Fabrication Techniques for Mems-based Sensors: Clinical Perspective

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Lecture – 24

Hi, in last class what we have seen? We have seen how we can measure the mechanical property of tissue. So, we were interested in measuring the elasticity of tissue right. And for measuring the elasticity of tissue what kind of sensor we have designed? We have designed a piezo resistive micro cantilever.

So, just to quickly recall we have a tissue, we have a tissue placed on a glass slide and we have a cantilever, that we are pressing on the tissue, and a cantilever bands depending on the elasticity of tissue the cantilever will bend.

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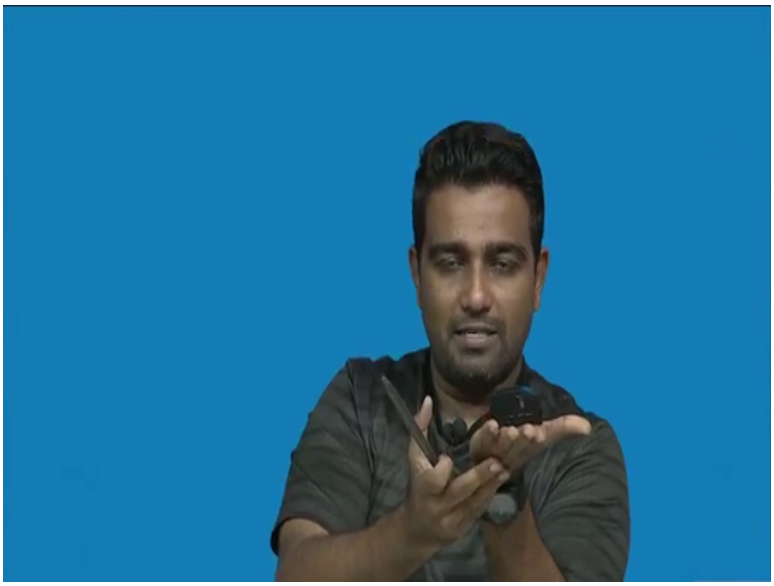

Now this cantilever is embedded with what piezo resistor. So, when it bends, there is a change in the resistance of the cantilever. This change in the resistance of the cantilever can be correspond or can be equate to the elasticity of the tissue. That is what we have seen, right and if we can measure the mechanical property of tissue, then how about electrical property of tissue. So, when I talk about electrical property of tissue, what it can be? It can be a resistance; it can be impedance.

So, today's module is focused on how to design a sensor based on micro technology to measure the electrical properties of tissue. Now what are we getting by measuring the electrical property of tissue? Our goal is that as the cancer progresses, as disease progresses will the electrical property of tissue change? And if we can correlate somehow using this sensor that as the disease progresses the tissue property changes, then that can be a marker apart from the existing gold standard that is the biomarkers IHC, MRI, mammography.

Now, we are adding one more modality based on the electrical property. Last time we have seen mechanical property. So, how can we design this sensor? How can we design this sensor? And it is again the heart of micro technology is photolithography right. So, let us see extremely easy way of designing this particular sensor using the photolithography and it is application in measuring the electrical properties of tissue.

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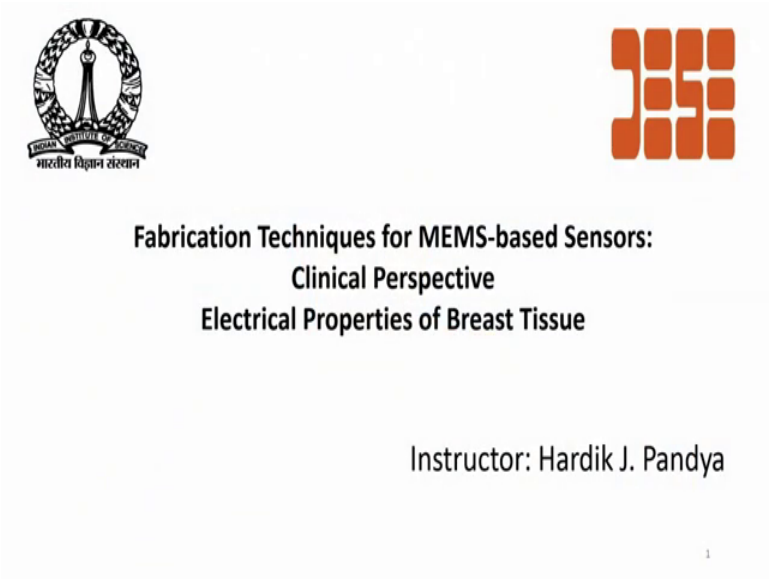

