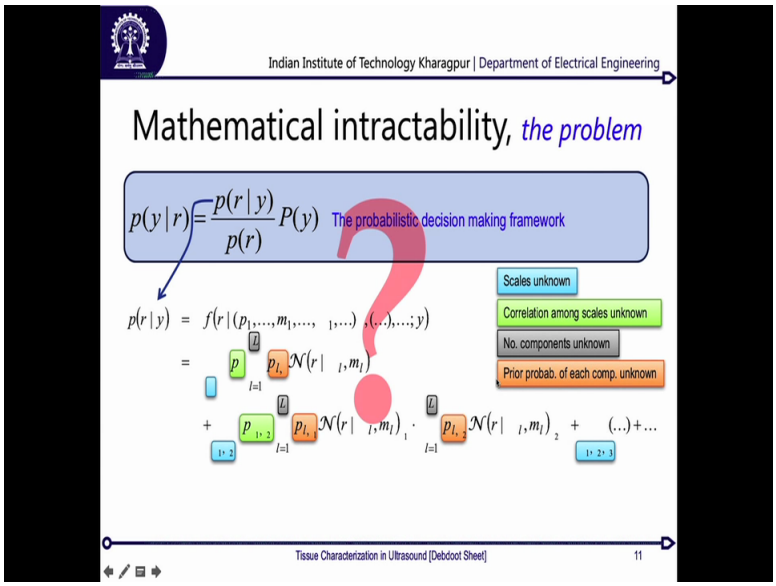
So say I take this region over here which corresponds to this region and we know that this part is Lipidic by looking into the histology on the histology reports. Now, over there we keep

on looking into multiple times of this ultrasound going down and then looking to what the probability curve looks like. Similarly we repeat the same thing for Fibrotic tissues, we repeat the same thing for Calcified tissues. Now if we look carefully over here across multiple measurements there is a mild variation, but more or less the shape of the curve is quite similar as well as the height of the curve is similar. Similarly, for Calcified and Fibrotic also we have a similar trend and each of this different kind of tissues exhibit a different kind of curve.

So that definitely means if I have a parametric form of representing and that parametric form of representing is my Nakagami distribution, so some parameters of my Nakagami distribution should be specific to Lipidic tissues, so there should be a bound of parameters or group of parameters within Nakagami, which will specify that it comes from Lipidic tissue, there will be a group of parameters which would specify that it is Calcified tissue and there would be a group of parameters which would specify that it is Fibrotic tissue and this is what we make use of in our problem.

So there were a lot of papers in earlier days who had also made use of these kind of properties in order to discriminate, but under an assumption that you need to manually delineate a mass of tissue and then find it out because whenever you are going to do some sort of a parameter estimation within and estimator framework, you would need the number of samples or (()) (22:28) samples to take down for doing it. So that would mandate that you have a very cohort group of samples coming down over there which is similar to each other.

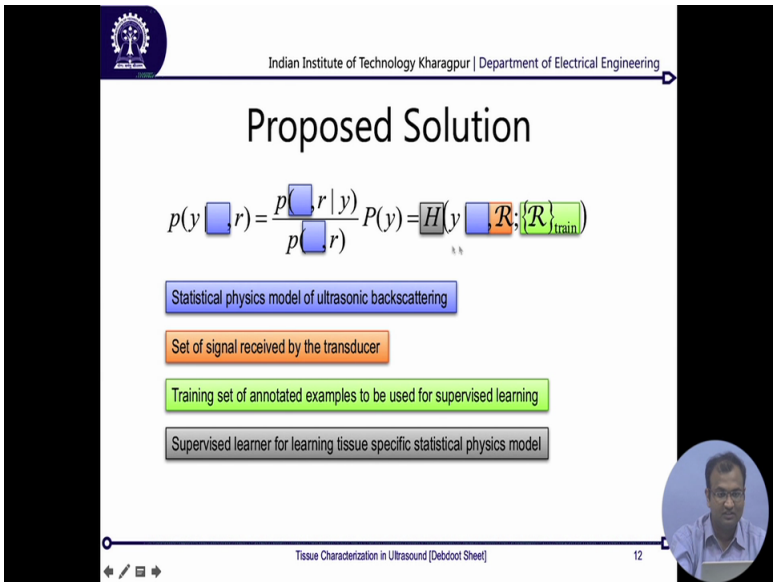
(Refer Slide Time: 23:00)



Now, although like they were doing it manually, but our task over here is to make it a totally automated process where you get signals and you just analyze them, the clinician over here is not going to point out that this is my cohort region which I would like to segment out actually. So in order to do that what we try to do is let us think of putting it into some sort of a probabilistic decision making framework. So given that I have a value of signal r coming down or my intensity of the ultrasound image, I want to predict out what is the probability of belonging to a particular type of tissue y and this is what it would look down in a Bayesian standard Bayesian paradigm in including your likelihood and your prior probability and the evidence over there.

