**Electronic System for Cancer Diagnosis**

**Dr. Hardik J. Pandya**
**Department of Electrical Systems Engineering**
**Indian Institute of Science, Bangalore**

**Lecture – 26**

**Techniques in cell morphology analysis**

Hi welcome to this module, in the last module what we have seen we have seen brush, that we can use to take out the cells from the oral cavity right. And that brush was attached to a motorized stage, where we can change the speed of the brush. So, as to get the tissues from the a from the from the deeper region right in a oral cavity. Now, what we have focused in the last module was what are the advantage or what is the advantage of that particular motorized module over the existing way of taking out the cells.

And we saw that compared to the expert even if the brush is used by a non skilled person, then we can have enough number of cells that too with uniformity and we can use it for further analysis that is for further analysis of the cytology or cytopathological analysis whether the cell morphology is changed or not so right. So, the first stage is to take out the cells the second stage is stage is to understand the cell and to do the image analysis and to then to come out with the diagnosis saying the cells are atypical or not. If atypical a person has to go for the next study which is goes under histopathology where the tissues are taken out.

So, that procedure now we know right, but how can you as an engineer develop this motorized stage we have seen particular (Refer Time: 01:59) and in this one in this particular module, let us see what are the challenges associated with the general procedure of the morphological analysis. Also we will see a how we can develop a system that can scan the slide coated with the cells and can understand whether there are atypical cells or not ok.

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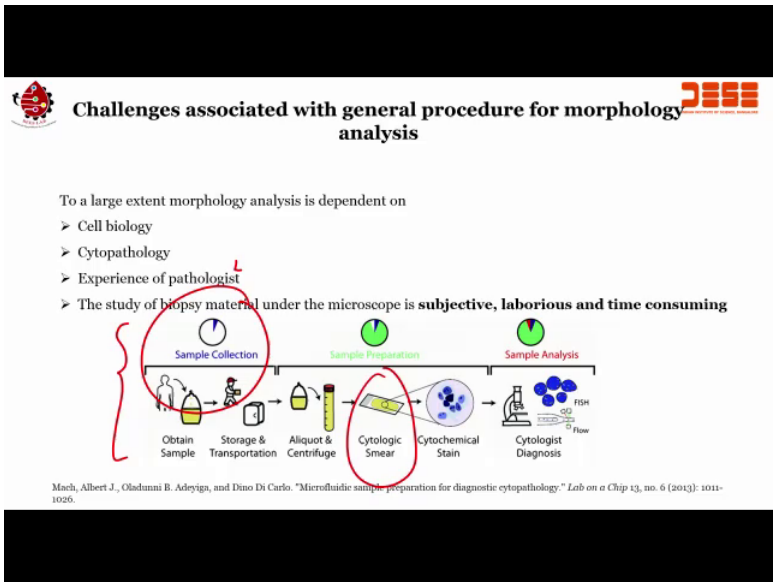


So, let us see the slide the slides talks about the challenges associated with the general procedure and we are talking about the morphological analysis. So, the large extent the morphology analysis or morphological analysis is dependent on first is cell biology, then set of pathology then experience of a pathologist. And finally, the studies of biopsy material under the microscope is subjective, laborious and consuming these are the difficulties or challenges associated, when we are talking about morphology analysis.

First is how it is dependent cell biology if the biology of the cell is different the said set of pathology, how good we are in understanding the cells, when we are talking about several parameters one such parameter is a cell morphology that we have seen in the earlier modules. Then how good a experience pathologist is that he can deal nearly between premalignant and malignant cells, premalignant is pre cancer malignant is a cancerous.

Finally, the study of biopsy material when the tissue is taken out it is sliced and it is so, for the stain with different biomarkers and the study is done by a expert it is laborious job, it is time consuming job and of course, it is subjective so, these are the limitations or challenges. So, here you can see how we are doing the process first is to obtain the sample, then the storage and transportation right this is a sample collection time.

Further you have to (Refer Time: 04:01) prepare the sample. So, how you are going to prepare the sample by aliquot and centrifuge and, then you can do a smearing you can do

a smearing with a cytospin we have already seen the cytospin in the videos earlier or you can do a manual smearing. Once you do that you can stain it with cytochemical for example, h and e stain staining and then the sample preparation take consumes time, then we have to send it to a pathologist. So, this pathologist will understand the cell morphology in the microscope and analyze it and come up with the diagnosis.