So, if you come into slide, we are interested in measuring the electrical property of breast tissue.

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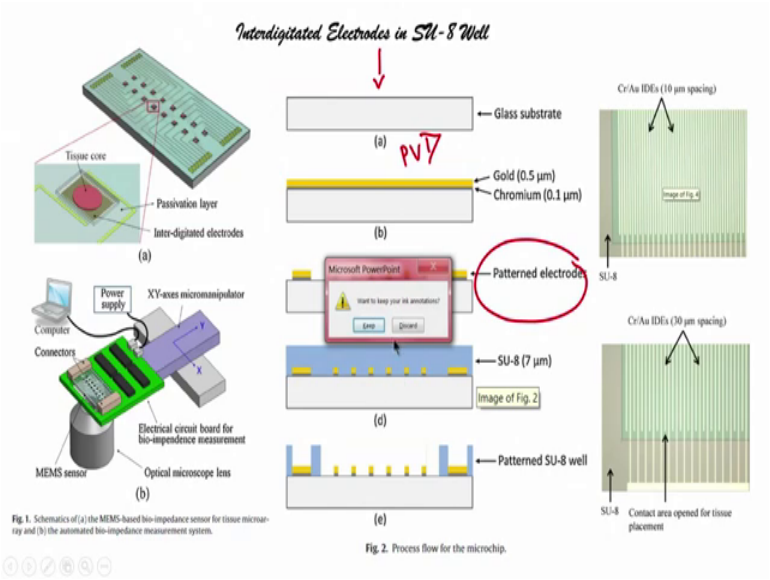

Fig. 1. Schematics of (a) the MEMS-based bio-impedance sensor for tissue microarray and (b) the automated bio-impedance measurement system.

Fig. 2. Process flow for the microchip.

So, this is the process flow what we can see? If you see on the left side, this particular chip, these are array of sensors and each sensor consists of an inter digitated electrodes inside SU-8 well. So, if I place a tissue which is shown here onto this inter digitated electrode are inter digitated electrodes, can I measure impedance? Can I measure impedance of this tissue right; so, let us see.

So, if you concentrate on the this process flow, the first process, first step is to take a glass substrate. Then we will use physical vapor deposition, either E beam evaporation or thermal evaporation to deposit chrome gold; followed by patterning electrodes, followed by patterning electrodes. So, how we can pattern this electrode? Right, how we can pattern these electrodes? So, let us do like this. Let me draw the process flow for you so, it becomes easier, it becomes easier.

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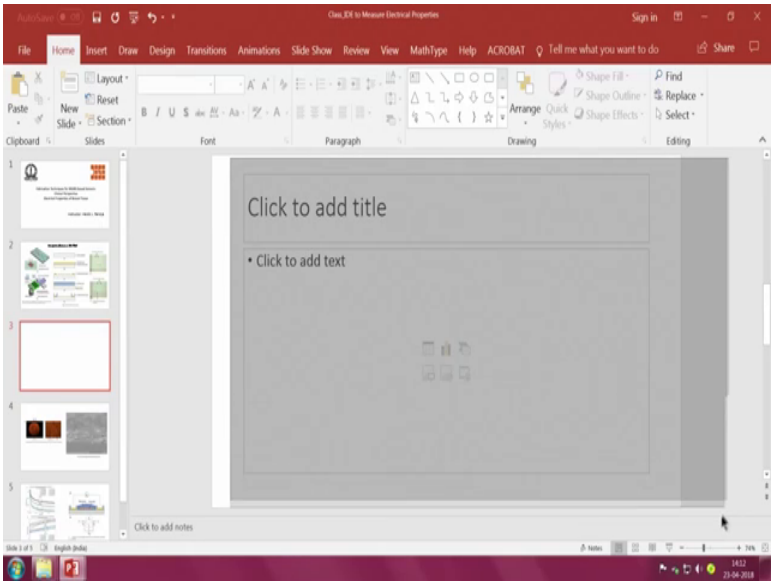