Now from this if we look into this likelihood function, what you would see is this that likelihood is going to be some sort of a summation of multiple Nakagami coefficients and then there would be a weighted combination of all of these different ones across different scales and together this is going to expand into different kind of polynomials.

(Refer Slide Time: 24:06)



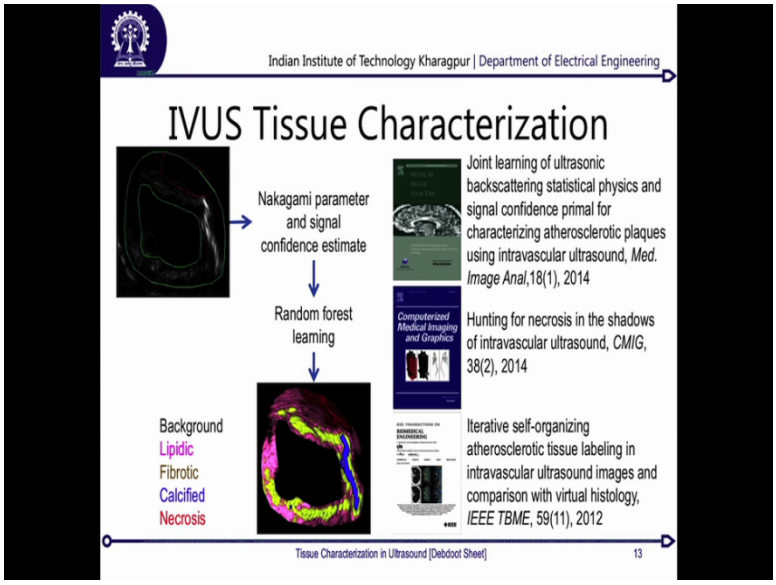
Now, in total these introducers are major challenge that we do not know what are the scales over there, what are the correlations between the scales, then the number of components and the prior probability of each of these components. And together that makes this whole problem as a intractable problem. Now in order to solve this what we end up doing is we have some sort of a proposed solution in which what comes down is that say this probability is posterior probability of belonging to a tissue type y, given a particular signal value r and some unknown factor, so we need to figure out what this factor is. If we use this unknown factor as some sort of guidance across all of them we should be able to get that work out.

Now what we decide is we call this unknown factor as this statistical physics model of ultrasonic backscattering and will come down to how that thing is computed out and it was a it is a very simple process by which you can compute out. Now, what at the end we can do is that given that any kind of a bunch of signals come or one single acquisition over there, then on that you will have to figure out this factor over there and given that you have a good set of training data then using all of them you can always train a classifier which can solve this whole problem and this is what typically would be called as a transfer learning problem because you are going to transfer your knowledge from one set of attributes which you have learnt to learning another set of attributes over there.

So from this what we end up getting is this sort of a total framework in order to do tissue characterization. So the idea is something like this that you want to estimate the Nakagami parameters and for that what we would do is since I said that you need a finite number of samples, which are coming from a cohort. But the problem is that now it becomes a Chicken Egg problem, until I can see what tissues are there I will never be able to delineate what is a homogeneous mass of tissue over there, until I eliminate and isolate one homogeneous mass of tissues so that I get down all my readings perfectly, I will never be able to calculate what is my estimator over there.

Now what do we do in that case, so what we make use of is again that sort of a pyramidal decomposition framework. So we start by assuming that there is some sort of a homogeneity at a scale. So say be starting on a small neighborhood of 3 cross 3, then we expand this neighborhood to 5 cross 5, 7 cross 7, 11 cross 11 and then keep on going.

