Mathematical Aspects of Biomedical Electronic System Design
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Thermal Properties of Tissues and Modelling

Welcome to the next session. In the earlier session we talked about how to quantify the ultrasound that is acoustic attenuation coefficient as well as the optical properties of the tissue. In optical we talked about reduced scattering coefficient and the absorption coefficient for the tissue bulk properties of the tissue. In now, in today's session we will talk about the how to quantify the bulk thermal properties of the tissue.

So, by meaning what do we mean by bulk thermal properties is that we want to quantify the thermal conductivity of the tissue and the heat capacity of the tissue. Why do we want to quantify it? One of the reason to quantify it is you want to delineate between normal and cancerous tissue. So, let us see how do we do that. So, as you can see on the screen.

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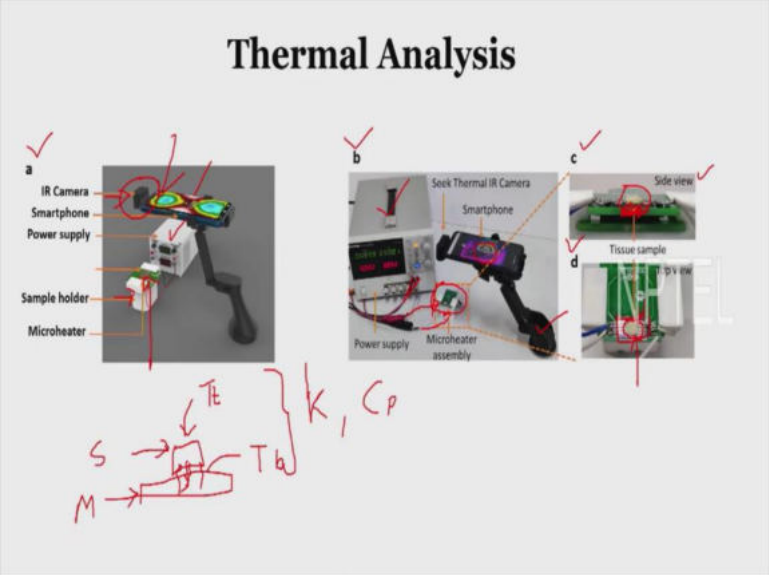

What do we have is one of the configuration that we build we have the power supply over here and we have the sample holder over here and then we have the micro heater. So, this micro heater which is placed just below the sample. So, the micro heater is like over here and then on top of it there is a sample so, this is the tissue sample and this is the microheater. This microheater actually heat the bottom part of the tissue.

So, we have the T_b that is the bottom temperature of this tissue and then we want to quantify what is the T, T_t that is a top surface temperature of the tissue. How do we quantify the top surface temperature of the tissue? We actually use the our mobile camera so, this is the mobile

phone but not mobile camera but we are using this mobile phone which is connected to an IR camera.

So, this is an IR, IR camera. In this case we use this seek thermal compact pro, IR camera which is which can easily get connected to your mobile phone and through your mobile phone you can then image the tissue sample. Once you image the to sample, you can see as you can see over here you can see the temperature of the tissue, we can quantify the temperature of the tissue very accurately.

And once you know the top surface temperature and bottom surface temperature, you can actually get the tissue properties such as thermal conductivity k and specific heat C_p. How do we get this? We will come to it in some time. So, a schematic is seen on the left side. So, this is the schematic and on the right side what we observe is the actual experimental setup. So, this is again the power supply and we use the power cables over here and connect it to the micro heater.

So, this micro heater is used to locally heat the sample tissue. And it is very finely tuned the rise in temperature at the bottom part of the template of this tissue using the micro heater. So, we calibrate that. We perform the experiment 3 times and then we calibrate to use using the measurement of 3 times. And once we do that, we quantify the temperature on the top surface as you can see over here.

So, this is the temperature profile seen on this arrangement of the tissue as well as the microheater assembly over here. And from this, you get the top surface temperature, you can see that we use a mobile holder over here which actually is used to very tightly connect or hold the mobile phone so, there is no misalignment of doing the measurements. And then we use the as you can see on the right side, the c and the d part, the c part d, the side view and it is the zoom part of this particular tissue sample and the tissue holder.

