Introduction to Biomicrofluidics
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Lecture - 19
Microfluidics for Healthcare

In the previous few lectures, we were discussing about some fundamental aspects of microfluidics, of course, keeping the biological applications in view. However, we have not specifically discussed how microfluidics can impact the healthcare scenario. And in the remaining two lectures, we will be focusing on some aspects of microfluidics for healthcare. So, I would like to let you know that microfluidics for healthcare is very much specific or centric to the location at which the healthcare is delivered.

So, microfluidics for healthcare should not be treated in the same way as for example, it is done in an advanced country as compared to what is done in a resource limited setting. So, one has to be careful and it has to be an integrated teamwork that delivers the healthcare at the location using microfluidics as a tool. Before getting into the details of how this is possible, let me talk about a specific example. Let us say that there is a patient who is suffering from fever in a rural place.

Now, normally when the patient is suffering from fever; it I mean one ways for may be 1 or 2 days or 3 days, because in most instances the fever will go away by itself within just a couple of days or may be three days like that. However, there are instances when that is not the case and then further intervention is necessary. So, when we say further intervention we of course, mean some basic diagnostic tests. So, these diagnostic tests may involve blood as a body fluid.

So, when we take a this into account, we have to keep in mind that the person who is there in a rural sitting and may be at extreme remote location, the person has to travel a long distance to go to a primary health care center where the blood sample is taken. And remember that this distance on an absolute scale may not be too large, but in a condition when the patients health is not so good, the road conditions are not so good, and the transport available is not so modern, it becomes very very challenging to take the patient to that location, forget about cost and time; even the hazard issues that play a big role.

Then in a primary healthcare center some blood sample is drawn and it is normally like it depends on how many tests are done, but normally at least one syringe full of blood and depending on the age of the patient that can itself give rise to an agony. For example, it is it may get very challenging to get to take this blood sample from very young child because of obvious reasons; and then this blood sample has to be transported from this primary healthcare center to another pathological lab which depending on the need or the level of sophistication demanded, it may still be located at a far away distance and then this test will be executed.

So, after this tests are executed then these results come out and sometimes it takes one or two days for this tests results to come out. And then actually by the time the result is available with the doctor treating the patient, the patient's condition may worsen. So, it is it is not a question of just the money that the patient can afford for the test, but also the time and other hazards. So, instead of this kind of a paradigm can we think of a situation, where instead of bringing the patient to a hospital, we make a small handheld hospital which is a mobile device and bring it to the patient make a finger prick and take one drop of blood, blood I am talking about as an example; but it could be urine, saliva or any type of body fluid.

And then using these we perform a diagnostic test on the handheld device itself, and very rapidly we can get a readout which we can then use for subsequent treatment of the patient. So, it not only saves time, not only saves hazards, but also brings down the cost considerably. So, if implemented in a appropriate manner with a appropriate controls and appropriate studies, validations studies prior to the implementation, then such a diagnostic procedure may actually revolutionize the way in which diagnostics is done in the rural scenario.

So, not just diagnostics there could be many other applications where microfluidics could be used in this way. And to emphasize the need of a team work, it is not just the question of microfluidic as a science or microfluidics as a technology, it is a team work between social workers, medical practitioners, entrepreneurs, engineers, scientists all together to come up with solution of such challenging problems.

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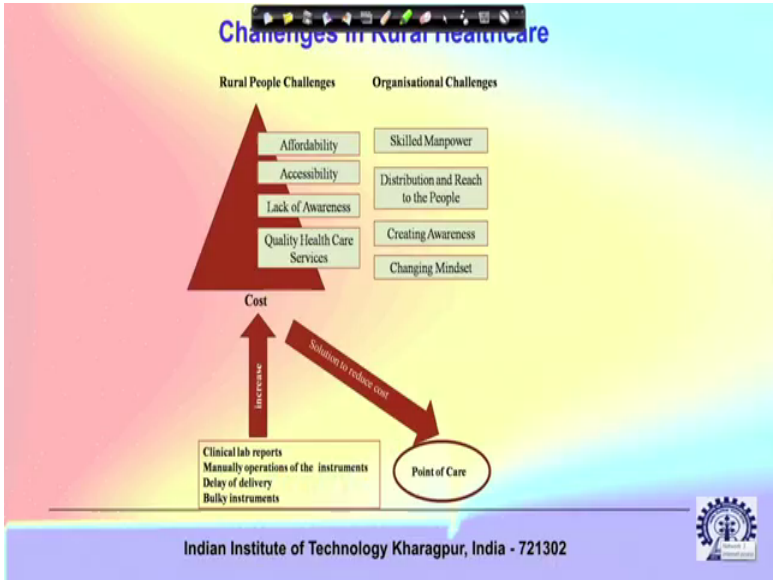