So, this is the challenges and if you can reduce this whole process right over here, when the sample is collected and if you can put on the slide and can get you the analysis that is great.

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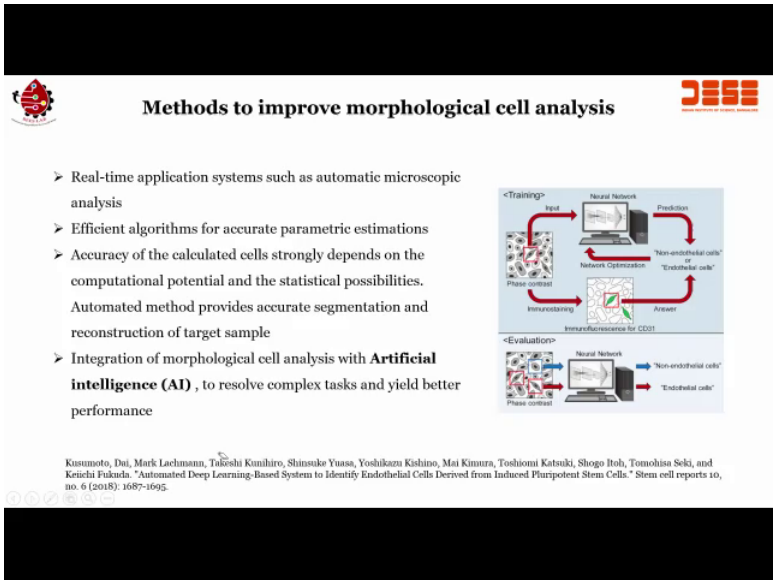


So, let us see how we can do that, what are the methods right methods to improve morphological cell analysis, first is that we have to take the face contrast images that to input with the neural network. We can use the immunostaining we can get the answers we can use the neural network to predict it and we can get non endothelial cells or endothelial cells are there say.

So, we can use one of this technique to understand the cells, but also the there are another techniques which we will talk in the following slides, but for this time let us see real time applications such as automatic microscope analysis this is one of the improvement that can be thought of, efficient algorithms for accurate parametric estimations, accuracy of calculated cells strongly depends on computational potential and

statistical probabilities also possibilities automated method provides accurate segmentation and reconstruction of the target sample.

Finally integration of morphological analysis with machine learning algorithms well artificial intelligence, to resolve complex task and yield better performance, though this as then the methods to improve the morphological analysis.

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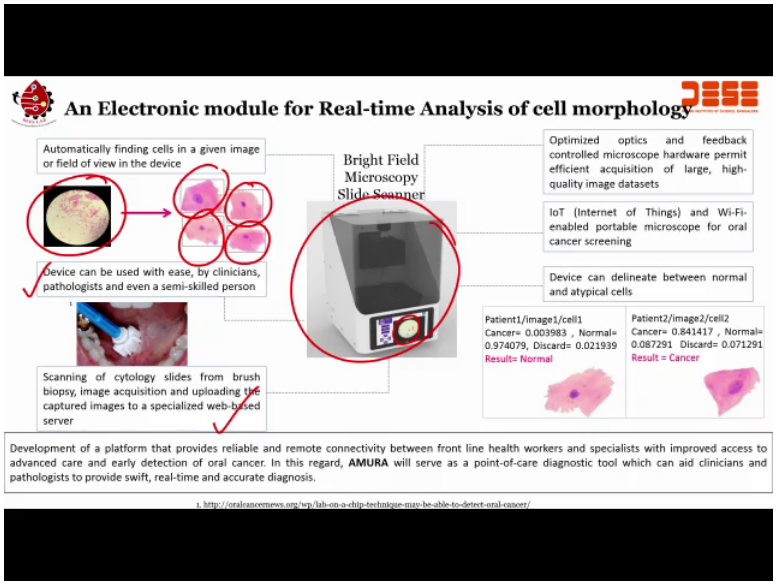


Now, the looking into that particular concept let us see ha what we have developed ok. So, let us see here the first one here we can see the brush is used to take out the cells from the oral cavity. So, and then you have to put the cells a on to the glass slide smear it down, or either use manual smearing or you can note the cells with PBS in the cytospin and smear it down in the glass slide load. The glass slide into this particular platform, this is the microscope with image analysis with machine learning algorithm. So, what it can do ok.

