INDIAN INSTITUTE OF TECHNOLOGY ROORKEE

NPTEL

NPTEL ONLINE CERTIFICATION COURSE

Biomedical Nanotechnology

Lec - 11
Nanomaterials for Cancer Diagnosis

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Hello everyone I welcome all to this 11th lecture of this course.

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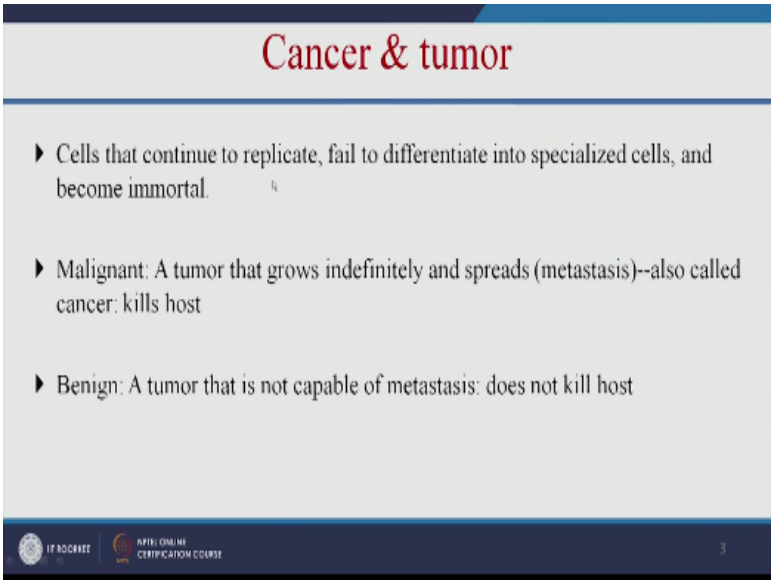

So this 11th lecture is on nanomaterials for cancer diagnosis. So let us see what is the difference between cancer and tumor okay, the cells that continue to replicate and fail to differentiate into specialized cells and become immortal, this is called as cancer cells or tumor cells. And the main difference between the cancer and tumor is malignant cells okay. So a tumor that grows in definitely and spreads that is called as metastasis okay. As and is also called as cancer cells and which kills the host.

And the meaning is a tumor that is not capable of metastasis and does not kill the host. So the main difference between the cancer and tumor is, the tumor cells are localized and it grow undefinitely okay. And it grows more number of cells the particular location and it could be removed by surgery, but in case of cancer the tumor cells spread from all location to other location and it is going to kill the host that is called as cancer.

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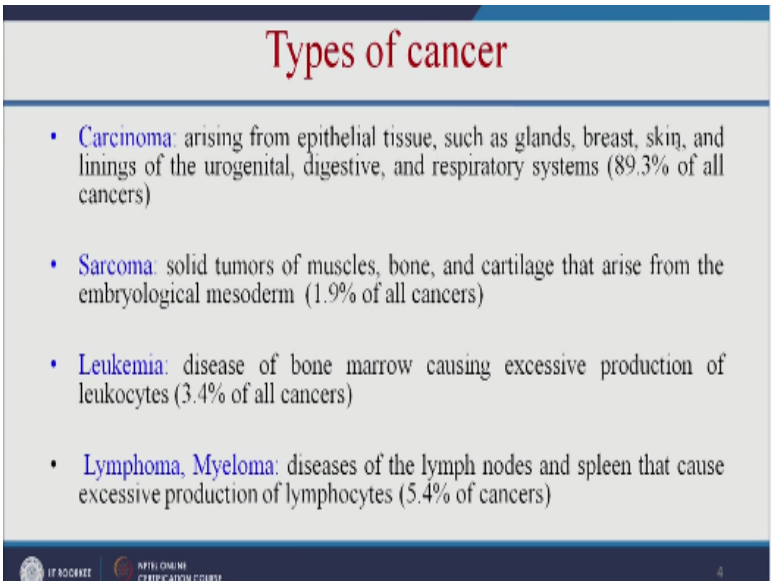

So these are the various types of cancer carcinoma, so it is arising from the epithelial tissue such as glands, breast and skin okay. So this carcinoma constitutes mostly like 90% of all the cancers and again sarcoma is solid tumors of muscles and bone, it is 2% of all the cancers and leukemia is the bone marrow, this is a bone marrow okay. So this is constituting 3.4% of all cancers. And lymphoma and myeloma this is constituting like approximately 5.4% of all the cancers.

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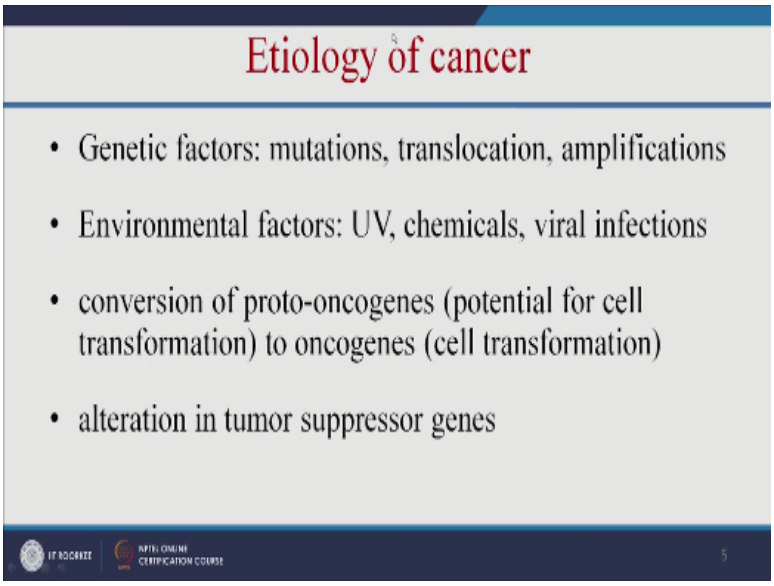

So let us see what is the reason for the cancer, first is genetic factors, it may be due to mutations or maybe due to translocation, and it may be also due to heritary okay. And next reason is environmental factors like UV or chemicals or viral infections. So when a person working from chemical industry he has high chance for getting the cancer. And what is happening in the cancer, the conversion of proto-oncogens to oncogens.

So each cell will be having proto-oncogens all the cells will be having proto-oncogens if the proto-oncogens is connected into oncogens the normal cell became a cancer cell. And also the alteration in the tumor suppressor genes, so each cell we have tumor suppressor genes which suppress a tumor growth okay, and if there is some alteration in the tumor suppressor genes there is a high chance for getting the tumors of cancer.

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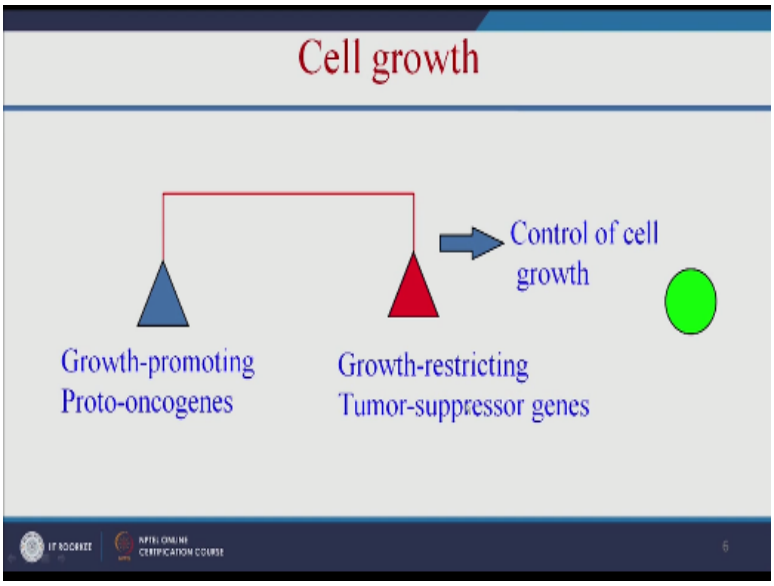

So this growth promoting proto-oncogens and growth restricting tumor suppressor genes this should be properly balanced for a control of cell growth.

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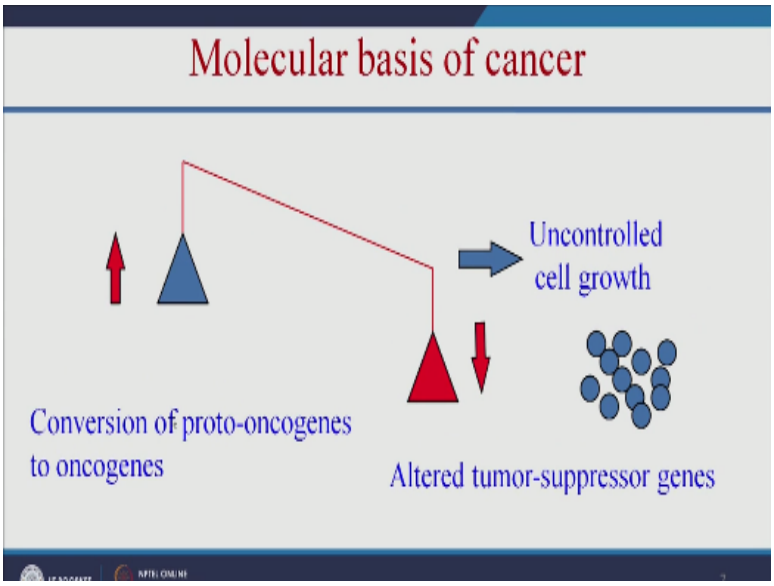

So if there is a imbalance the conversion of proto-oncogens to oncogens will happen and it leads to altered tumor-suppressor genes. So due to this, what happen there will be an uncontrolled cell growth, so that is called as tumor. So the uncontrolled cell growth is a tumor and if the tumor spreads from one location to the other location that is called as cancer and this spreading is called as metastasis.