So, here you can see this is the sample tissue over here. And this microheater is placed below the sample tissue over here. So, here is the microheater and what you see over here is the top few of these this microheater over here. So, we have the microheater over here again and this is the area where it is heating up locally heating up the domain and then we have this is the tissue.

So, this is the tissue which is getting actually heated up and from this we actually; so, we have two different steps. The first is without the sample tissue so, that we can calibrate this

microheater and the second step is with the sample tissue, so, that we actually can quantify the top surface of the tissue sample and from there we calculate the bulk properties of the tissue.

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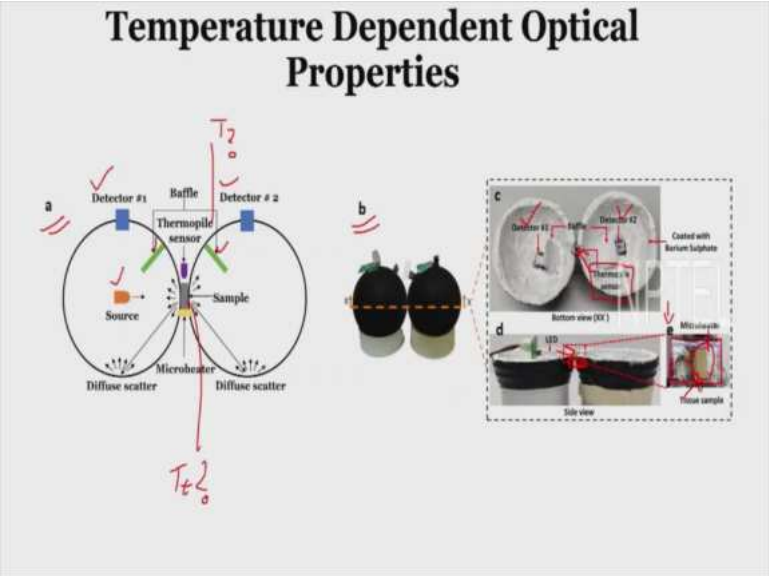

So, now, let us move forward and try to evaluate earlier we evaluated the reduced scattering coefficient and absorption coefficient for different different wavelengths that is 850 nanometres, 940 nanometres and 1060 nanometres. Now we also wanted to study the temperature dependency on these bulk optical properties. So, how do we quantify the temperature dependency?

So, in that case, what we do is we again go ahead with the earlier double integrating spear there is a detector 1 and detector 2 and over here we again have the same source with different different wavelengths. But in this case, we were assured that at 940 nanometres, they have very good delineation between normal and cancer. So, we used only a single wavelength over here 940 nanometres, you have the baffle over here.

So, that there is no direct light being detected from the backscatter as well as the forward scattering of these light from the sample. But now, at the same time, I also we also want to quantify the temperature of the tissue. So, what is the tissue temperature? So, how do we do that? So, in that case, to locally heat the sample tissue, we again use the microheater. And in this case, we also not just want to heat it.

But we want to give the feedback to the system as what is the tissue temperature. So, to give this feedback new thermopile sensor. So, this is a schematic on the left side and on the right side is the actual system. So, again, the double integrating sphere remains the same. And if you

cut open it from the bottom, you can see the two detectors, but in addition to it, you also see a thermopile sensor over here.

So, this is the thermopile sensor which is attached to the top part of the cross section of the in the top integrating spear from the side view, what you observe is the microheater assembly. So, this is the micrometre is placed somewhere over here. And therefore, you can just see from the top view that his image e you can see this is a micro heater which actually locally heats the tissue and this is the actual tissue.

This is the actual tissue over here and the light actually passes through the tissue here and then backscattered and forward scratches both, it happens. So, with this let us see with this arrangement, how do we actually quantify the bulk thermal properties that is the thermal conductivity as well as the heats specific heat specific heat of the tissue.