So, the scanning of cytology slides from brush biopsy image acquisition, and uploading the captured images to a specialized web server. This device can perform this particular aspects 1 2 3 4 5 6 and then we can help the remote oncopathologist to come up with a solution, whether the cells identified as atypical by the AMURA, or by this particular real time analysis electronic module are correct or not that is the atypical cells that are identified by this particular electronic modules are atypical or not, that can be decided by a remote pathologist.

So, what are talking here let us see one by one first is the development of a platform that provides a reliable remote connectivity between front line health workers. So, the people who are taking the cells right from the oral cavity and specialist a remote specialist acclimation oncopathologist, with improved access to advanced care and early detection of oral cancer, that is the goal of this particular platform. And in this regard we will say that this device which we called an electronic module will serve as a point of a diagnostic tool here, what you see what you see here is that the scanning of cytology slides from brush biopsy image acquisition and uploading the captured images to a specialized web server can be done.

Second this thing is device can be used with ease by clinicians pathologist and even a semi skilled person, automated finding automatically findings cells in the given image of or field of you. So, if this is the field of u the device the system will be able to delineate the cells from the background the and thus only focusing on the cells. Further it will also find out whether the cells are having the same morphology, or they have a different morphology. If it is a different morphology the system you see here a the system will tell that if these are the cells that have different morphology and those cells would be sent to a remote pathologist you got it.

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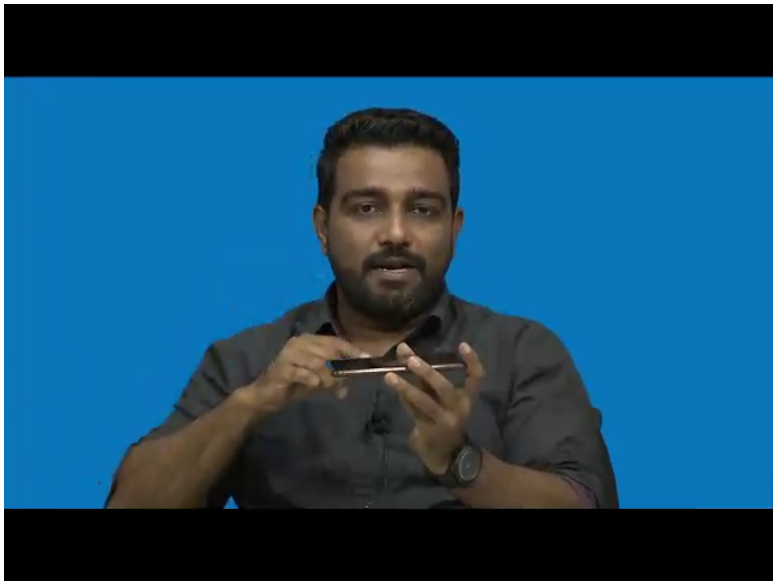

So, now the advantage is if I have a slide coated with cells, I load the slide press a button it will scan the slides find out the cells which are having different morphology and

identify those cells and sending to a remote pathologist, will save lot of time in screening the cancer. So, the screening can come down with the help of this particular tool. So, it is a nothing, but a bright filled microscope with a integrated with image processing algorithms and a machine learning algorithms very basic machine learning algorithms to identify atypical cells from the normal cells using the morphological analysis.

Then if you see the slide the another advantage is that optimized optics and feedback controlled microscope, hardware permit efficient acquisition of large, high quality images, then we have internet of things where Wi-Fi enabled portable microscope for oral cancer screening. So, IoT because we can transmit the way you can transfer the data from the microscope to a remote pathologist and finally, device an delineate between normal and atypical cells.

So, you can see here if it is cancer it will be of low value compared to normal and if you discuss, then its 0.00 0.021 very same we when talk about patient two, you can see the cancer is 0.84 normal is 0.08 and discarded value is 0.07 result would be cancer right. So, it is very very easy to identify whether it is cancer or not from the values obtained to the microscope.

Here you can see normal is very high and the normal value is extremely low, the cancer value is extremely low from a cancer value is extremely high right. So, both images we can take it and we can get the cancerous cells over the normal cells or we can delineate cancer cells over the normal cells alright. So, let us further see what exactly there is there within this particular microscope.