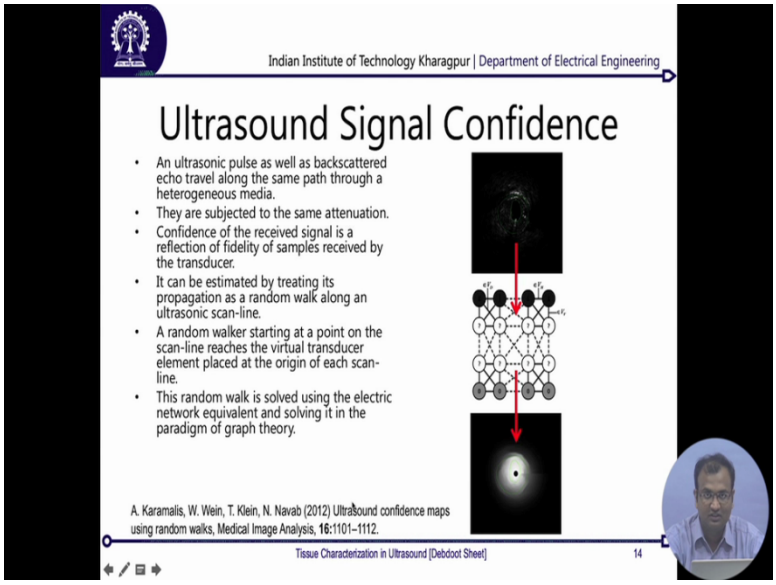
(Refer Slide Time: 26:02)



Now as you keep on expanding what would happen is that say at 3 cross 3 it is homogeneous, say at 11 cross 11, it is homogeneous, then obviously at 7 cross 7, a lower scale also it is homogeneous and any of the lower scales it will always be homogeneous that is how it is supposed to be. But then say at 5 cross 5, it was homogeneous, but at 7 cross 7, it is not homogeneous ok, but all the other scales over there had a very good estimator. Now if you try to create at each pixel level a whole stack of these estimators over there, so that would in term end up being an array of estimators and these would be something like features of a single pixel over there. But it is no more features in terms of textures or coherence matrices or local binary patterns, but these are now features in terms of some estimators which have a basis is in the statistical mechanics of ultrasound, ok.

And using all of those features we train a random forest and then so that it can do a very good estimation solving over here. So this output is just a color blended output of the probability ones. So this blue one is what denotes a Calcified tissue, red over here is what denotes the probability of having a Necrotic tissue, yellow is what denotes the probability of having Fibrotic tissue and although if you we have examples later on where I would show you a sharp distinction between the Calcified and the Fibrotic which we could identify with this method and pink over here is what signifies the Lipid deposition completely over there.

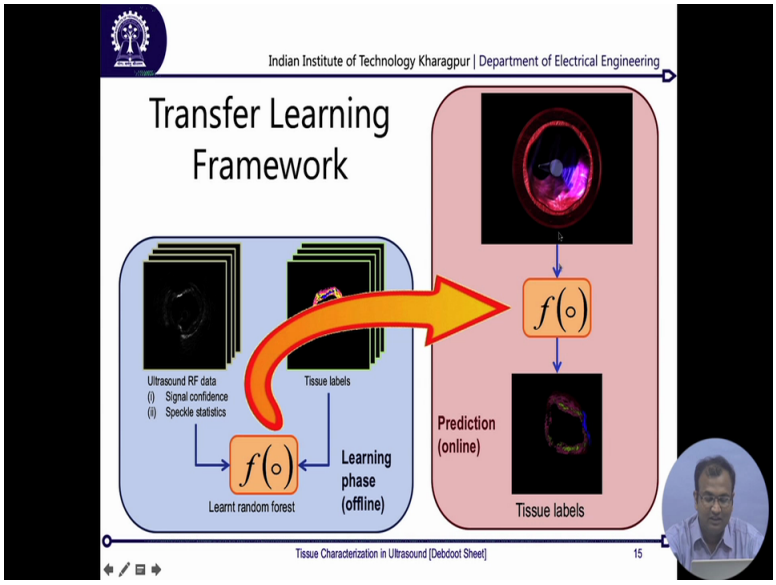
(Refer Slide Time: 27:39)



Now another important aspect which we make use is borrowed from this one of these papers by in the journal of medical image analysis and this was about understanding ultrasonic signal confidence and the cue what we use is that since ultrasound as it propagates two tissues and we have studied it is going to attenuate significantly and if there is a significant attenuation, then we will not be getting very good reliable estimates. So we need to find out some sort of estimation about how reliable the signal is, and that is what is called as ultrasound signal confidence.