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And the interesting fact about the cancer is at least once a day your immune system destroys a cell that would become a cancer cell if it lived. That means everyday at least some cells are trying to become a cancer cell; if your immune system is strong it can destroy the cancer cells.

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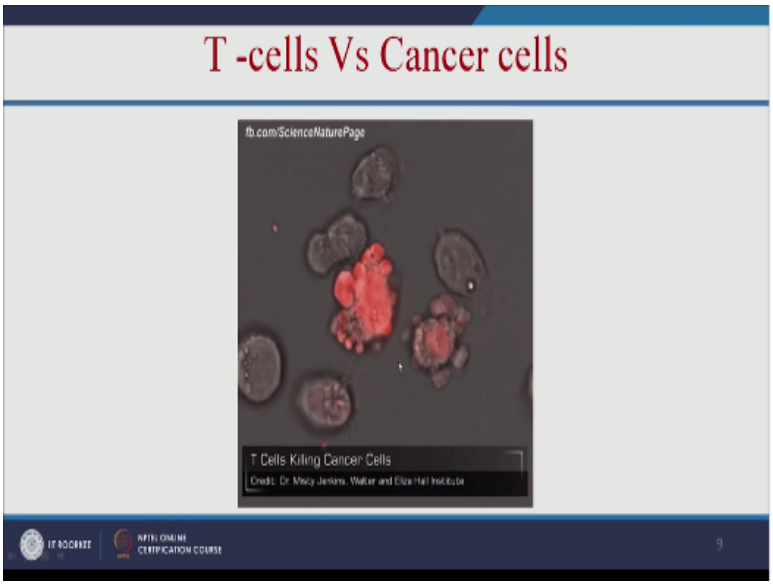

So let us see this animation so the, the long cell is the cancer cell, and this one is the T-cell that is your immune cells. So it is coming and attacking your cancer cell and destroying it, that means if your immune system is strong it will at least productive from developing cancer or tumor.

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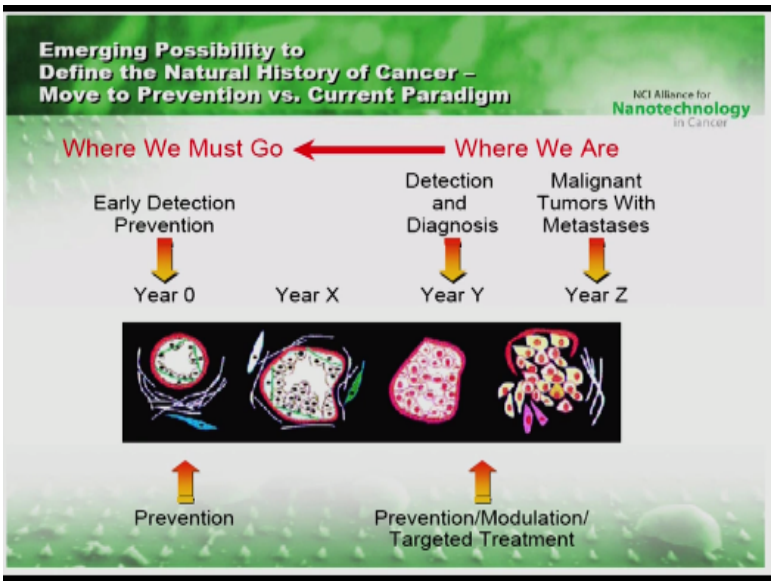

So what is the major problem in the cancer diagnosis? The main problem is you are not able to diagnose a cancer in the early stage, so with the present tradition with us we are able to diagnose the cancer only in the later stage and in the later stage we have to go for targeted treatment or we have to go for radiation and chemotherapy. So by using nanotechnology we can go for early detection of cancer and we can protect the patient from the cancer death.

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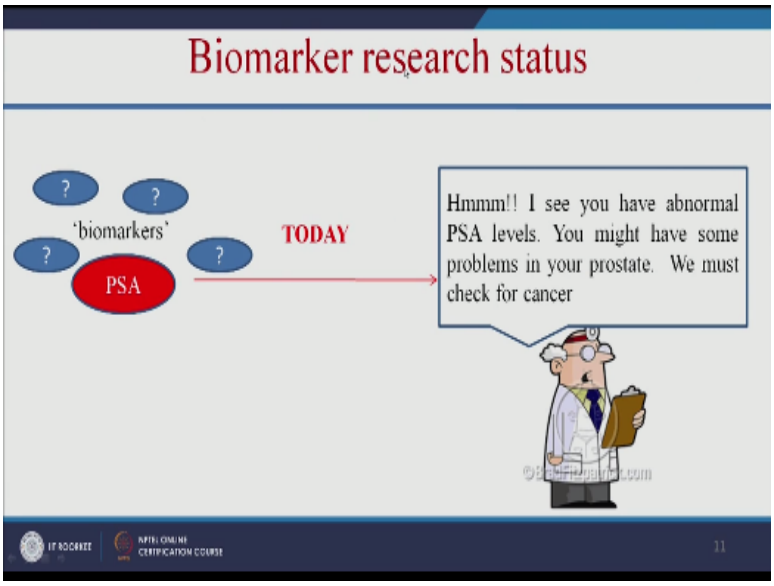

So this is the biomarker research status okay, so this PSA means Prostate-specific antigen. Suppose if the person is having more amount of PSA that means he has high chance for getting prostate cancer. So that is the today's biomarker research status, so if some person is diagnosed with the more level of PSA that means he has high chance for prostates cancer.

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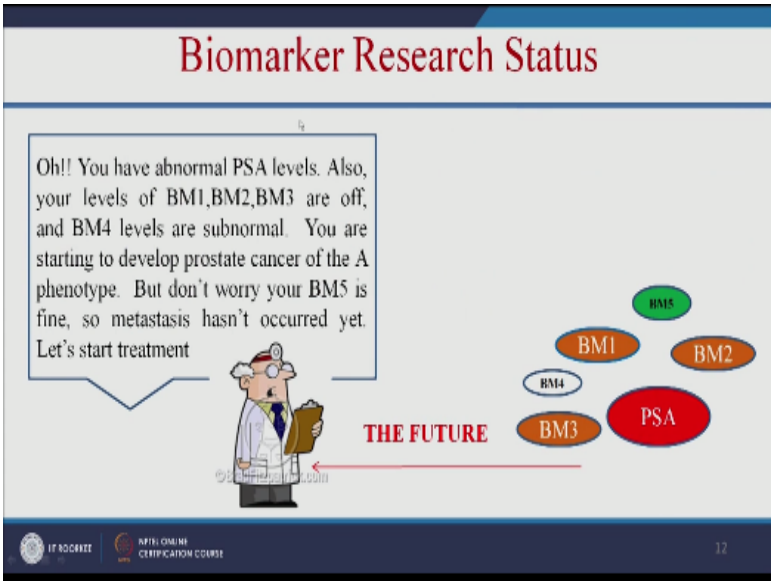

So let us see the biomarker research status in future. So in future we will be able to tell you the prostate specific antigen is over expressed, but also we can also check it what are the other markers involved in this expression okay. So based on that we can tell like if it is a BM1 or 2 or 3 and we can give drug occurring to that. So here in this example you can see here the marker 1, 2, 3 are in off condition, and marker 4 is subnormal.

And for example, the marker 5 is fine, so there is no metastasis okay, so we can go for treatment accordingly. So each cancer have several kind of markers septons on the top okay. So we can easily detect which type of marker is over expressed or which type of marker is down regulated. So accordingly we can select the drug and we can target and start the treatment process, and which will save lot of time as well as we are not giving more amount of drug consideration to that particular person.

So this condense personalized medicine, instead of giving the generalized medicines, so if suppose a person is having cancer instead of giving the medicine for all the 5 types of markers we can given drug only to attach the particular marker. So instead of giving the generalized medicine we can give the personalized medicine. For example, if the marker 1 is over expressed we can give drug only to suppress the marker 1, instead of giving drugs for all the various markers okay. So that will analyze a therapeutic efficiency.