So, what we have seen? If you see we will be, we will be concentrating on these steps these 2 steps. From depositing chrome gold on glass to formation of pattern inter digitated electrodes. How can we do this ok?

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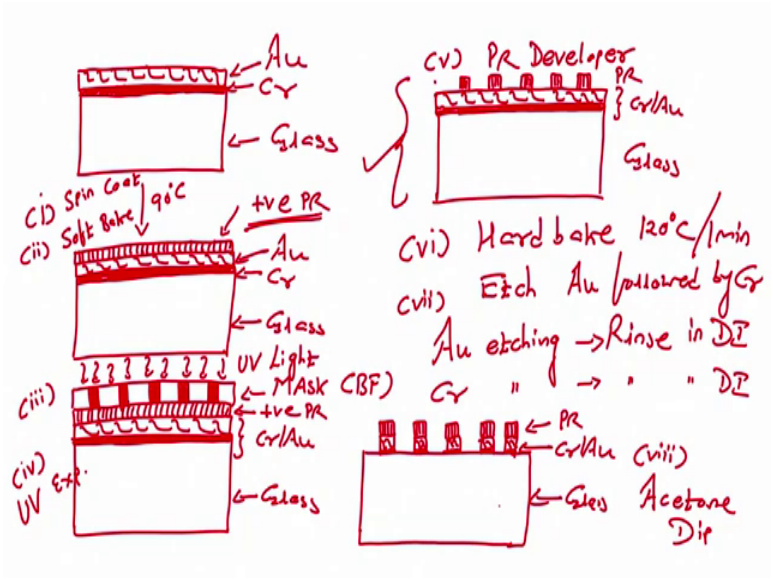

So, what we have? We have a glass substrate on which we have a thin layer of chrome and gold, gold chrome glass. So, what will be the first step? First step would be to spin coat photoresist, to spin coat photoresist which kind of photoresist? Positive photoresist so, let us draw photoresist in this particular format, this design and we have our gold and

we have chrome; so, glass chrome gold and positive photoresist. Next step, what is the next step? Next step would be to load the mask, to load the mask what kind of mask bright film mask, right. Now it should be very easy for you guys to understand, what kind of mask you will use? For which kind of pattern we have to use?

If we are using positive photoresist, then which kind of mass we can use if there is a negative photoresist, then which kind of mask we can use right this can be now very easy for all of you to understand, since we have learned photolithography in detail in our earlier lectures. So now on this I will load, I will load right film mask, right. A bright field masks field is bright. So, it is bright field mask what kind of photoresist we have? We have positive photoresist. So, what will happen? If I expose this wafer if I expose this wafer, then the area which are not exposed, the area which are not exposed by UV will become stronger.

The area which are exposed will become weaker, right this is your mask. This is positive photoresist right. And this one would be your chrome gold, this is your glass. So, first step is step one would be to spin coat for positive photoresist. After that, step 2 would be to perform soft bake right. Spin coat second would be soft bake 90 degree centigrade 1 minute. Step 3 would be load the mask and this is what kind of mask? Bright field mask, step 4 would be UV exposure.

So, step 4 would be we will expose the wafer with UV light right. Next step would be, step number 5 would be to unload the mass gain photoresist developer. So, when you dip the wafer in photoresist developer what you will get? When you dip the wafer in photoresist developer you will get pattern which I am drawing right now, correct? We will get this particular pattern. So, what would be my next step? Step number 6 would be hard bake, 120 degree centigrade 1 minute, right.