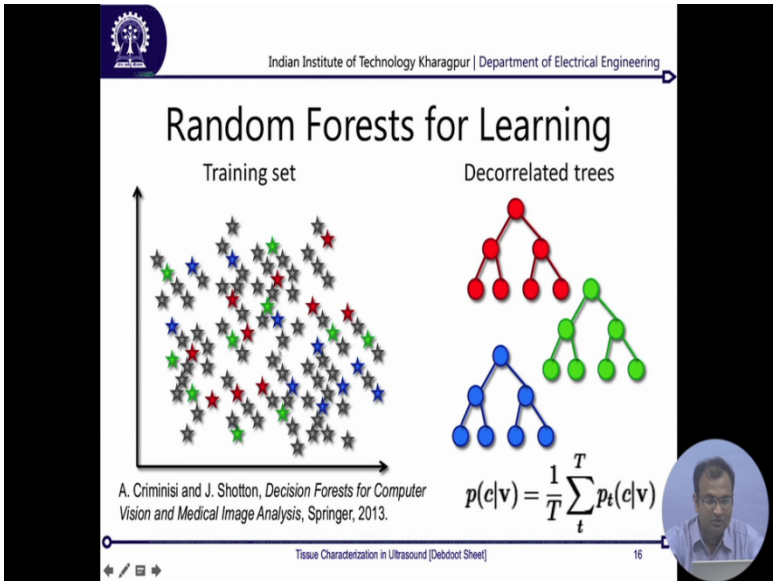
So we use a typical random works like solution framework in order to get down signal confidence and so that is quite beyond the coverage areas, you can read more details about on this particular paper as well. So what it gives out is at every point on this signal acquisition space, it will give out a probability in the range of 0 to 1. 0 would denote that the signal has a very low confidence over there of returning back and so the estimator might be a weak estimator or rough estimate, whereas, wherever there is a high value or close to 1 probability, it means that the estimation is very good over there.

(Refer Slide Time: 28:45)



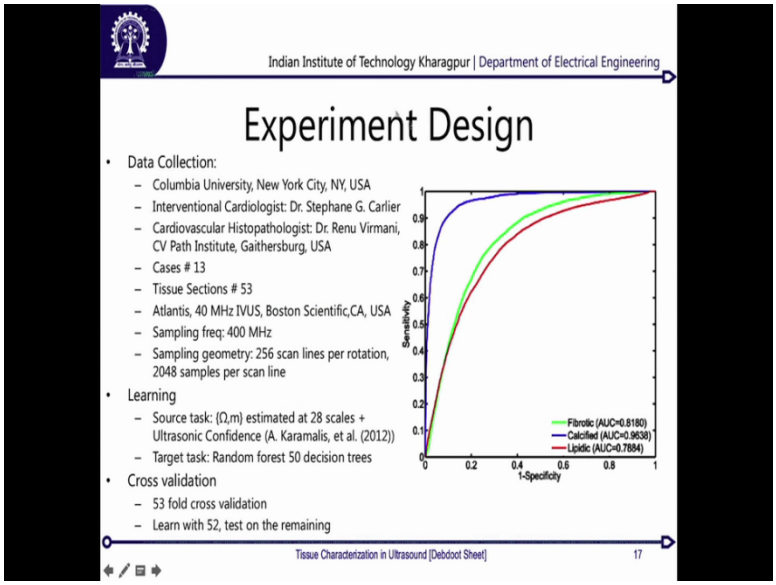
Now, using all of that we fit that into a transfer learning framework so what we do is we have one estimation of signal confidence, also an estimation of these speckle statistics of ultrasound using those Nakagami parameters at multiple levels. And then from ground truth labels we learn down a random forest, now ones this is done, this is what is carried down in the offline process, after that we start with the online process in which what happens is given that there is a signal acquisition happening over there. Immediately all of these estimators are carried down and then this model is transferred over here such that you do a feed forward through this model and then you get down the probabilities and coming down for different kind of tissues.

(Refer Slide Time: 29:25)



Now one good thing is that we use a random forest for learning over there such that this makes our whole process independent of topological behaviors of samples as we had studied in the random forest lectures. So you do not need to understand typically as to what is the prior probability of the samples or you will not be needing to a priori know about the topology of the feature space on which you are going to have your discriminator coming downs, so whether you have a linear discriminator or quadratic discriminator it is independent of that and that beauty of random forest is what helps us in learning this whole feature space in a much stronger way.