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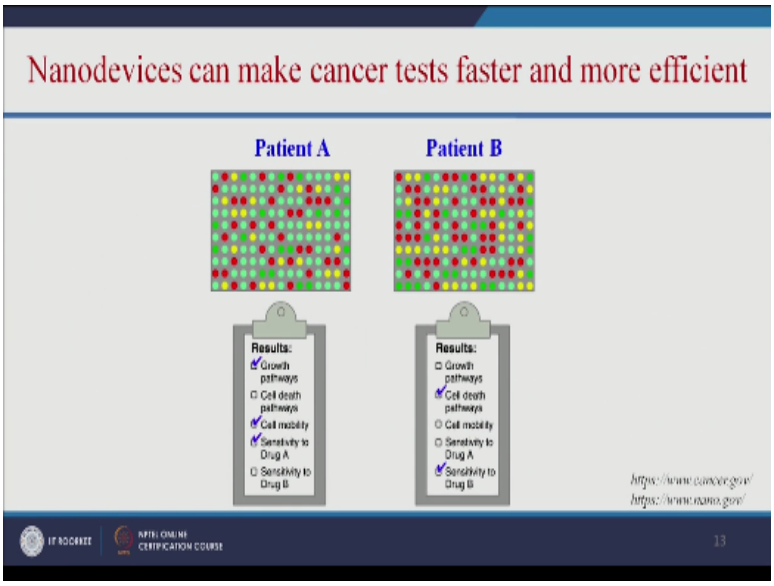

So let us see another example, so here the nano devices can make cancer tests faster and more efficient. So we can see the example, this is patient A and patient B, and we can check all the pathways and everything and also insensitive to drug and we can give the drug according to the patients need. So in the patient A you can see here the growth pathways are okay, and cell mobility is okay and he is sensitive for drug A.

And in case of patients B he is sensitive to drug B and since the pathways and everything is okay. So the cancer even though both have the prostate-cancer so they will be having different kind of need, like as I told you like they will having expressing the different kinds of biomarkers, so we can give the drugs to the specific need that is called as personalized medicine. So in the cancer diagnosis various nanomaterials play important role.

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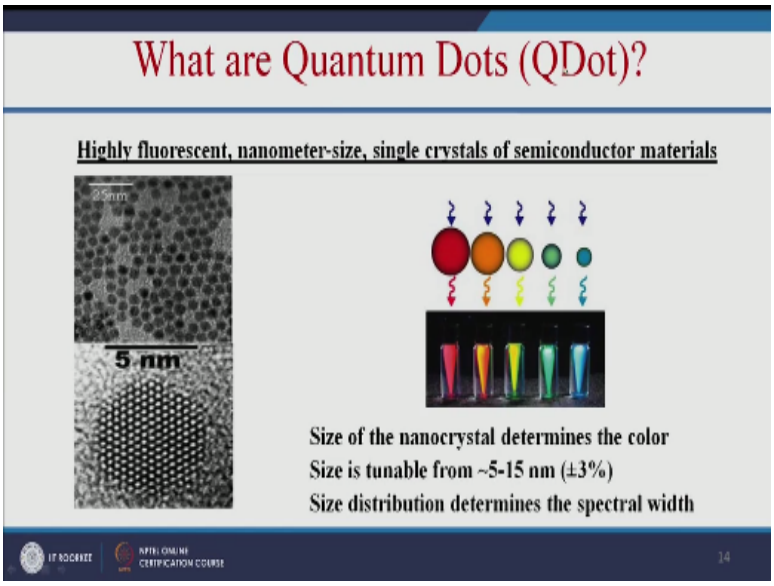

The main important nanomaterial is quantum dots okay. So the quantum dots are highly fluorescent, nanometer-size, single crystals of semiconductor materials okay. And with respect to size it will give a different color. And the size is tunable between 5 to 15 nanometer, so based on the size it will give different fluorescents that are our role of these quantum dots.

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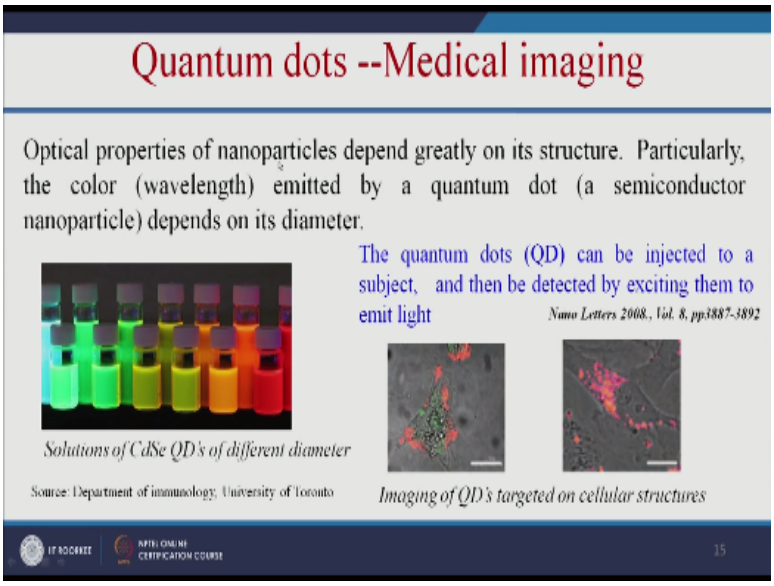

And here the optical properties of nanoparticles depend greatly on its structure particularly the color okay emitted by the quantum dot and depends on the diameter. So as I told you it depends on the size, it is going to give different kind of colors. So here the quantum dots can be injected to a subject and then be detected by exciting them to emit light okay.

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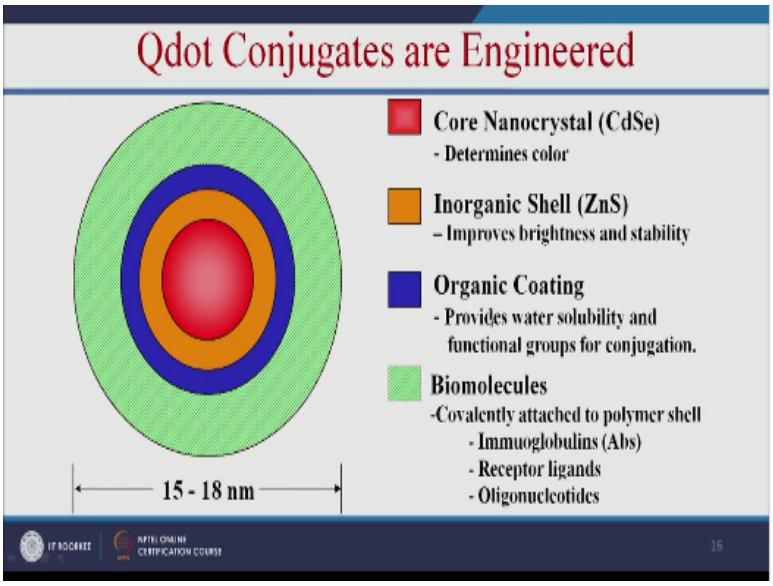

But the quantum dots are toxic it is not biocompatible, so how to make the quantum dots biocompatible and also soluble. So we have to engineered these quantum dots, you can see here this is your core nano crystal which determines the color and we have to give a inorganic shell this will improve the weightiness and stability and followed by we have to give the organic coating, so that will provides the water solubility, and functional groups for conjugation.

So we can add any antibody or peptides okay, and we can specifically target these quantum dots for cancer diagnosis.

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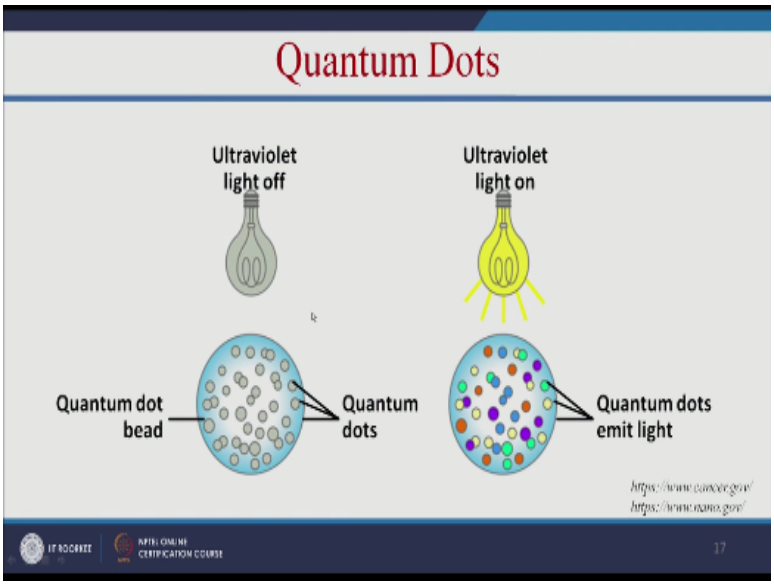

So you can see here this example, so the quantum dots are not fluorescents when you apply the UV light it will emit light.

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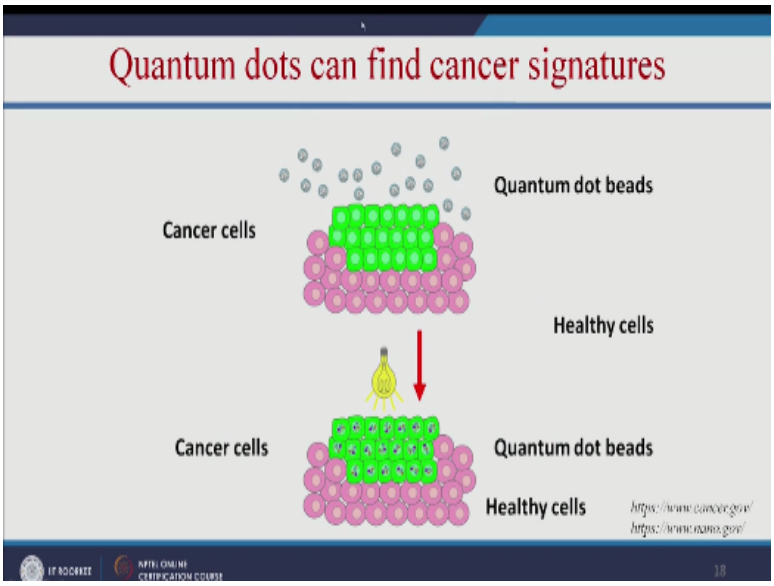

So here you can see that the quantum dots are attached with some antibodies which is specifically go and bind into the cancer cell. So when the quantum dots bind into the cancer cells and when you apply the light, so only the cancer cells will emit fluorescents and healthy cells there is no fluorescents.