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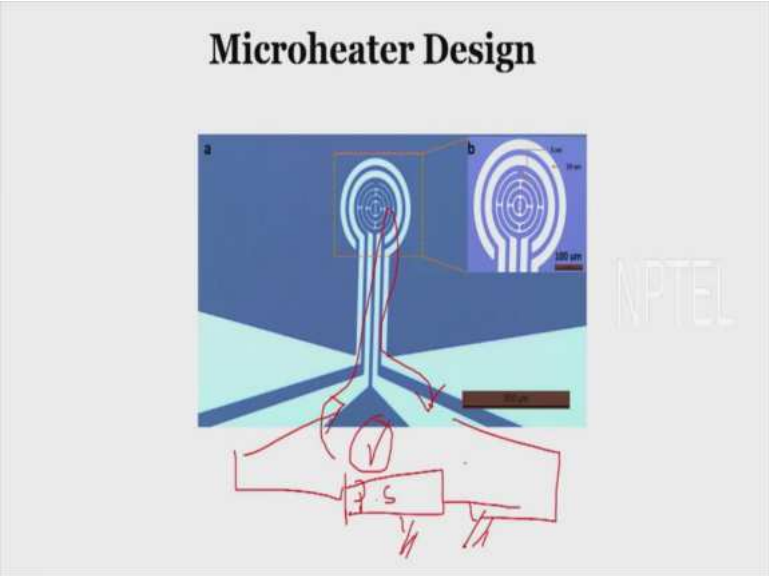

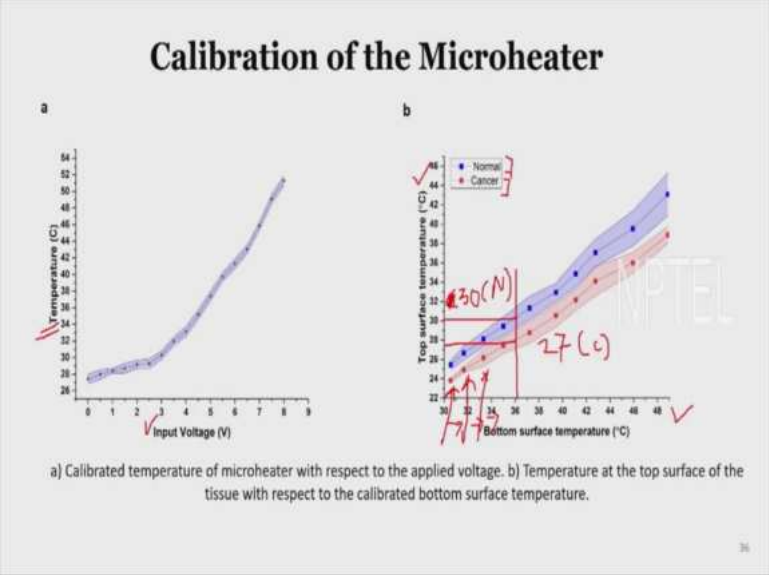

To quantify this. So, this is the design of the microheater, how does it looks like so, we have a circular arrangement of the electrodes and one part of it is getting the input over here and then it is the power supply that we give to the complete arrangement. So, this is actually grounded over here.

So, the first thing is the calibration of the microheater. So, we actually give an input so, this is the voltage input that we were talking about the this is the voltage input to the microheater, and the current which actually passes through this to this microheater. They are specifically designed for locally heating this tissue. So, we give different different inputs to the microheater, and then we quantify the temperature on the top of the microheater.

And that is done using the infrared camera that we have over here. And we do it for multiple times and then we average it out and that is what you see a band, error band over here. Then we quantify the different different normal and cancerous tissue. For different different normal and cancerous tissue, we quantify the bottom surface temperature and the top surface temperature.

So, what we observe is that if we heat for example at 36 degrees Celsius. If you heat the bottom of the surface of the tissue at 36 degrees Celsius what we have observed is that at the case of cancer the top surface of the surface of the tissue we get heated up by for example 27 degrees Celsius in the case of cancer, but in the case of normal it gets heated up very quickly.

So, example over here it gets heated up for around 30 in the case of cancer. So, it is around 3 degrees more in the case of normal as compared to the normal. So, in the in the normal it gets heated up by 3 degrees more as compared to the cancer. So, what do we do over here is that

for each step we keep heating for 2 minutes and then we go for the next step get it heated for 2 minutes again the next step so, this is the step by step process that we follow over here.

So, now we know for each normal and cancerous tissue, the top and the bottom surface with the function of time. So, from this how do we back calculate the thermal properties?