Next step 7, next step would be to dip or etch, etch gold for load by chrome etch gold followed by chrome. How can we do that? We have to dip this wafer, we have to dip this wafer in the gold etchant after gold is at, we can live the same wafer in chrome etchant. And after you dip the wafer in gold etchant, you have to wash, you have to rinse it. You have to so, after gold etchant after etching gold, gold etchings you have to rinse wafer in DI ok, deionized water.

Then you have to perform chrome etching followed by rinsing in DI ok. So, when you will do that, what you will achieve? You will get, you will get wafer with chrome gold protected where there was photoresist. And when therefore, where the photoresist was not there the chrome and gold got etched right, chrome and gold got etched. So, this is your photo resist, this is your chrome gold and this one is your glass.

Next step would be next step would be, step number 8 would be acetone dip acetone dip. Why did I base it in acetone to? To strip of the photoresist, to strip the photoresist, we have to dip the wafer in acetone. When we dip the way for an acetone what you will have? You will have this pattern; you will have a pattern of inter digitated electrodes. If you see here, what we got a pattern of inter digitated electrodes from a glass coated with chrome gold, right.

Now, what we said that, we said that these inter digitated electrodes should be inside SU-8 well right. So, for that what are the process? So now, we know that we know that so, I will just clear this one. We know that we have a wafer a glass wafer with inter digitated electrodes right. We have glass wafer with inter digitated electrodes and what we want? We want we want that the interdigited electrodes should be within a SU-8 well within a SU-8 well.

So now we have to perform we have to perform a photolithography in a way that we can create SU-8 well, we can create a SU-8 well. And when we look inside the well we can see the inter digitated electrodes. When we look inside the well we can see the inter digitated electrodes.

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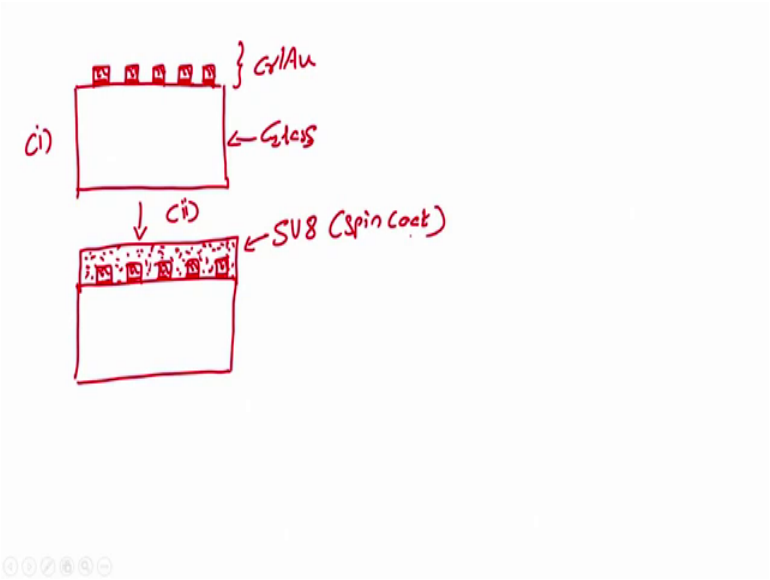

So, let us start the process. This step one, step one would be to take the wafer, last wafer with inter digitated electrodes right, chrome gold. Chrome and gold next step; next step would be to spin coat, spin coat positive as spin coat SU-8 onto the wafer right. We had to spin coat SU-8 on to the on to the wafer having a pattern of inter digitated electrodes su-8. Just let me draw the SU-8 with some different design; which is your dotted one, dotted design alright.

So, what we have done? This is we have taken wafer with chrome gold glass wafer, then as step one what we have done? So, this is step one of course, the step 2 would be to spin coat, spin coat SU-8 onto the wafer right.