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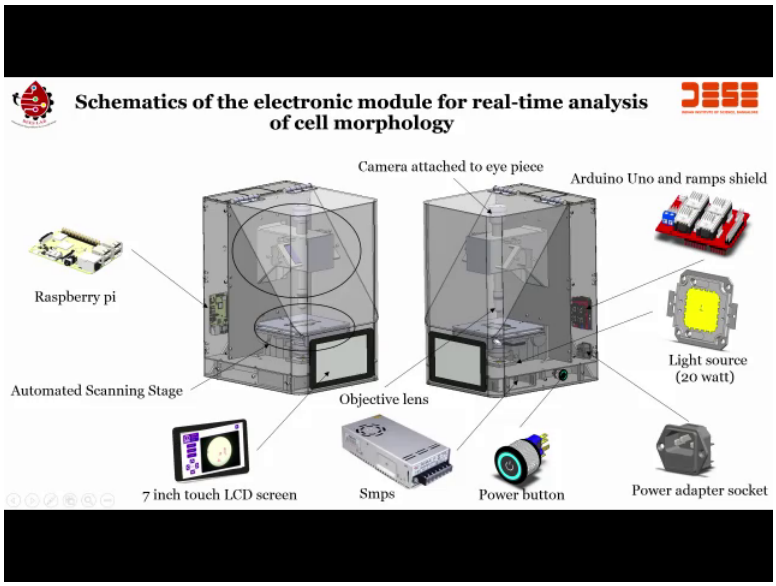


So, first is there is a electronic module or microprocessor or controller, you can say this is a raspberry pi, you all have learnt raspberry pi we can use a raspberry pi to do the processing there is a automatic or automated scanning stage which is right you can see over here right, this is a automated scanning stage and then we have the camera attached to a eye piece which is right over here we have Arduino Uno and ramps shield we have a light source which is a array of LED lights, then we have a power adapter socket, we have a power button and we have we have Smps.

So, it is when you attach everything to whether, then you can get the image of the cell which are loaded on this particular glass light. Again I am helping you out to understand that you can use an integrate all things together to come up with an technology, that can be used for such application I am showing you one application which is a screening of oral cancer patients, but you can use it for several other applications as well alright.

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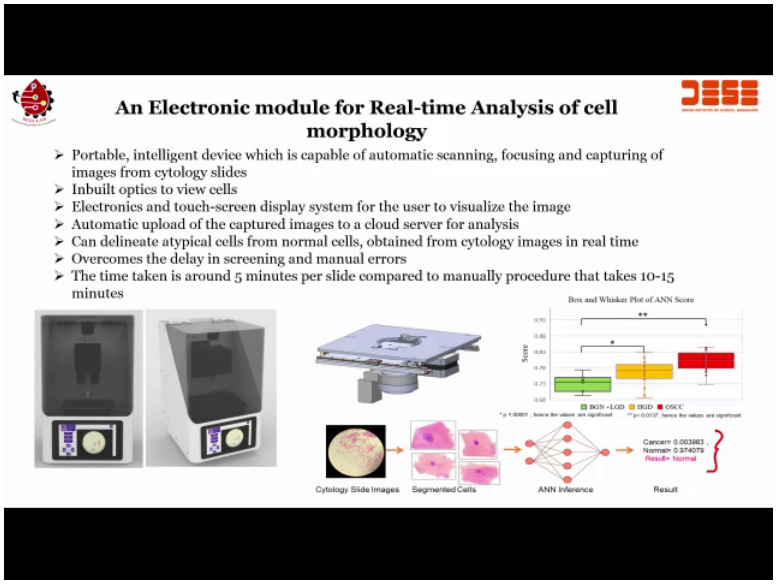


So, if you go further and you see how this can be used then you can see here that f, if you are given a cytology slides then it can segment the cells can we can run through the ANN interphase. And, we can get whether the cell is a normal or cancer, or which cells are cancerous which cells are not you can clearly see that benign plus low grade is different than high grade and is different than the OSCC.

So, you we can clearly delineate the cell type as well this can be seen from the box and discuss lot of N and score so, what exactly the system consist of the system is an portable intelligent device it is capable of automatic scanning. It has a inbuilt optics electronic center screen display for visualizing the cells, or automated upload of the capital image is to the cloud server final analysis.