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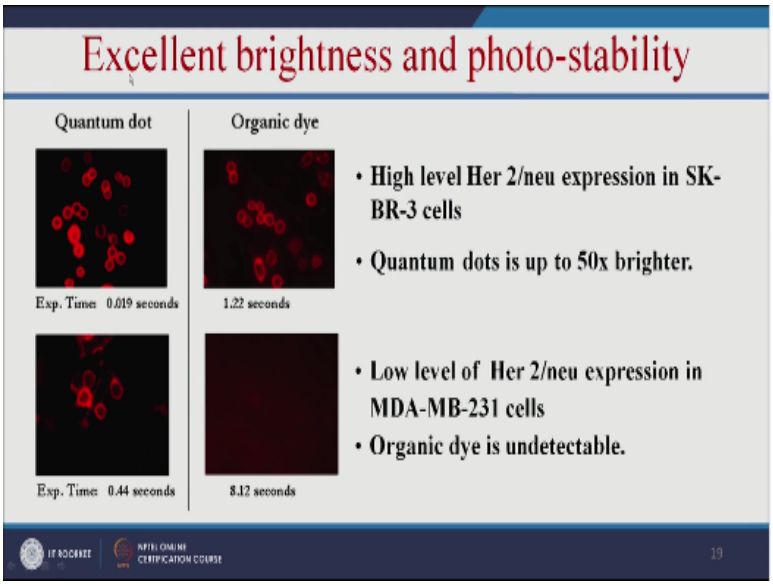

So we can easily diagnose the cancer cell. And quantum dots have excellent brightness and photo-stability. So in this example you can see the difference between the quantum dot and organic dye. So here you can see here the exposure time required for quantum dot is 0.019 second and organic dye it need 1.22 seconds. So in this picture the first two pictures is the cancer cell which have high level of expressing o the particular cancer marker.

That means ,it is like the cancer cell which is expressing more number of the markers okay, and you can see here ,when comparing to the organic die the quantum dots is showing 50 times brighter ,okay. and the another thing is it is the cancer cell which is expressing low level of markers and we use the quantum dots and the organic die and in the organic die there is more flows and the signal ,it will give a first negative result.

It means the person is having the cancer bit we use the quantum dot and it use for the diagnosis and there is now flows and the signals, so we need to get the result like the person is negative for cancer but the person is having the cancer when we us rte quantum dots.

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We can see here it is giving her the flows and the signals, even it is the low level and the expression of the marker is the quantum dot is to able to bind and it able to see the flows and the signals, so this is the advantage and this quantum dots.

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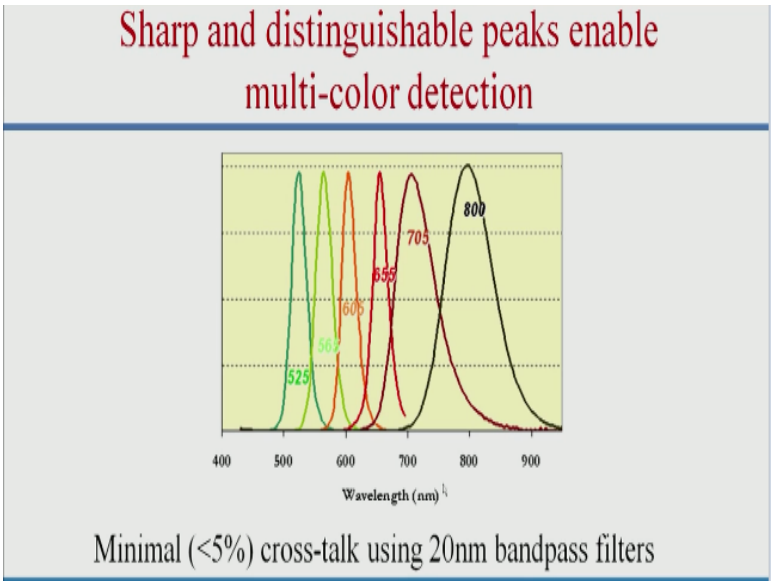

And the another advantage is as I told with the respective size and it will give the different kinds of the fluorescents and when we use the traditional and the organic dies, so there is chance for the over lapping of the fluorescents, and this case there is no over lapping and the fluorescents and there is no cross talk.

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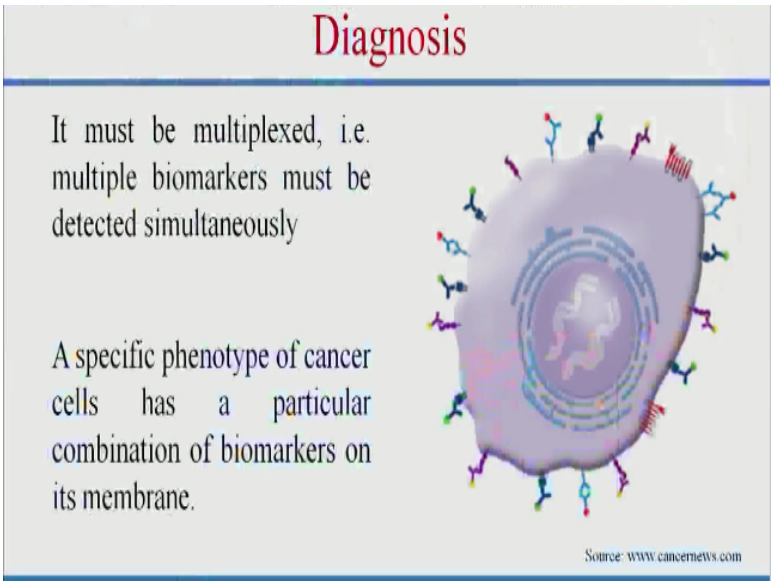

And this is the diagnosis should be multiplex that means as I told you the earlier the cancer is that have the multiple bio markers, so that should be detected simultaneously okay, so this example you can see here this cancer cell is expressing different types of the markers and the cell surface, for the example this is the blue color or t purple color or the red color okay, so this is the different types of the marker are expressing on the surface of the cancer cell so the diagnosis should also multiplied.

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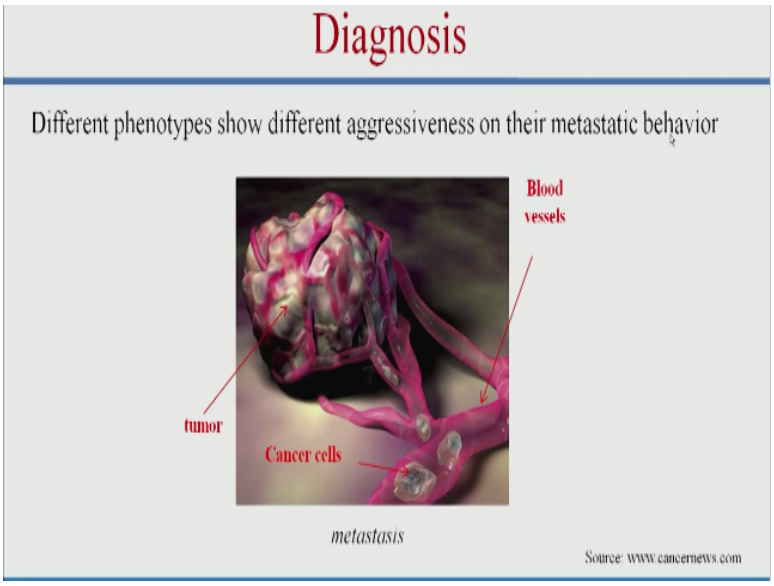

And the fellow types will show the different aggressive nests and their metastatic behavior so depends on their marker, so we will come to whether the person is in the early stage of the cancer or he is in the advantage stage of the cancer.

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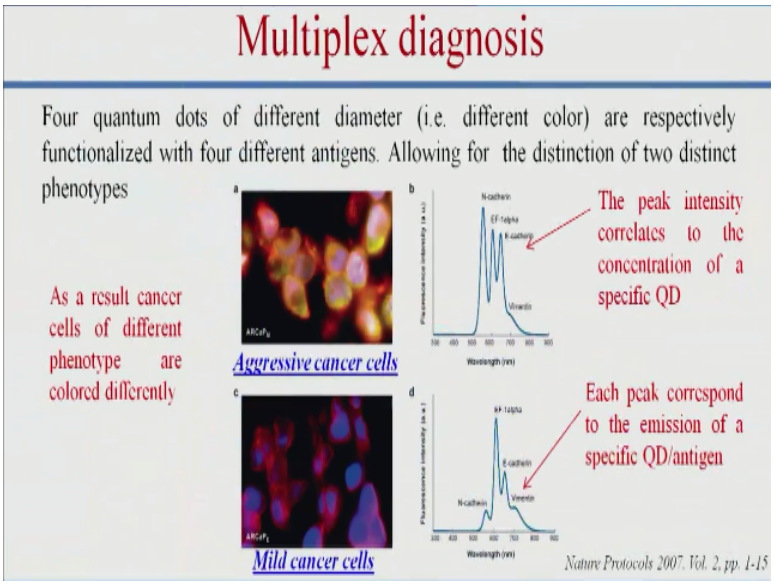

So let us see the multiplied diagnosis, here the four quantum dots are in the different diameter and in the different color or respectively functioned with the four different antigens, that means if I cancel the expressing four different kind of marker are recited as this quantum dots are go and band to the four types of the marker and the receptors and the all the four is giving in the floor cells and that means the person is in the advantage stage of the cancer.