So, let me discuss then some of the challenges in rural healthcare these challenges are important, and I would say that some of these challenges are possible to be overcome by microfluidics based technology. So, first is affordability, second is accessibility, third is even lack of awareness, which is itself a big thing in resource limited settings and the quality of healthcare services. So these are challenges mainly related to the rural scenario. And eventually all these aspects result in an increase in cost, there are also organisational challenges like there is scarcity of skilled man power who can do pathological work or sophisticated pathological work, distribution and reach to the people who need medical attention is quite poor, creating awareness is a challenge and changing the mindset of people is a challenge.

So, these people if they are essentially depending on the clinical lab reports and then there are certain associated implications like manual operation of instruments, delay of delivery, requirement of bulk instruments all these essentially increase the cost. So, one should go for a solution which is rapid and at the same time cost effective and that essentially is the paradigm of point of care diagnostics.

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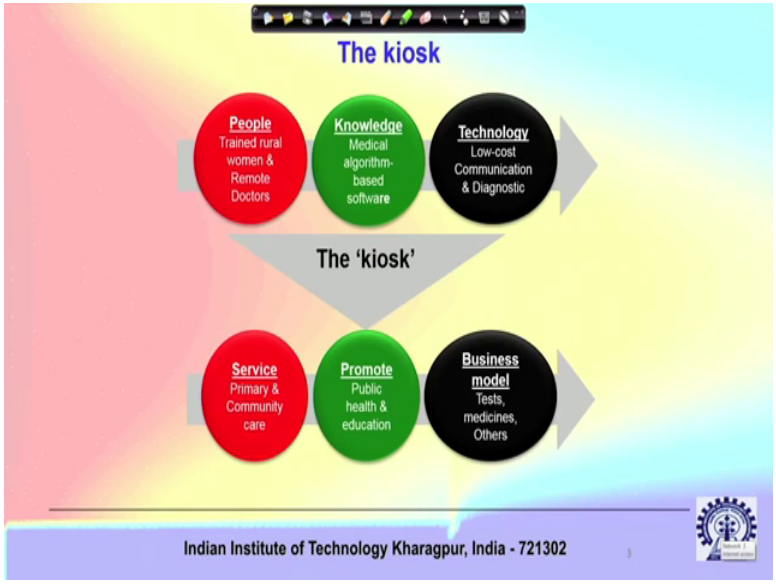

So, when we talk about point of care diagnostics we should have also a broad perspectives. So, what is point of care diagnostics? It is essentially that instead of bringing the patient to a diagnostic center or a hospital; you make a handheld device which you bring to the patient and wherever the patient is there; may be at the hospital bed, may be at home or wherever you bring that device and use that device for the diagnostic purpose. So, it may use the body fluid or it may not use the body fluid, it may use some other body signals may be so, but it should be at the site of the patient instead of been located at a fix site.

So, now I want to talk about something which is a broader perspective. So, where will this be implemented? So, already there are avenues by which it is possible that by remote technology or by using the internet of things combined with telemedicine and other remote technologies, it is possible that even though most of the sophisticated doctors are not physically there in front of the patient, but the patient some care is given to the patient through computer based database system where the interface between the patient and the technology is not very sophisticated doctor, but train rural women and remote doctors. So, this is the resource that you will have as human resources.