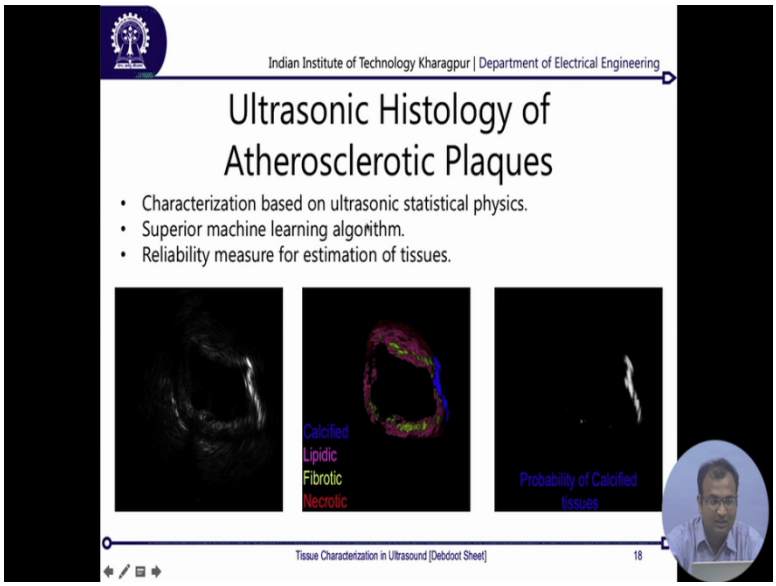
(Refer Slide Time: 30:02)



So together with that we did prove it on an experimental data which was in vitro and they were all acquired at 40 megahertz intravascular ultrasound from Boston Scientific with sampling frequency of 400 megahertz coming down such that we had in one 360 degree rotation of this you had 256 such scan lines and each scan line had 2048 samples over there. So the whole signal space for me has basically 256 columns which is one scan line is one column and you have 2048 number of rows, such that each row denotes one sample along a scan line. We in total had 53 such acquisitions from 53 different slices which were from 13 different cadaveric hearts.

So there were different arteries on the heart, where different plaques were there and for each plaque we had one typically acquired signal taken down which was with consultation of our interventional cardiologist and cardiovascular histopathologist, so they were the ones who were responsible for choosing out which locations to actually sample down and analyze further.

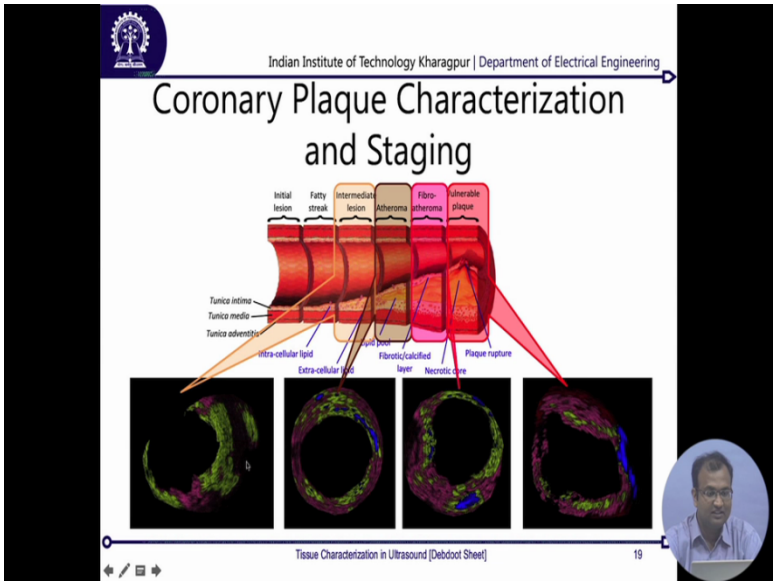
(Refer Slide Time: 31:15)



Now with that what we got down is something like this so we have a method which is quite good in characterizing so on this side, on the right hand side you would be seeing a relative probability changes over there. So this is the probability for finding out Calcified tissue, now this is the probability of finding out Fibrotic tissue now if you look over here the region where you had Calcified tissue there is no Fibrotic tissue at all collocated and that is quite say that is biologically quite relevant and correlated. Now this is the probability of getting down Necrotic tissue and this is the probability of finding out Lipidic tissue. Now if you carefully look between both of them since Necrosis is a latest stage of Lipidic, so they need to coexist

in some way and you can see this co existential probability quite distinctly coming down over here, ok.