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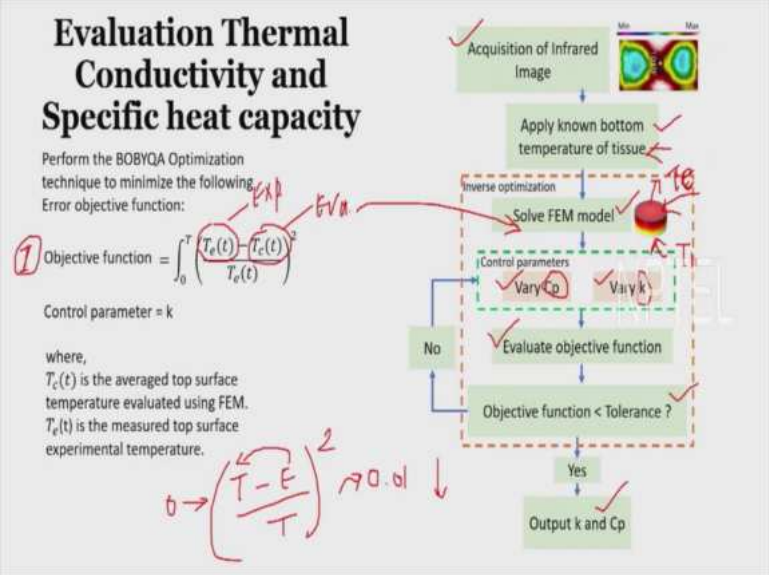

So, what we use is a inverse optimization technique. Inverse optimization technique is used when you do not know the tissue properties for example, in this case the thermal conductivity and specific heat of the tissue and from there you calculate the so, you do run off different different parameters. For example, over here thermal conductivity and C_p. C_p is the specific heat and from there you actually get the actual values of C_p and k.

So, let us see it a step by step. So, what do we do over here first thing is to define an objective function. So, this is the first thing to do the objective function is something like it is a variable which defines the $\left(\frac{T-E}{T}\right)^2$. So, when once this evaluated becomes very much close to this target value this actually turns out to be moving towards 0 and this it would be like very very small value and the square of that would be even smaller.

So, we try to minimise this value of the objective function and as you go ahead and minimise this value of the objective function. How we will minimise? By varying the value of control parameters that is C_p and k in this case. So, as you can see on the right side what we have is the acquisition of the infrared image. Then we apply the known bottom temperature of the tissue and at the same time we solve the FEM model.

So, we solve the FEM model of the tissue of this same uniform sample same dimension that is 5 mm diameter and thickness of 2 mm and then we give the same bottom temperature tissue bottom surface temperature to this over here have for these FEM model and we see the top temperature surface and then so, this this is the evaluated top temperature surface and the evaluated or the target temperature is actually the experimental value.

So, this is the experimental that we already know and T_c which is the evaluated that is actually coming up from the FEM model. So, we then vary this C_p as well as k and we do the time dependent optimization and then we evaluate the objective function if it is less than the tolerance, then if it is yes then it will give the output of k and C_p if it is no then it will it will actually again vary the value of C_p and k.

So, it will keep on wearing the C_p and k as long as the objective function is becomes very very less or because less as compared to the tolerance. So, in this case so, what we observe is that from this actually we can actually quantify the value of C_p that is the specific heat and the thermal conductivity k. So, this is the time dependent optimization problem that we perform and from this we calculate the value of C_p and k.

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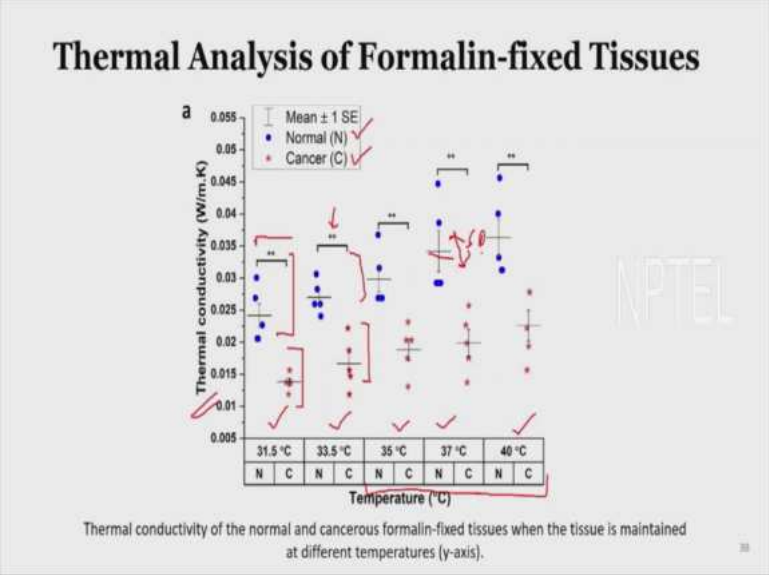