So, the human resources are essentially you know some young girls, who are trained to take care of the minimal requirements of interrogating the patient and putting that information in a database; and making basic physical examination like may be blood

pressure, height, weight and all these things. The knowledge based is medical algorithm based software and the technology that is supposed to be there associated with it is low cost communication which is a part of the communication technology and diagnostics.

So, based on this there is a concept called as health kiosk, which one of our collaborators I will acknowledge all the collaborators who have effectively contributed to our research here in this domain. So, essentially they have setup some small health kiosk. So, these health kiosk are basically small centers, where the service is primary and community care, the objective is to promote public health and education and also develop a business model for tests, medicines and others.

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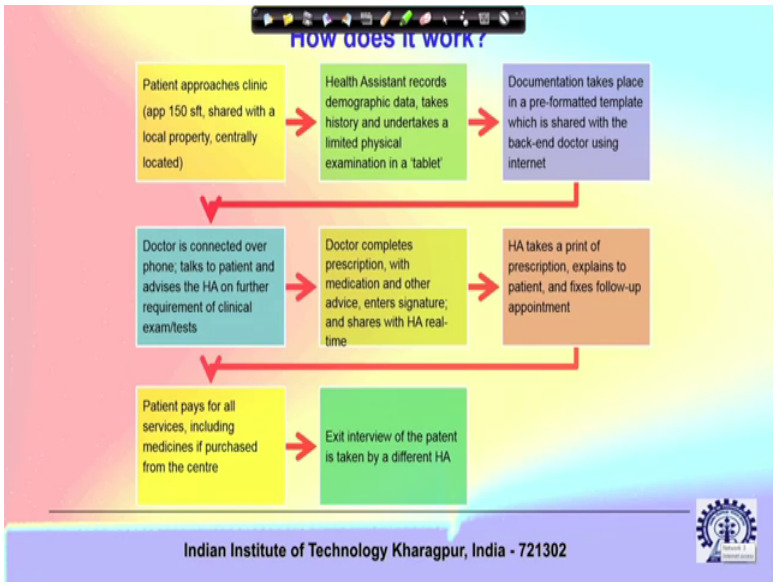

So, question is how does this work? The patient approaches the clinic which is approximately 150 square feet shared in a local property, which is centrally located in the village. The health assistant records demographic data takes history and undertakes limited physical examination in a tablet, then documentation takes place in a preformatted template which is shared with the backend doctor using internet. Then the doctor is connected over phone, talks to the patient and advices the health assistant on further requirement of clinical exam or tests.

Eventually the doctor completes the prescription with medication and other advice, enters signature and shares with health assistant in real time. The health assistant from the computer takes a printout of the prescription, explains to the patient and fixes a

follow up appointment; this is not free of cost or driven by charity that patient pays for all services including medicines if purchased from the center. And then ether is exit interview of the patient taken by a different health assistant.

So, now an obvious question will come to your mind that what is the cost that the patient has to pay for this. So, because of the limited infrastructure that is used and large number of patients attending a kiosk, may be only a few rupees the patient has to pay as the part of the consultation fee. And of course, the price of medicine as per actuals; however, the bottleneck is the cost of diagnostics.

So, for example even if the patient is paying rupees 10 for a medical consultation which may be affordable, but if the patient now has to do a set of medical tests what thousands of rupees, it may not be easily affordable. So, the real bottleneck of implementing this kind of technology or implementing this kind of a concept in a paradigm where the essential feature is low cost, the entire technological bottleneck is making the diagnostic procedure of low cost.