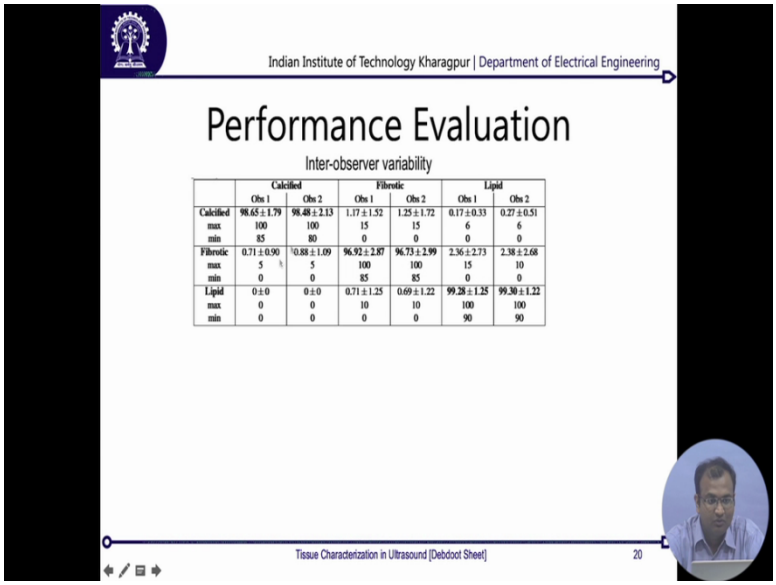
(Refer Slide Time: 32:06)



Now this is almost quite towards the end of it, so now for different staging is what we had. So what we had done was we had for different arteries which were in different stages of plaques and then for each of them we decided to look into how the behavior comes down. Now from a machine learning perspective in the context of medical image analysis you would often note that some of these samples have missing classes. So over here say there is no Necrosis and there is no Calcification at all, this is an early stage. Still it is going to predict and there are no false positives coming up, this is a stage when in these 2 stages also there is no Necrosis coming and it comes only over here. So there are missing classes in the data itself and it is still very efficiently going to predict it out, including like learning hem perfectly.

But obviously if you try to learn with this sample without any Necrotic example, then your model will not have any Necrotic learning ability as such. So that is one thing which you need to keep in mind as to how to choose down perfect examples for learning.

(Refer Slide Time: 33:00)



	Calcified		Fibrotic		Lipid	
	Obs 1	Obs 2	Obs 1	Obs 2	Obs 1	Obs 2
Calcified	**98.65 ± 1.79**	**98.48 ± 2.13**	1.17 ± 1.52	1.25 ± 1.72	0.17 ± 0.33	0.27 ± 0.51
max	100	100	15	15	6	6
min	85	80	0	0	0	0
Fibrotic	0.71 ± 0.90	0.88 ± 1.09	**96.92 ± 2.87**	**96.73 ± 2.99**	2.36 ± 2.73	2.38 ± 2.68
max	5	5	100	100	15	10
min	0	0	85	85	0	0
Lipid	0 ± 0	0 ± 0	0.71 ± 1.25	0.69 ± 1.22	**99.28 ± 1.25**	**99.30 ± 1.22**
max	0	0	10	10	100	100
min	0	0	0	0	90	90

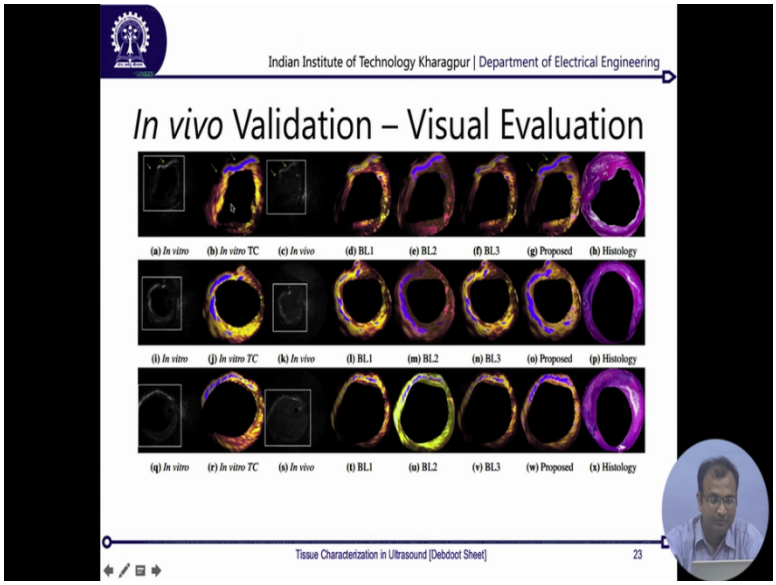
Now from there I come down to this performance evaluation so what we had done was we had compared our predictions with observers and we did do an Inter-observer and Intra-observer variability scoring by assessing our predictions with respect to the histologist over there and this was done by clinicians who are train to interpret cardiovascular histopathologies directly, so ours is a computational model and you have a actual histology to compare with. So if you look over here the diagonal line over here shows down quite close to 100 percent some of the highest values which you see and the cross diagonal shows very lowest values. So they definitely signify that the method is quite consistent as far as inter and intra observer variablities are concerned, and you can read through the papers which are linked down at the end of it for much more details.