For the example out of the four only two only one is given n the floors and the signals in the person is in the early stages, cancer if we you can see her this is he early stage of the cancer and this is the advance of the cancer and it is the two receptors you can say that the different between the early stages you think in the receptors.

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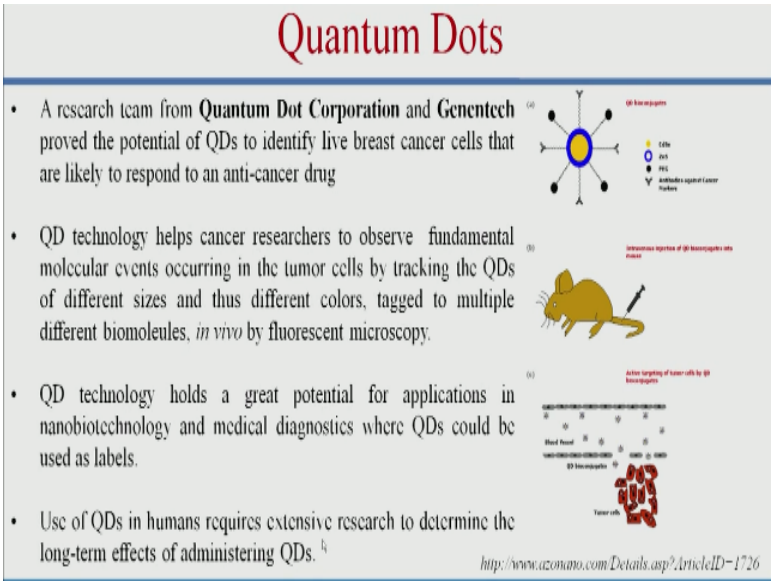

Ni the sixteen from the quantum dot from the so the medium quantum dot to the identify in the best cancer okay this technology you are available for and the mouse model. And we can also use it for the various and the cellar application, but the use of the sane quantum dot and it is the recovery and this is the different types administrating quantum dot in the earlier and the quantum dot is made earlier.

And it is earlier quantum and it is made up of quantum materials in the use of the quantum dots and in the human dots and we need a lot of lots of the clinical in the repairs human application also.

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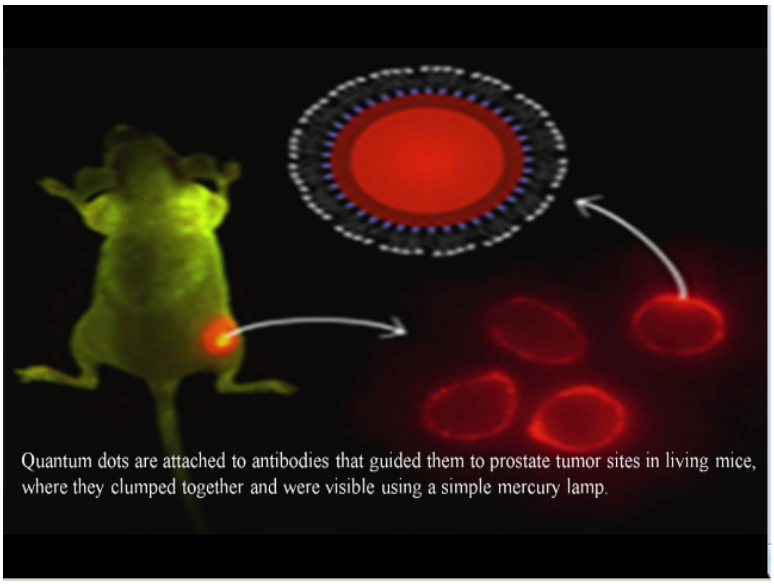

They use the quantum dots attach to the anti bodies okay that will go and specifically in to the pro state and in the humor size and it minimize where they clump to it will visible under the ray mercury lamp so they injected this quantum dots it is specifically and do and bind in the pro state cancer. When I apply this light it will give the flows and the signal and it will easy for the diagnosing the cancer in the mouse model.

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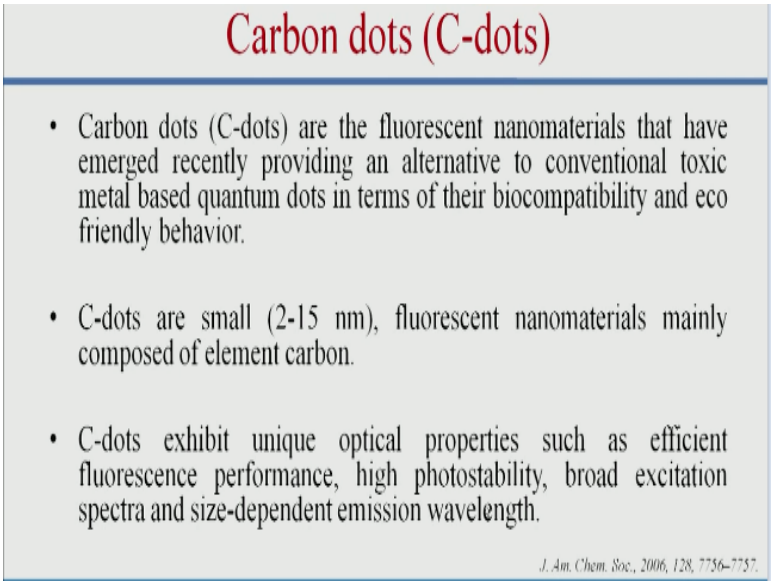

Let us another nanomaterials this carbon dots so this are the florescent ant the nanomaterials so that have emerged in the recently providing an alternative conventional toxic material quantum dots okay, so this carbon dots are made up of the carbon and the highly biocompatibility okay. And this carbon dots are small in the size to the 2 to 15 nanometer and it is mainly composed of element carbon and the carbon dots are exhibit in the high photo-stability in the respecter similar to the quantum dots

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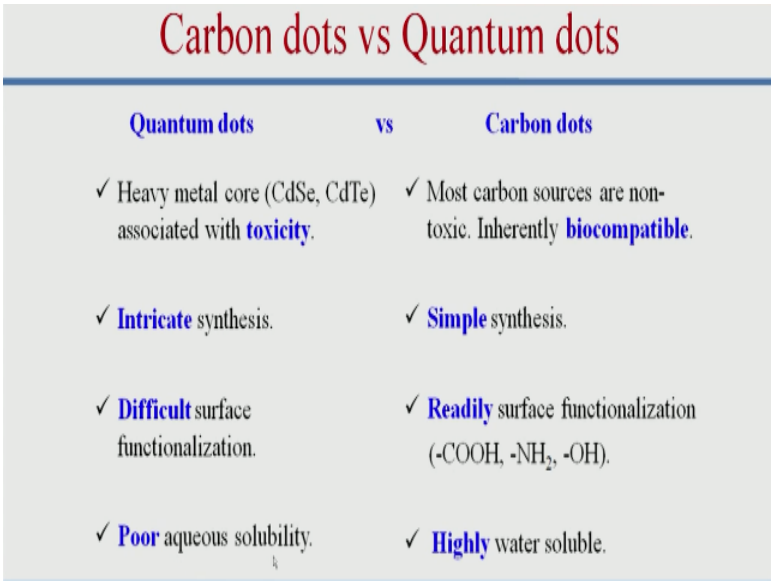

So you can see the different between the quantum dot and the carbon dots so the quantum dots are made up of the heavy metals and so it have to oxides and the carbon dots are the mostly carbon sources. So it is highly bio comfortable and the synthesis difficult and there is the synthesis is very difficult and the difficult for the surface conclusion, here it is readily surface function and it is complication and as I told it is pure accurately solubility and here it is water soluble.

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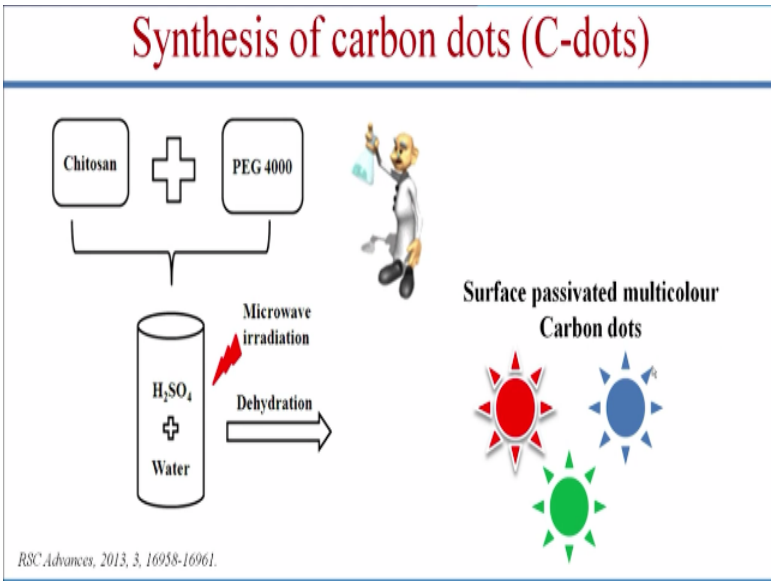

And I highly explain the synthesis of the carbon dots method okay and we use the synthesis of the carbon dots and this could be water plus sulphuric acid and you can apply the micro red and it and the de hydrotation process and you will get the surface passive items and in the multicolor carbon dots .