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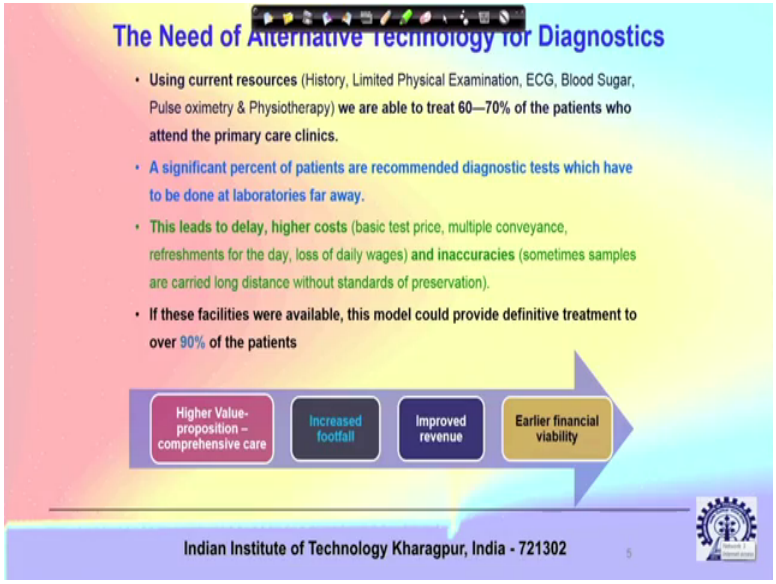

So, there is need for alternative technology for diagnostics. So, a significant percent of patients are recommended diagnostic tests, which have to be done at laboratories far away. So, this as per the current resource constraints is done in the rural health rural healthcare kiosk, these leads to delay higher costs and inaccuracies. And this is the very significant thing. The origin of this inaccuracy is that sometimes samples are carried long

distances without standards of preservation, because sample preservation is a very very important aspect of you know doing coming up with correct pathological results.

So, if a blood sample is taken and it is transported to a distant place without being preserved properly, this can give rise to erroneous predictions. Not only that, if there is delay in predicting the results that can lead to higher costs, not just because of basic test price, multiple conveyance, refreshments for the day, but also loss of daily wages of the patient because of long waiting time. If these were available, this model could provide definitive treatment to over 90 percent of patients.

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So, point of care diagnostics in a rural setting is a very big challenge, and then one requires the paradigm shift. So, when we go for a paradigm shift, this is where technological intervention is important, for example, power. So, in the rural places, the power supplies often erratic, often it is not available, and often it is of poor quality. So, one can go for innovation, for both battery and power operated systems. Environment, this is a big challenge.

Most of the times, the traditional pathological tests are done in very sophisticated air condition laboratories, where the conditions are very carefully controlled. Whereas, in the rural settings, we have heat, dust, humidity all these things are important. So, the technology must be robust, so that even in the presence of heat, dust, humidity, the results should be accurate.

Reagents, in the scenario, the refrigerators or air-conditioners do not work. Supply-chain, it does not exist. Skill sets, trained technicians are not mostly available. Blood draw, trained practitioners or trained experts for blood drawing are not available. And cost, there is a lot of price-sensitivity, so the cost needs to be cheap. So, you can see that for transforming, the pathological laboratory based tests. Two point of care tests, there are lots of technological challenges, and some these challenges are techno economical or techno social.

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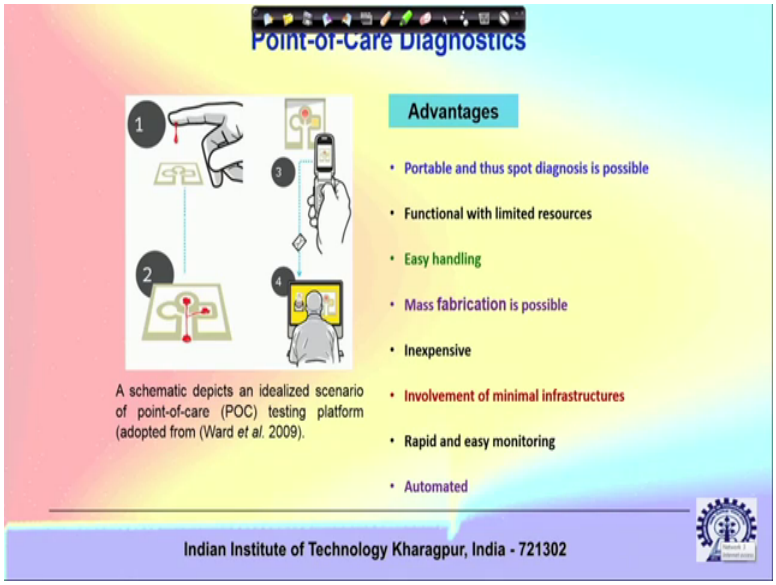