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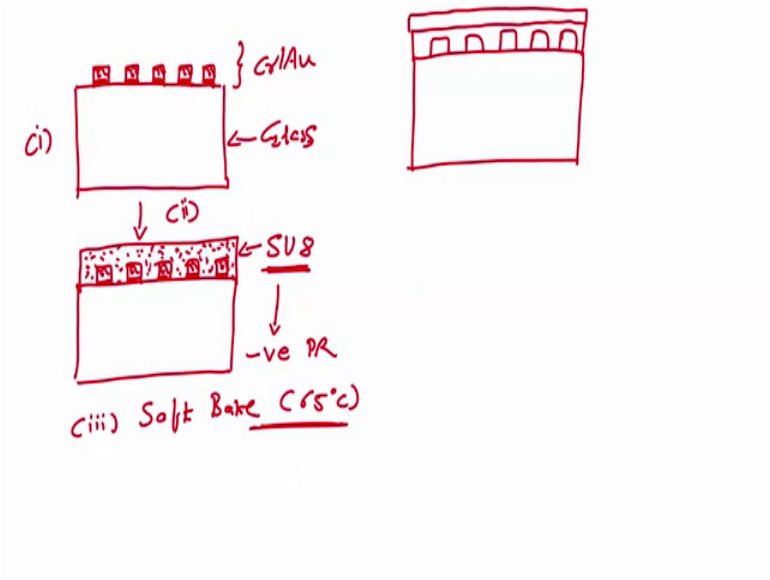

Now step so, what is su-8? SU-8 is a negative photoresist, SU-8 is a negative photoresist, alright; so, after you spin code su-8, the next step would be, step number 3 would be soft bake. Soft baked, now in case of su-8, the soft bake temperature is around 65 degree centigrade, depending on the thickness of su-8, the time for soft bake would be different. After soft bake, we have to load this su-8, load the wafer spin coated and soft bake with su-8, spin coated with SU-8 and soft bake with a mask with a mask. So, what kind of mask we will use? We will use a mask; so, let me let me draw it little bit in the center of the screen so that we understand clearly.

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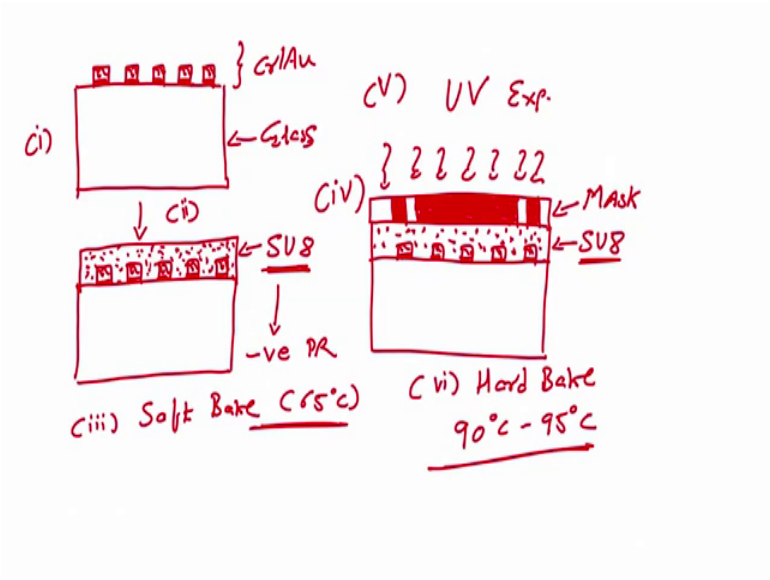

There is very important process, very important process ok. So, what we are talking? We are talking that we have inter digitated electrodes, covered bySU-8. And then on that we are loading a mask, SU-8 is SU-8 is a negative photoresist. So now SU-8 chrome gold and this is a mask. So, in case of in case of negative photoresist, what will happen? The area which is not exposed, the area which is not exposed will become the area which is not exposed will become weaker. The area which is exposed will become stronger right. What we want? We want well we want a well. So, what we will do? What kind of mask we should design? We should design a mask in this particular fashion.