From this what we observed is we. This is the results of the system after performing the inverse optimization technique, what we observe is that for different different temperature. So, for example, at 31.5 degrees Celsius, at 33.5 degrees Celsius, 35 degrees Celsius, 37 and at 40 degrees Celsius we observe what is the value of thermal conductivity k for normal as well as cancerous tissue.

So, as you can see over here in the case of normal the thermal conductivity is very very high as compared to the cancerous tissue. The same is observed for all the temperature and this is the range of frequencies that we are interested in because all the biological tissues are actually surviving at this particular temperature actually still even lower, but this is the region of interest broad region of interest that we are interested in.

The start over here points to the significance that is statistical significance, we perform Mann Whitney U test for this case and what we observe is that it is statistically significant very highly statistically significant the value of thermal conductivity for normal and cancer, over here. The mean so, the line in the centre is the mean value and the one that you see over here is the standard deviation and that is ± standard deviation 1.

But what about the temperature dependency diffractive the scattering coefficients that will come in in the next slide.

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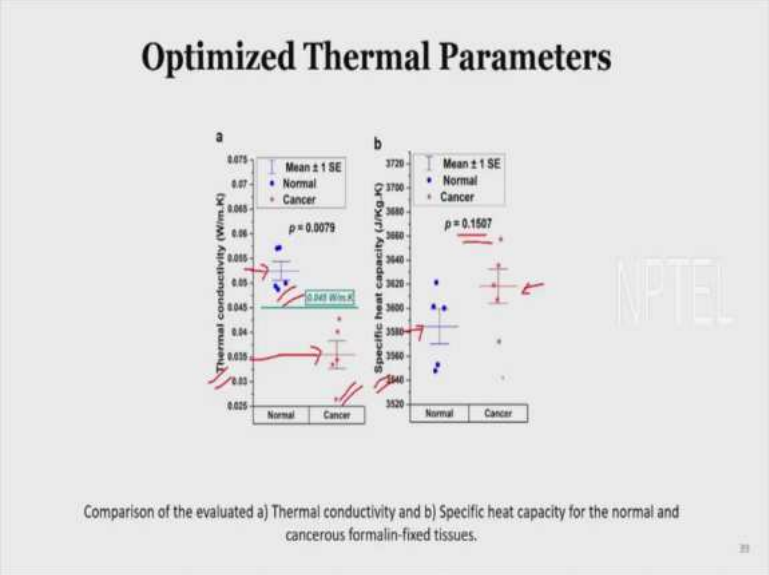

This slide talks about the average thermal conductivity and the specific heat. So, as we told earlier we will perform the time dependent inverse optimization technique and from there we calculate the thermal conductivity and the specific heat capacity of the bulk tissue properties. In this case what we observe is that again for the normal tissues the thermal conductivity is far higher as compared to the cancer's.

So, this is not a function of temperature now, but it is for the average along the complete ramp up of the temperature. So, the normal template and for normal a normal thermal conductivity was far higher mean around 0.05 to 5. But in the case of cancerous it was around 0.035 watt

per milli Kelvin the mean values. So, far difference in the normal and cancerous tissue and that is one of the reason behind this was the presence of the collagen in the case of cancers and the presence of lipids in the case of normal tissues.

So, the lipids have a comparatively higher thermal conductivity as compared to the other tissue constituents. So, you in the case of normal there are more lipid content and because of which the thermal conductivity actually increases. The increase in thermal conductivity also means that the heat can flow very easily through this tissue and that is why there is a very high rise in the top surface temperature in the case of normal as compared to the cancerous tissue.