So, this is the paradigm of point-of-care diagnostics that we talk about, so instead what we design is something like this. So, there is a handheld device, I will explain that what are these handheld device in the reaming part of this lecture and the subsequent lecture. So, look into this slide, consider the step 1, where from the fingertip one drop of blood is loaded on the device, then what happens is that this one drop of blood is passed into a large number of channels. If a large number of tests needs to be done or may be of small number of channels only if a few tests need to be done, so what is essentially done. So, I will talk about one particular example, which is called as calorimetric testing.

So, in calorimetric testing what is done is if there is a particular element or disease associated with a blood sample that will be associated with a particular antigen or antibody. Then if now you can assess that blood sample against a complimentary or a matching antibody or antigen, then because of antigen, antibody reaction, there will be a

change in color of the blood sample. So, the complementary antibody or antigen corresponding to which the disease particular disease is interrogated, may be embedded on the wall of a small handheld device, and that wall of the device may be itself the wall of a microfluidic channel, because the blood sample can be transported along different microfluidic channels to go to different reaction sites, where different tests will be done.

So, here in the step 2 in the diagram, you will see that for example, there are three different test sites. So, the blood sample can go to three different test sites, and three different tests will be done. So, the at this three different sites, three different chemicals are there. And the blood by reaching this places, it may change its color.

And sometimes the color change is visible that means, you can understand by looking into the change in color about the signal, but in most of the cases, we need a more quantitative information, so that means, that the image of the change in color that needs to be grabbed and processed. So, it is possible that one uses a camera like a Smartphone camera for example, to grab the image, and then image analysis can be done to give the result of the intensity of the pixels under investigation.

Now, there is already a calibration of the color intensity of the pixel against the biomarker that is being investigated, for example hemoglobin concentration or may be glucose concentration how much milligram per deciliter will correspond to what intensity of the pixel. So, once that against that calibration, this result is accessed from that calibration; one can tell that what is the particular blood parameter of that particular sample for that particular test. So, I hope, I could clarify that how these tests could be done.

There are many advantages of such tests that these are potable and thus on spot diagnostics is possible. These can be functional with limited resources like just capillary based blood drawing from the fingertip that needs to be done. Sometimes the device in which this blood is loaded that device needs to have a good capillary action, so that by surface tension driven flow or by capillary action, the blood gets transmitted from the source to the destination, where the chemical is there with which the blood will react.

There are very common diagnostic devices may using the microfluidic technology, where such capillary driven action is possible. Easy handling is one of the important aspects. Mass fabrication is possible. These are inexpensive. These require involvement

of minimal infrastructures. The tests are rapid and the patient can be easily monitored. And if necessary, such tests can be automated.

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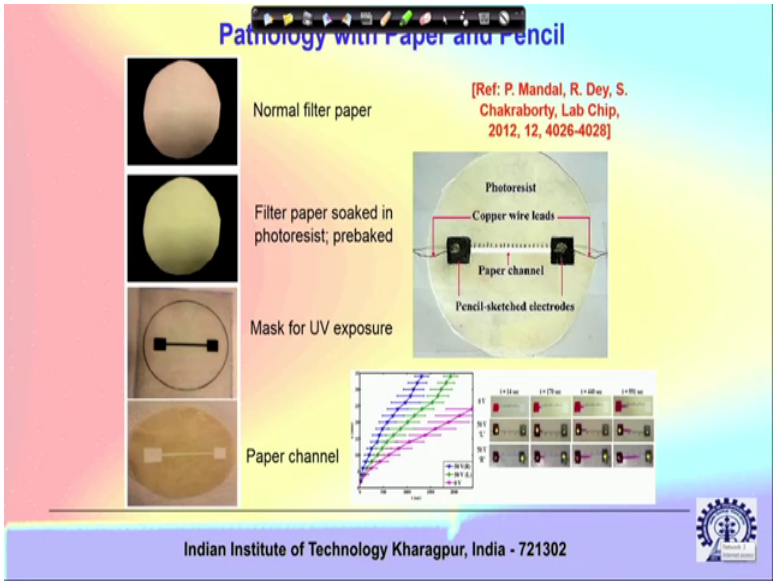

So, I will talk about one example in this particular lecture that is pathology with paper and pencil. So, normally paper based diagnostics is considered to be one of the very important research breakthroughs in the modern era and this paper based diagnostics was originally introduced by Professor White Sites from the Harvard University, USA.