So, stay with me the area which is which is not exposed will become weaker hm. So, if I draw a mask, in this particular fashion and perform you will lithography hm. Why we want to do this? You see here, you see here what I want? I want to remove from here, I want to remove from this area right. So, if I draw this kind of mask right, if I use this kind of mask and perform UV photolithography what will happen? The area which is not exposed by SU-8 will become weaker right, and the area which is exposed will become stronger will become stronger correct.

So, after UV exposure, after UV exposure what we had to do? Next step would be this would be 4th step and UV exposure would be fifth step right. UV exposure would be 5th step loading mask would be 4th step ok. After this 6th step would be hard bake. There is

little bit trickier compared to negative photoresist SU-8, after soft bake and UV exposure you to perform hard bake before you go for developing the SU-8 material.

So, hard bake is done around 90 to 95 degree centigrade for x amount of time depending on the thickness of SU-8, ok. So, that is the next step right, after hard bake you have to develop SU-8, develop SU-8.

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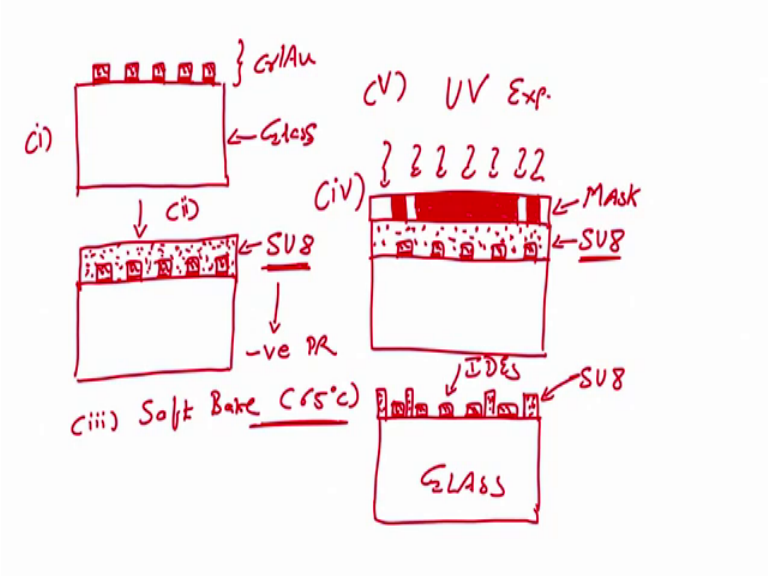

When you develop SU-8 what will get? You will get a wafer which looks like which looks like this. Sorry about that ok. And this would be correct. So, SU-8 and this one is our inter digitated electrodes with chrome gold right. So, this one would be my SU-8, this one would be my inter digitated electrodes right. And this is my glass right. So, when I perform this experiment what will I get? I will get a pattern SU-8.

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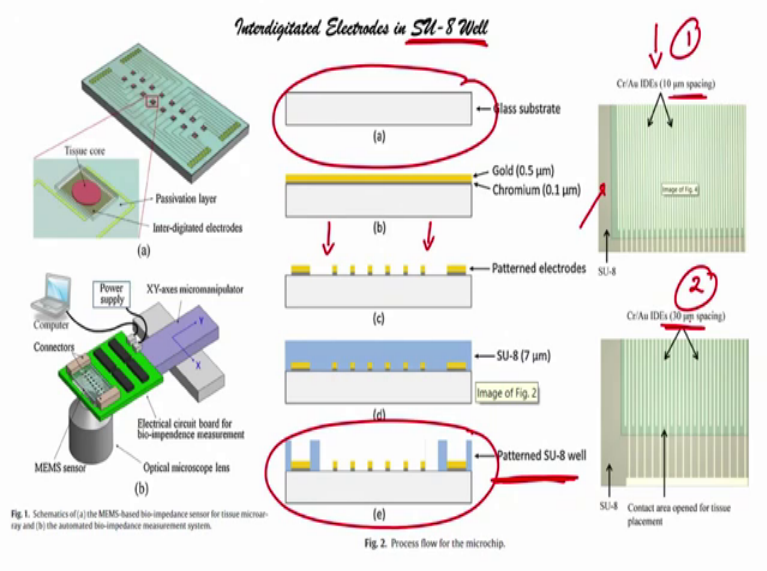

Fig. 1. Schematics of (a) the MEMS-based bio-impedance sensor for tissue microarray and (b) the automated bio-impedance measurement system.