We also quantify the specific heat capacity that is how much the tissue is able to hold the heat. In this case we will observe that the mean value of the normal is is lower as compared to the cancerous tissue. But there were regions where we were getting overlapping valleys of heat capacity. So, we there is no statistical significance with which we can differentiate normal and cancerous tissue.

So, thermal conductivity is a better variable to quantify the normal cancerous tissue as compared to the specific heat from this particular model. So, the next part is to quantify now, the optical properties and how the optical properties actually vary with the rise in the temperature.

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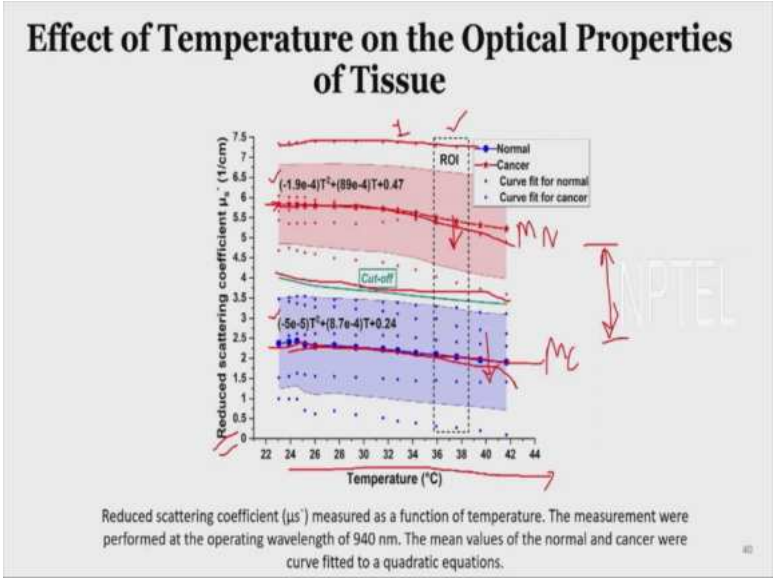

So, as you can see in the this slide what we observe is the rise in temperature. So, what we do is the rise in temperature of the tissue that is the experiment that we followed over here, this is

the experiment that we are now talking about the results. So, over here the as the tissue temperature rises, we quantify the reduced scattering coefficient.

Again, this is the inverse adding doubling method that we used using the Monte Carlo method and over here we get the M_r, M_t values give it to the system which runs the Monte Carlo method and then we quantify the reduced scattering coefficient as a function of temperature. Over here, each star that you see over here this each line over here represents a single sample tissue.

So, you can see multiple dotted lines over here and each of them represents a particular tissue. The centre line which you see over here is the mean value that is a mean for normal and the line that you see over here is a mean for cancer. So, this is a very high differentiation of optical scattering coefficient with normal cancer specifically for reduced scattering coefficient for all the wavelengths for all the temperature in the system and specifically in the region of interest that is around 36 to 38.

We see the very good delineation between normal and cancer tissue. We can also come up with a cut-off line that you see over here, which can easily differentiate normal and cancer. We perform this curve fitting and come up with the equation of how the temperature is related to the μ_s that is the reduced scattering coefficient. In this case, we come up with a polynomial equation with the second order quadratic equation.

The next thing that we observe is that the scattering coefficient actually reduces as we go on increasing the temperature. So, this trend of reduction of the reduce scattering coefficient was also observed and the main reason for this is because, as the tissue temperature issue goes on increasing what we observe is the volume expansion of the of the tissue and because of the expansion of the tissue, the scattering actually reduces.

And because the scattering reduces the scattering coefficient which account for the total number of scattering also reduces and that is why you see that as you go on increasing the temperature the reduce, scattering coefficient also reduces because of the thermal expansion or the volume expansion of the tissue.

This volume expansion would still be in order of like in order of few micrometres or so, which cannot be quantified very easily with the system that we have right now, but that is significantly enough to quantify the difference in the reduced scattering coefficient. And with this, how much is the slope of this lowering of this reduced scattering coefficient we can actually can quantify whether it is normal cancer.

As you can see over here for the normal tissue the slope of the reduction is very high as compared to the cancerous tissue. So, that could also be a factor with which you can actually delineate the normal in the cancerous tissue.