(Refer Slide Time: 33:52)

Now from here I come down to the significant point of that we needed to domain adapt definitely this whole thing and the major problem was because this has to go for in vivo instead of in vitro where it was trained. And so what we decided was we have this whole idea over here that once you have the train model which is in vitro trained over there, then we need to do some sort of an adaptation and for this adaptation part is when we make use of very small number of samples coming down in vivo but you do not have do not necessarily have a histology coming for that one.

You just have in vivo acquisitions and the whole idea was that unsupervised way how can you adapt these models when you do not have a tissue characterization, so the ground truth labels available in any of them. Now for that we did do, so the since that part is quite beyond the coverage which we can do over here you can definitely look into it.

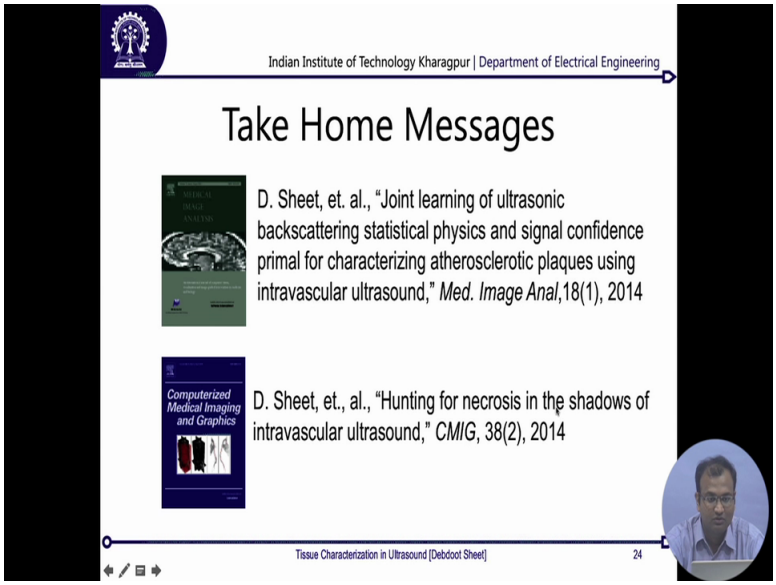
(Refer Slide Time: 34:45)



But to come down to a fun part as to what we could achieve by doing it is that we had fortunately for some of the animal experiments what we had was we could sacrifice the animal at later point of time. So you could do an in vivo acquisition and then take out once the animal is sacrificed or dead you can pluck out the artery and then do an in vitro acquisition over there and do histology. Now you can compare your in vitro prediction results with your domain adapted model for in vivo predicted results on that and with the histology. And if you look over here, then our method has quite consistent performance, this is the one for in vitro over there and this is the one with in vivo what we show.

Now our results which we show for this in vitro to in vivo are quite consistent with each other compare to other base lines which were very simple methods of trying to either train on directly on this in vivo data or trying to directly deploy the in vitro model in case of on the in vivo data itself. Now these are again extensions from the first lecture of this week, where we were studying about domain adaptation in case of retinal image analysis and the power you could gain by using a lot of in vitro data, or healthy data, or some other experimental data to pre-train your model and then just (()) (35:56) adapt it to be really superior performing than having to train on limited data.

(Refer Slide Time: 36:13)



So this is the particular paper on which you will find more of the details and I would suggest that you look through it. So with this we come to an end and to read more about them you can read refer to these 2 of our earlier publications. The first one has a much more detailing about the ultrasonic statistical mechanics and then how you can use it and then the whole concepts behind that. So with that I come to an end to ultrasound tissue characterization and thanks.