Now, although paper based diagnostics is a very simple procedure, what essentially we have to do is you have to make micro channels on paper. You may argue that can we do diagnostics without making micro channels on paper on a paper itself? Yes, you can do, but you can do only one test, because if you put a blood sample and if there is a chemical already embedded in the paper because of the diffusive or wreaking action, the blood sample will diffuse in all directions.

So, it could be blood, it could be urine like that. And in fact, there are common paper based devices paper based kits, although not micro fluidic kits, but paper based kits available in the market, these have been available for a long time like the pregnancy test kits for example.

Now, if you want to make multiple tests with a instead of blood diffusing in all possible directions with a particular reactions site, where your camera will focus and grab the

image. Then instead of you know allowing the blood to diffuse all along the paper, so this paper for example, could be a filter paper, nitro cellulose paper, these kinds of paper. So, what you can do is that you can make micro channels on the paper. So, to make micro channels on the paper, what you can do is you can use a very traditional technique like a photolithography for example, to make micro channels on paper, which is a very common procedure for a semi conducted industry, similar kind of photolithography you can use. But, one simple way to do it is to do a simple inkjet printing process.

So, in the inkjet printing process, what you can do is that you apply basic two step process. In a in a particular step you in the first step, you print the micro channel design on the piece of paper on both sides. And the in the second step, and the you print this in the inkjet printer. And in the second step, you heat this system on a hot plate.

If you heat the system on the hot plate, the toner particles which have come from the printer will melt, and they will block the pores across which you will have no flow, and you will have therefore, only flow in that direction in which the toner particle is not deposited, therefore you will get a unidirectional flow. And just by using a simple printer, and the paper, paper micro channels can be created.

So, this is the kind of innovation that we require in the context of the developing nation, but that is not all, how can we make this diagnostics faster. So, one possibility is that instead of using just a simple paper, we use an electric field on the paper to make sure that the blood sample by electro kinetic action. We have already studied electro kinetics in this course, so by this time, you already know what is electro kinetics. By electro kinetic action, there is rapid transport of the blood sample from the source to the destination. So, very quick diagnostics can be done.

Now, depositing electrodes for creating electric field is itself a channel challenge. In our research group, we overcome this we overcame this challenge by introducing a new technology for the first time, which we called as microfluidics with paper and pencil. So, what is this paper and pencil technology, it is a such a simple technology that even school children can use this.

So, what we essentially have done is that we have scratched or rather scribed the paper with a tip of the HB pencil. So, this black region is a the pencil sketch or the HB pencils sketch, so in because of the graphite in the lead of the pencil, this pencils sketch region

on the paper acts like electrode, and that makes it very convenient that, if you now connect copper wire leads across this electrodes, and electro kinetic flow of the blood sample can take place.

So, actually we make a massive innovation in this technology by implementing two things, one is a ultra-low cost fabrication of the paper channel by using an inkjet printer coupled with a hot plate to make micro channels just by using printer and printing those on a paper. And the second step is by pencil sketching electrodes, we combine the electrodes with the paper based micro channel to make a paper and pencil based micro fluidic platform. So, this can be a low cost platform at its best.

And the good thing is that research facilities which do not have advanced fabrication for microfluidics like micro fabrication, advanced micro fabrication labs or research labs, which do not have enough money for expensive experimentation for expensive equipment. Just by having a printer, paper and a few pencils, you can actually make this technology work. So, I believe, this is a very important innovation. And when translated into commercial practice, this could lead to very important paradigm shifts in the diagnostic world. Let us stop here for the time being for this lecture, we will continue again on this topic in the next lecture.

Thank you very much.