Then we will see how we can use the cloud server for analysis how can we store the images in a cloud server as a part of the experiment laboratory, I will tell you how we are taking the data using a 3D printer and how we are storing the data that what is the time left in the 3D printer, or what is the set of things completed by a certain set of equipment and you can store the data in the remote server.

We will talk about that in the laboratory further it is thus the e the system, that we I am showing it to you can delineate atypical cells from normal cells and it can overcome the delay in screening and manual errors that is the most important point. And the final is the time taken is around 5 minutes for slide compared to manual procedures by the oncopathologist, which seeks about ten to fifteen minutes depending on the expertise and

the advantage here is that we can delineate the premalignant cells and the malignant cells. So, it is very important in premalignant cells from benign cells also, that is also very important that in the premalignancy stage we can screen the patient. And if you can screen the patient at early stage of cancer, then you can treat the patient well that is the advantage.

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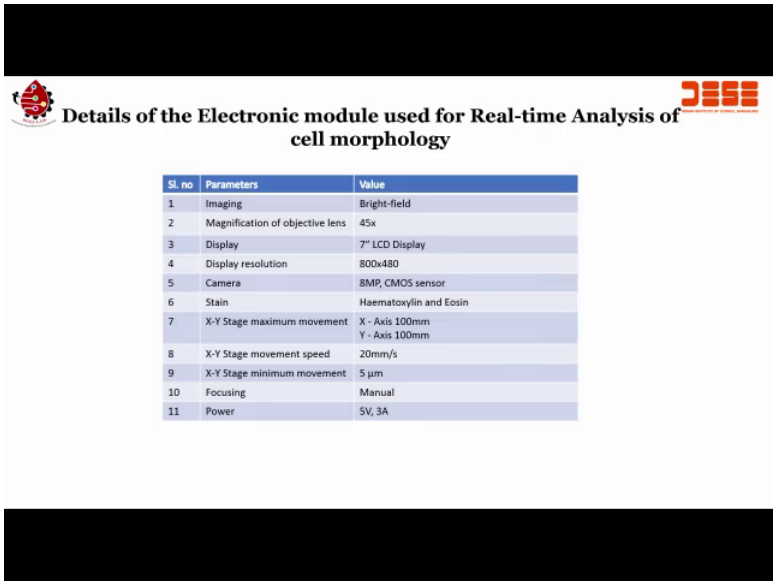


If you see further features what are the parameters and the value that we have used to build this particular system and same system you can develop in your laboratory as well, the imaging parameters with bright field magnification 45 X this display is about 7 inch LCD display and resolution 800 by 480. Then we have camera which is 8 8 megapixel CMOS sensor, we have stain which is HME staining X Y stage with a 100 millimeter by 100 millimeter and X Y stage movement speed is 20 millimeter per second.

The X Y stage minimum movement would be 5 micrometer which is really important right. So, this is the max and focusing is manual right now and we have using about 5 volts of power voltage and about 3 amperes of current. So, there is a power requirement for the system ok.

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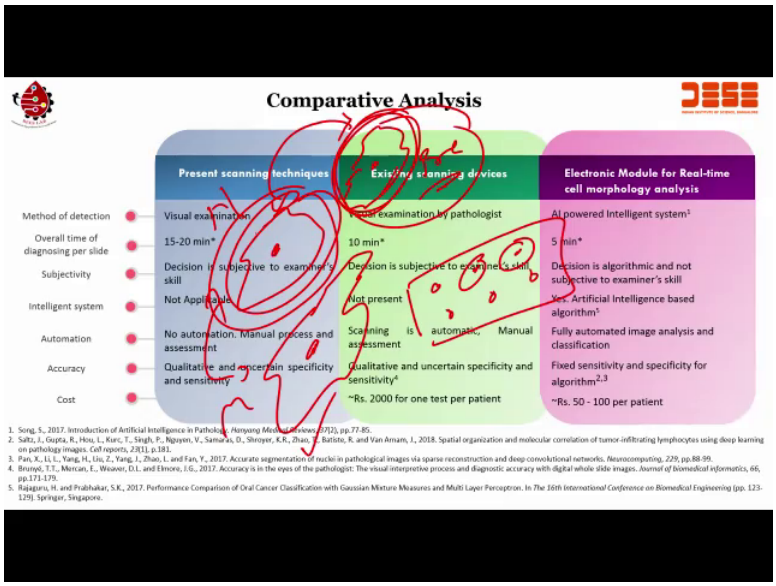