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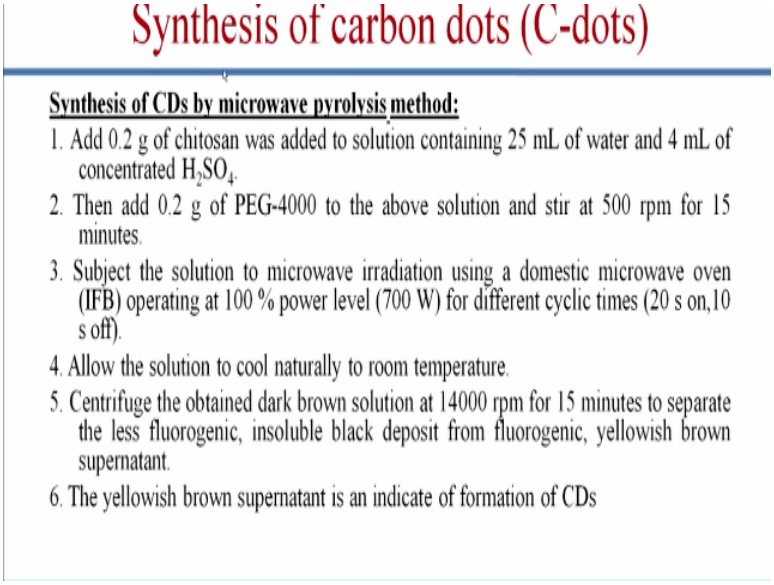

So this protocol has been developed the lab so let me explain in the protocol in the microwaves and in they use in the solution and in the water and the 4 ml of the acid ,then add the v0.2 gram of the above solution to the 500 rpm in the 15 minute and then subject the solution to the microwave in the integration and the domestic wave oven so in this case we have micro oven in the 700 watt and the different cyclic times.

That means the 20 seconds on the 10 seconds off and ten to get color dots and the solution okay then allow the solution to cool in the naturally to the rooms temperature and in the region and the centrifugal in the obtained in the solution and in the 15 minutes and then separate the less insoluble in the black deposited from the and it will open it and yellowish brown will open and indicate on the formation of the carbon deposited and the by using the deposited and then proto cal and in the florescent in the carbon dots in the lab and in the domestic microwave in the deny carbons .

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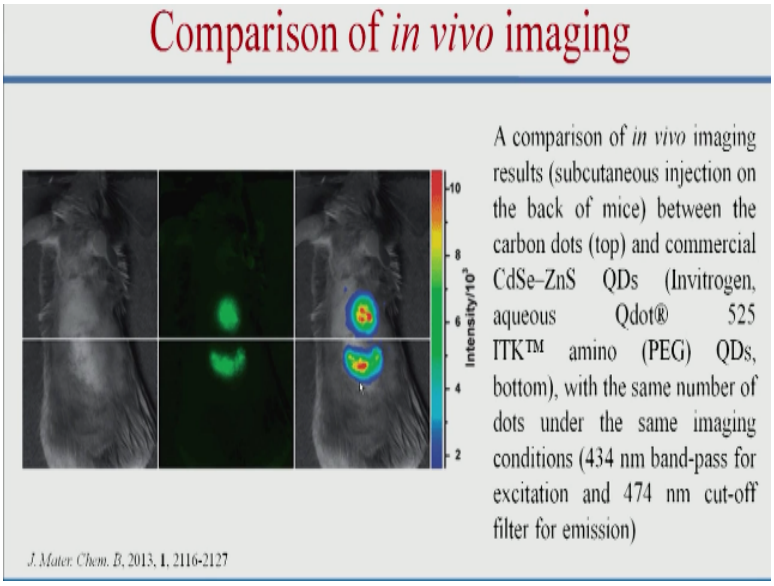

And this is the compilation and in the imaginary and in the carbon dots and in the carbon dots and with they use in the mouse model and in the in and this is the carbon dots and the bottom in the quantum dots so this quantum dots is in the commercial dots this is the carbon dots so it is the giving equally efficiency in the carbon dots are in the. Equally efficiency in the and it is another advantage in the major in the future.

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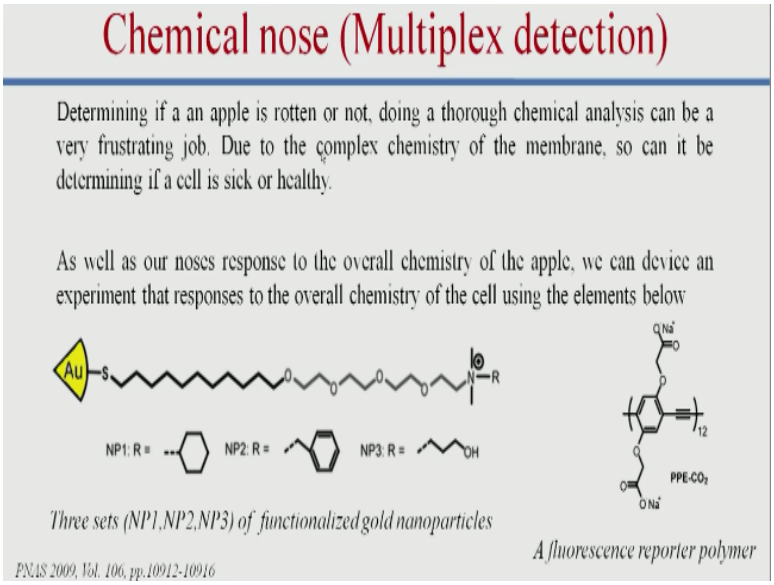

And this is the chemical in the suppose in the energy n the and the bunch up of the bunch of the so you and tell in the throttle in the in the chemical nose in the can be injected to the person in the finding cancel cell in the florescent reporter chemical.

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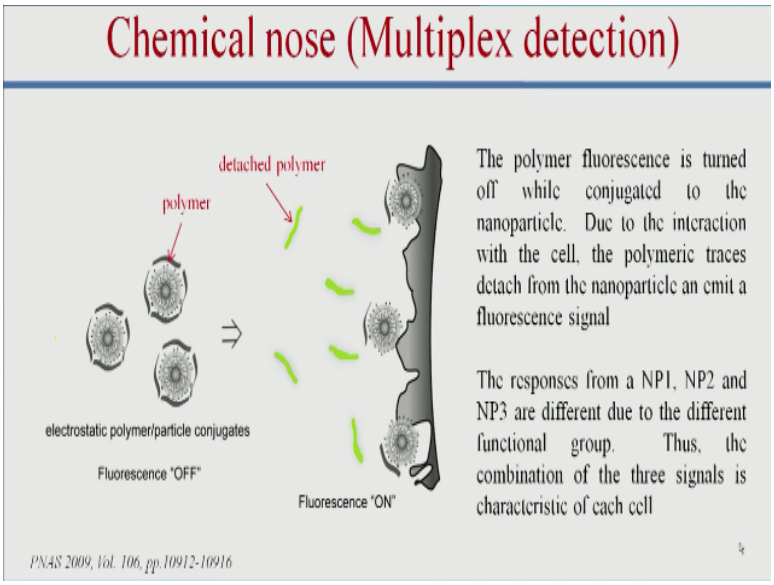

So you can see here the person is having the cancer you will having the various markers on the cell surface and the you can see this is the nanoparticles and covered with the polymer and the florescent this if off, when this nanoparticle bind to the cancer cell and this will remove the polymer, so when the polymer and the removed in the given the in the floors and the signal in the floors and the signals and they will be one.

And this is the yellow and the and the red flows and the green flows and that means the flows in the one the person is in the advance stage of the cancer suppose out of these only one particular is gives the fluorescents signal that means they can see he is the early stage of the cancer due to the exportation and in the particular marker so accordingly we give drug to the person for the cancer therapy. And we can and the diagnosis using another moment and the so the cancer cells appear the more elevated in the normal in the local temperature.

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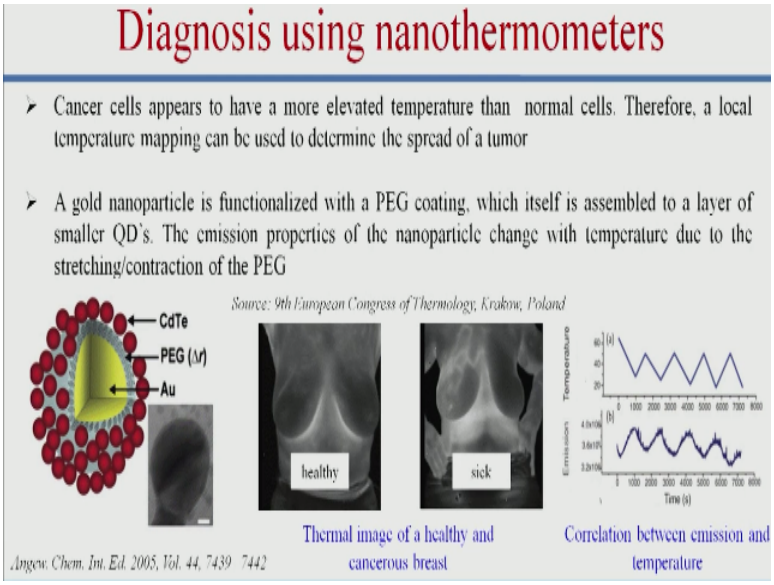

And the mapping can be used in the determine in the spread of tumor, so when compare to the normal person the cancer cells will be having more metabolism and there will be more generation of the heat at the particular location and we can make a gold nano particle funiculate with PEG, that is polyethylene glycol coating okay and on the top of that we can add the quantum darts.