Fig. 2. Process flow for the microchip.

I get a pattern SU-8 well right so, from glass to and inter digitated electrodes within SU-8 well we are seen the process. So, how it will look like? I will look like, it will look like the one shown in this particular figure. What is this figure? All about it there are inter digitated electrodes which are off chrome gold, and this inter digitated electrodes are within SU-8 well. There is some difference between this figure number 1 and figure number 2. What is the difference? You see closely this spacing between the inter digitated electrodes is about 10 microns.

The spacing between individual electrodes in figure number 2 is 30 microns. The width of the inter digitated electrode, each electrode the width is 10 micron; so, 10-micron width 10-micron spacing, 10-micron width 30-micron spacing, ok. So, this is how we can fabricate an inter digitated electrode in an SU-8 well, you can also say that this is a biochip, this is a bio chip. Now, on these inter digitated electrodes we will place tissue.

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So, if you see this particular figure what you see here is, we have placed a breast tissue core a breast tissue core on to the inter digitated electrodes right. And the thickness of breast tissue core is close to 4 microns. 3.83 to 4 microns, this is a cross sectional image of the breast tissue core, this one, SEM image cross sectional image of the breast tissue core.

You can see here the in the inter digitated electrodes at 20 x magnification, this is at 4 x magnification, inter digitated electrodes inside SU-8 well, on which the breast tissue core is placed. So, what we will do now? Once we place the breast tissue core, to keep the breast tissue core in a intact position we have to load something called PBS forceful buffer saline, alright. So, that the tissue is preserved so that the tissue is preserved.

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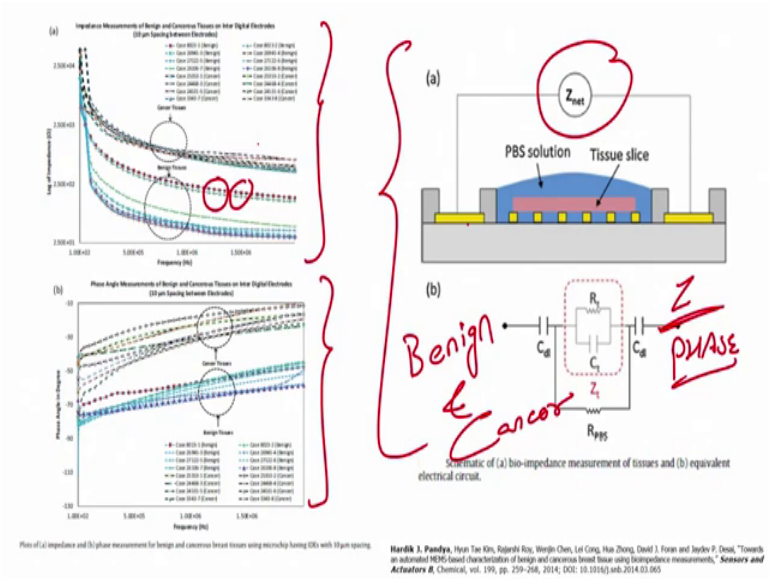

So now, if I load this PBS on to the tissue, then it should look like this right; that I have the contact which is for measuring the impedance, I have a tissue slice, which is my breast tissue slice, and then I have PBS solution to preserve the tissue. So now, if you so closely see, what we find? We find that the electrodes from here to here forms a double layer capacitance, from here to here again forms a double layer capacitance.