Now, if I go for comparative analysis very important and like always I am giving you few slides few research articles to read, it is very important to read this articles to understand further how a AI can be used in pathology, how special organization and molecular correlation of tumor infiltrating, lymphocytes can be used using deep planning algorithms, how can use the accurate segmentation of nuclei and pathological. Images using AI you can also understand how you can compare the oral cancer classification with Gaussian mixtures using multilayer perception and lot of thus also. If you have chains and if you get chains then please access this research papers a 5 in numbers for you to see.

So, now let us see if we are comparing three different things, present scanning technique existing scanning devices and electronic module for real time analysis of cell morphology, that is what we have been learning and we had developed in the laboratory, this is advantageous for you so, that you can compare it in terms of method of detection or subjectivity or its intelligence or automation accuracy as well as cost. So, if you talk about method of detection in case of presence scanning technique is a visual examination right, existing scanning devices that are there is visual examination by the pathologist and where here we have the AI powered intelligent system.

Second is take about 15 to 20 minutes this take about 10 minutes this takes about 5 minutes right, then third one is that subjectivity you meant about subjectivity, then reason

is subjective to examine the skill for the present devices for the existing devices this is when is subjective to examiners skills and finally, if it is our device the system that you are guys are learning, then this one is algorithmic and or I can I should say this one is algorithmic and not subjective to examiners skills. Finally, there is no intelligence c present in the present scanning device, where only our system right now what you have learnt you can have the AI module indicated to that.

So, what is what is at least AI and why you want to use the AI in our present module the role of AI, in the present module is that a suppose you have this cells right you have this cells. Now, which cell is atypical and which cell is not you can only know when you have the different in the cell morphology. So, if the cell is changing its morphology at premalignancy, you will not be able to understand the change between the normal and the plain malignant cells ok, but for normal and malignant it is very easy, suppose we say that this is a malignant cell this is a premalignant cell, this is the normal cell then normal and premalignant is difficult normal and malignant is easy.

But with the machine running algorithm, you can delineate the premalignancy with respect to normal. That is the advantage of machine learning which is not there in any of the existing devices and that is why the system that we are talking about that is so, easy you guys may be learning a part of machine learning, you may be learning part of the electronic module design, you may be learning part of the you know mechanical design like cad drawing right you all go to a workshop.

So, how can you integrate your knowledge together in a team and work on this kind of system that can be used for screening different cancer, you can talk about cervical cancer you can talk about oral cancer you can talk about any cancer the in which you are relying on the cytology studies right. So, screening of the patient based on cytology you can develop such kind of system ok.

Coming back to the automation part; so, automation there I no automation manual process and assessment in the present scanning technique, scanning is automated and manual assessment is also there in the existing scanning devices, while in this one fully automated image analysis is done finally, accuracy quantitative qualitative and uncertain in this case qualitative uncertain specificity and sensitivity, while here is fixed sensitivity

specificity for the algorithm cost is about 2,000 for one test patient is about 550 to 100 per patient.

So, in any case we are focusing on developing a system, that can be a low cost accurate system based on the imaging of the cells and relying on the change in the cell morphology, by relying on the machine running part integrated to the system itself. That is all about the scanning of the slides during the image analysis removing the background which is not cells. So, these considered as a noise and as a all the artifacts we do not have to consider only signals we have to consider. So, we have to develop a algorithm that can delineate the artifacts from the cells which are our signal cells well right.

So, that is the combination of multiple things like I said we will talk about little bit about how we can store the data in the server in the in the laboratory class, you just go through this come up with a novel idea that is a part or you know my interest of teaching, you this whole course is that this is more like a search oriented course. Where, you can understand what kind of techniques or how can we use your existing knowledge to develop a system, that can be used in identifying the cancer at earlier stage and that too at a low cost and that can also be used by a semi-skilled person ok.

So, I will see you in the next module where we will talk about how can we take the images within the oral cavity and what kind of system, we can develop for the same till then you take care I will see you in the next module bye.