And the emission properties of nano particle change with respect to temperature due to the strutting and contraction of the polyethylene glycol, you can see here inside is goal nano particle and the top layer is polyethylene glycol is polymer and the topes layer is your quantum dots. So if there is a change in the temperature the polymer will stretch or it will stink, so according to that it will give the different kind of florescence.

So here we can see here this is the healthy person and this is the sick person so there is a temperature difference. So based on that we can easily diagnose the beast cancer and based on the temperature and the emission we can easily identify whether the persons in the early stage of cancer or advance stage cancer.

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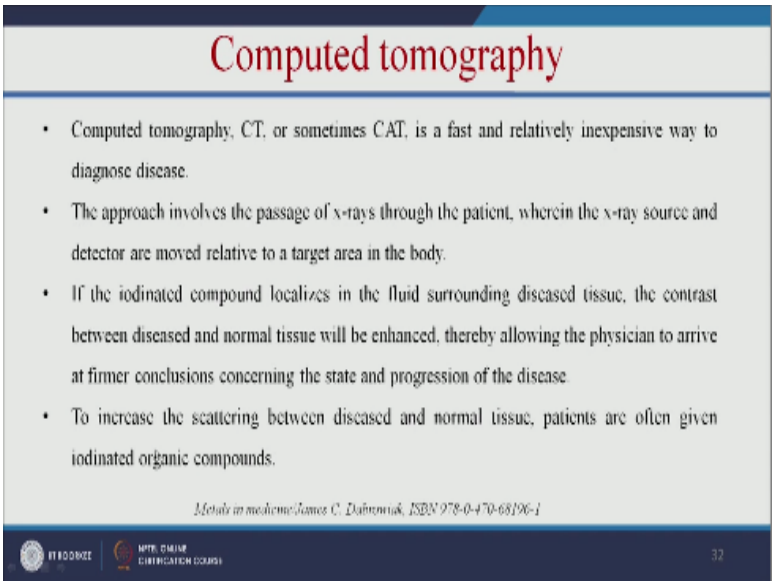

Let us see what is the role of nano materials in the traditional methods like CT scan and or MRI scan how we can improve those techniques by using this nano materials, so computed tomography that is CT or CAT scan okay it is s fast and relatively inexpensive way to diagnose disease. And this approach involves the passage of x rays through the patient and the x ray source and the detector are moved related to a target area in the body.

If the iodinated compound localizes in the fluid surrounding diseased issue the contrast between the diseased and normal issue will be enhanced, so thereby allowing the physician to arrive conclusion like whether what is the state of the disease and what is the progression of the diseases okay, and to increase the scattering between the disease and normal issue patients are offend given iodinated organic compounds.

That means in the traditional methods like a CT scan so the patient will be given iodine compound okay and will be applying the x rays to diagnose the different between the disease issue and the normal issue. And here we can use the gold nano particle okay so we can use the gold nano particle quarter with the polyethylene glycol.

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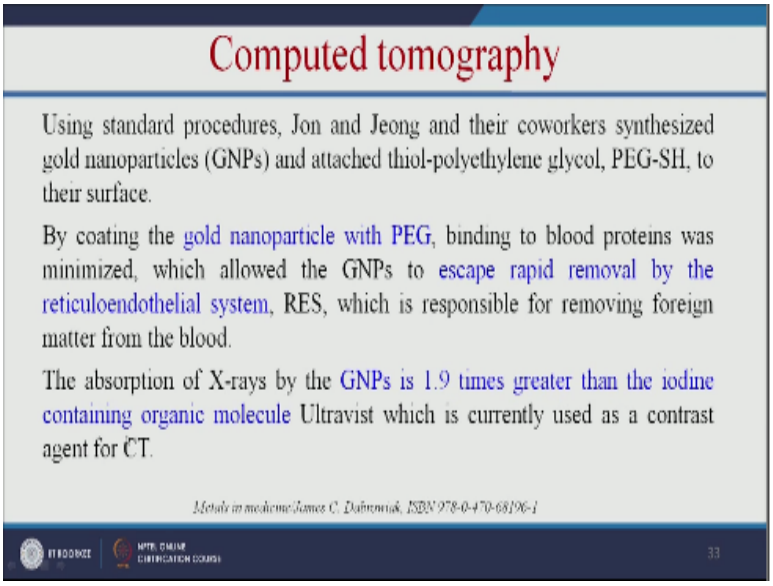

And it will allow the gold nano particle to escape from rapid removing by the reticuloendothelial system which is response for removing the foreign matter from the blood, so when you coat the gold nano particle from the polyethylene glycol it will give the bio-comfort ability and also it will allow the nano particle to escape from the immunity system. So here when we use the gold nano particle for CT scan so the absorption of x rays by gold nano particle is 1.9 times greater than the iodine containing organic molecule okay.

So when we use the gold nano particle for CT scan it is improving the efficiency two times more than the normal iodine compound okay, so this will reduce the expressed of patient to the x rays and it will be having high sensitivity okay.

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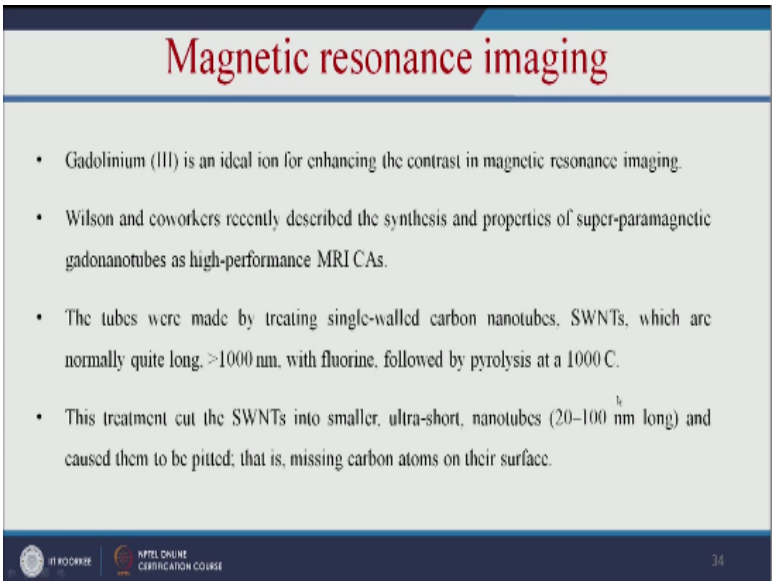

So let us see how this nano particle can improve the MRI Magnetic resonance imaging, so Gadolinium is an ideal ion for enhancing the contrast in magnetic resonance imagine. Here we can use this single walled carbon nano tubes okay which are usually 1000nano meter long and by pyrolysis that means your treating this carbon nano tubes at 1000^0 C this carbon nano tubes can be broken in to 20 to 100 diameter long and due to pyrolysis there will be a pit formation so that is a missing carbon atoms on the surface.

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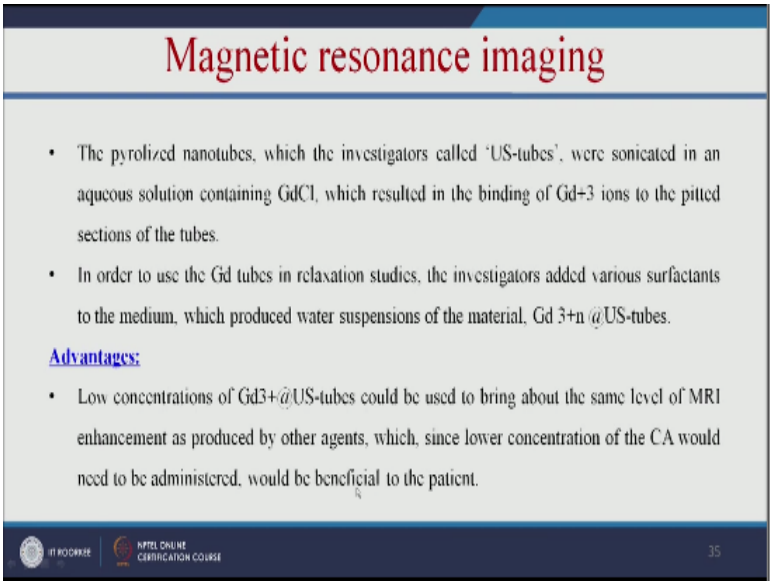

And we can add the Gadolinium ions to this Gd nanotubes and you can do the sonication, so when you do the sonication this Gadolinium ions will go and bind to the pit regions so the advantage of this carbon nanotubes is low concentration of this Gd nano tubes could be used to bring about the same level of MRI enhancement as produced by the other agents okay. So here we are using the low concentration of contrast agents so that will be beneficial to the patient.