This tissue and PBS solution will form the resistance and capacitance; which will be your Z t there will be resistance of the PBS solution, which is your R PBS; so, schematic of the bio impedance measurement issue an equivalent circuit you can see from this particular figure, right. So, what we are measuring now? We are interested in measuring the impedance of the tissue; which is your net impedance, which is your net impedance. So, how to measure that? How do we say that? We will use, we will use impedance an impedance analyzer, will use an impedance analyzer and we have tried 2 different kind of tissue, one is benign and another one is cancer, benign and cancer.

And we have measured impedance as well as the phase impedance and phase. So, what we found? We found that around 200 kilo hertz, around 200 kilo hertz, we were able to delineate the cancerous tissues from the breast from the benign tissues; the cancerous tissues from the breast or breast cancer tissues from the benign tissues, benign tissues.

Now, this method of using the inter digitated reactors within the SU-8 well can be used to delineate between benign and cancerous tissues right, if we have the impedance analyzer. And we are consider several cases; which we can see in this particular figure. And which kind of electrodes we have used? We have used the electrodes which are 10 microns in spacing and 10 microns in width, because the 10 microns in spacing and 10-micron width electrode would cover a better area cover a large area of the tissue compared to a 30 micron wide electrodes, the sensitivity will be different. If not at all in a simple terms, the sensitivity of the electrodes which is this electrode number 1 would be higher compared to the sensitivity of the electrodes which are 30 micron spaced and 10 microns in width.

So, the results that we can see here are obtained using 10-micron width electrode with 10-micron spacing. Same thing if you can see for the phase angle, you can clearly see that we can delineate the benign tissues from cancerous tissues based on phase as well. Now, one thing to measure here are to understand here is that, if you see these cases right, these cases are much more closer to cancer tissues. What could be possible reason? What could be possible reason?

The reason was that this tissues where order, this tissues where way older. So, how we got this tissue? We why we got this tissue from tissue bank so, in the tissue bank they preserve the tissue. So, these tissues were older compared to this tissues, this is used when comparatively freshen, newer and with time also you see the change in the property of the tissue. So, the our idea is not to wait and get the tissue from the tissue bank, but to understand the properties of tissue from the biopsy, from the immediately after biopsy.

Immediately as soon as the tissue is taken out, we should have some kind of technology, that can measure the electrical, mechanical and thermal property of tissue and get the understanding between the normal tissues, benign tissues, invasive ductal carcinoma, lobular carcinoma and as well as in situ. Lobular carcinoma in situ right, ductal carcinoma in situ, invasive lobular carcinoma, invasive ductal carcinoma, benign, normal; this delineation can be made. And, we can aid the clinician we can aid the pathologist using this tool that we are planning to develop. For understanding the electrical mechanical and thermal property of tissue, first thing is to understand the mechanical property of tissue, then we can measure with the help of cantilever.

Now, we in this in this lecture on this module what we have seen electrical property of tissue. So, how can we integrate electrical and mechanical both sensors onto one chip? And, if we can measure electrical and mechanical what about thermal property; can we indicate all 3 2 things together? Electrical mechanical and thermal properties and have a bio chip, on which we can load the tissue and get the measurements and get the delineation. Along with the existing technologies, we are not replacing any technology, what we want is we can aid the pathologist to reduce the false positive and false negative signals, right?

So, what we understand from here is; now we can measure the mechanical property of tissue, now we can measure the electrical property of tissue. So, in the next module we can design a sensor that can perform both electrical and mechanical property of tissue, right. So, we will I will see you in the next class, till then you just go through this particular module once again, understand it how you can fabricate a simple sensor to measure the electrical property of tissue.

Now, when I talk about tissue is not just limited to tissue, it can be used for understanding the properties of cell. So, if you load the cell and measure the property of cell you can again delineate between normal cells and cancerous cells right. So, I will see you in the next class, till then you take care. And read this thing once again so that when we understand the next sensor in the next module, you can correlate the understanding of this particular module with the next one.

I will see in the next class, bye.