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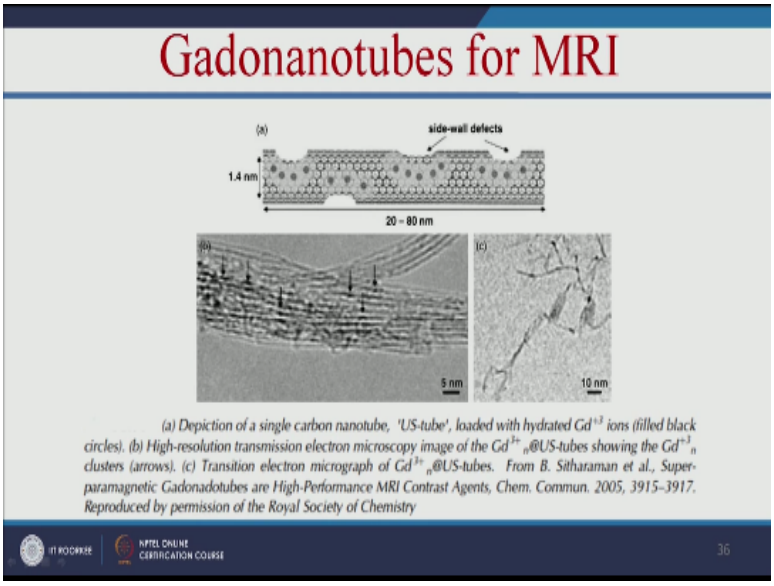

You can see here this is the carbon nano tubes and due to pyrolysis there is a pit formation when you add the Gadolinium and do the sonication this Gadolinium can come and attach to the surfaces so this is called as Gadonanotubes and which will enhance the MRI imaging.

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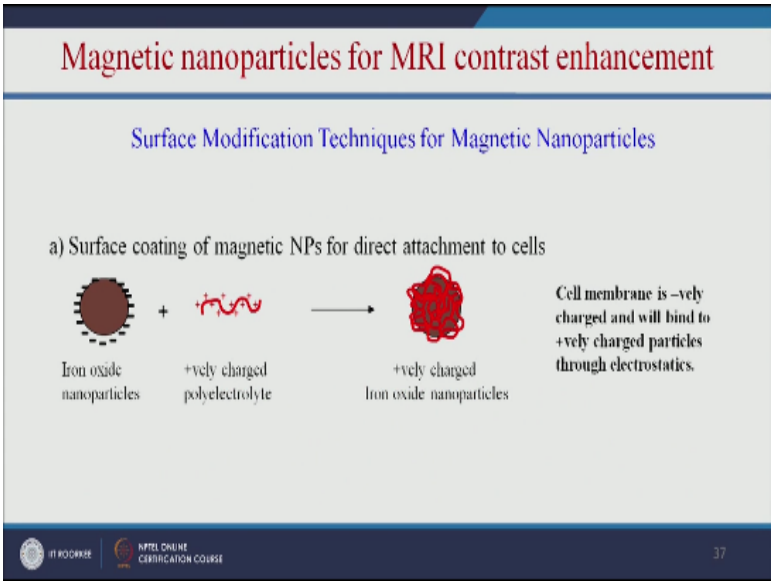

And we can also use the magnetic nano particles for MRI contrast enhancement, so we can make the Iron Oxide nano particle that is iron oxide nano particle is usually negatively charge, so we can add a positively charge poly electro light. So when you add this you cell member is negatively charge so it can easily bind to the cells by its positive charge through a electrostatic interaction, and it will enhance the MRI contrast.

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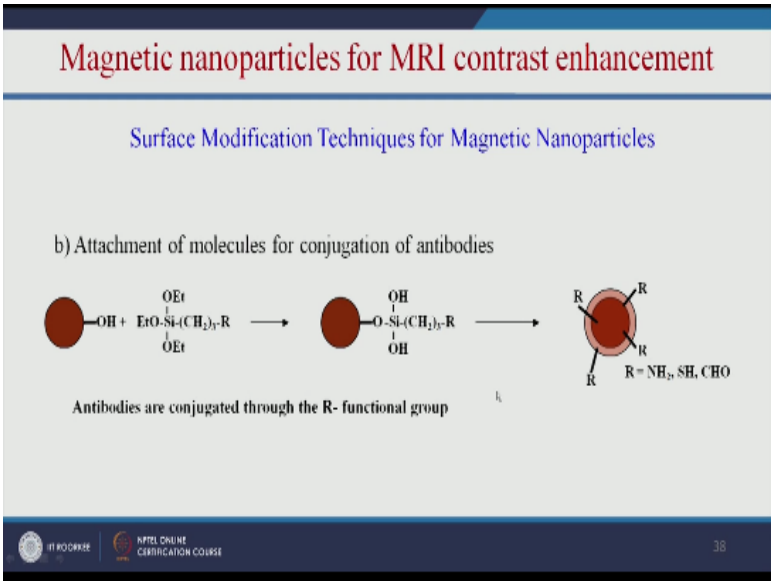

And next example is to this iron oxide nano particles we can also add anti bodies which can specifically go on bind to the cancer cell and it can also improve the MRI contrast.

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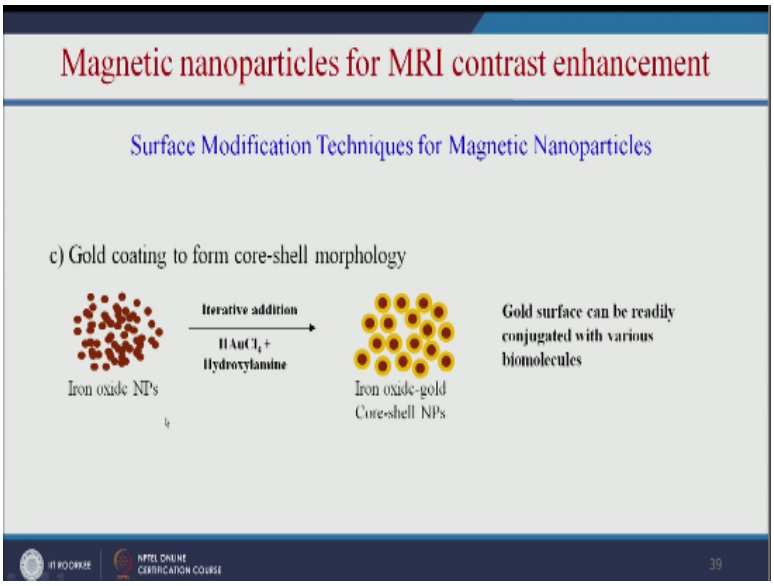

So another example is we can do the gold coating to form core shall morphology of iron oxide nano particles so here iron oxide will be the middle and falling you will be having gold coating okay, so the gold surface can be readily conjugated various bio molecules and it will be having like a multiple function like we can use the iron oxide for MRI enhancement also the gold is also will enhance the MRI contrast enhancement.

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So let us see how to make a paper based diagnostic for cancer so recently professor Sangeeta Bhatia, so from MIT they developed a paper based diagnostic kit that can redact the cancer by identifying bio molecules in the patient's urine. So let me explain to understand a simple way.

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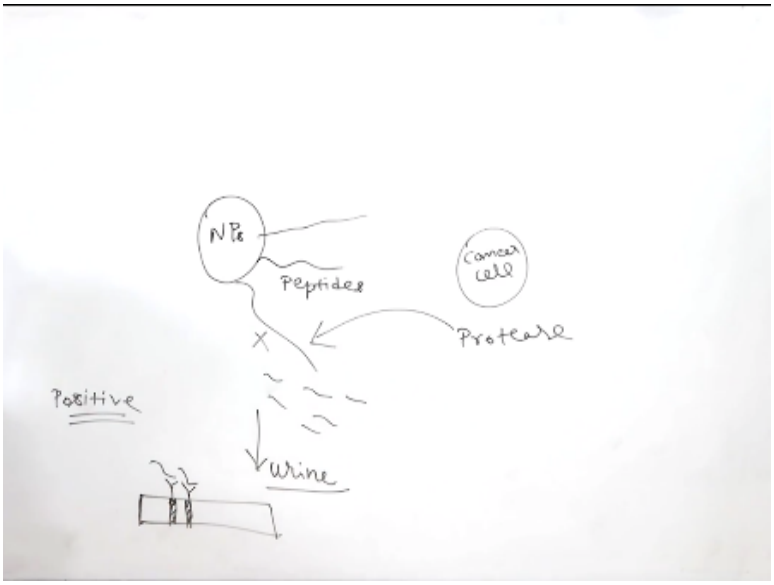

So what we have done is they have taken a nano particles and conjugated with the some peptides okay and usually the cancer cell express some amount of protears so this protears will specifically break the peptides start to this nano particles okay. So this peptides will be broken on to small, small pieces so that will be scatted to the urination process okay, so when you add the drop of urine to the paper based kit, so this paper based kit will have anti body specific for you're the peptides okay.

When the peptides come and bind to this it will give a color line so if the person is getting this kind of color line that means it is positive for the cancer. So it is simple paper based kit, so they made a nano particle and attached the peptide okay and cancer cells produce some kind of protears and this protears will specifically cleat this peptides and break the peptides in small, small pieces and this will be excerpt in the urine and this paper based kit will be having antibody specific for the peptides and this anti body is a some kind of color beats.

So if the peptide is come and bind to this it will form a kind of color line that means the person is positive for the particular cancer.

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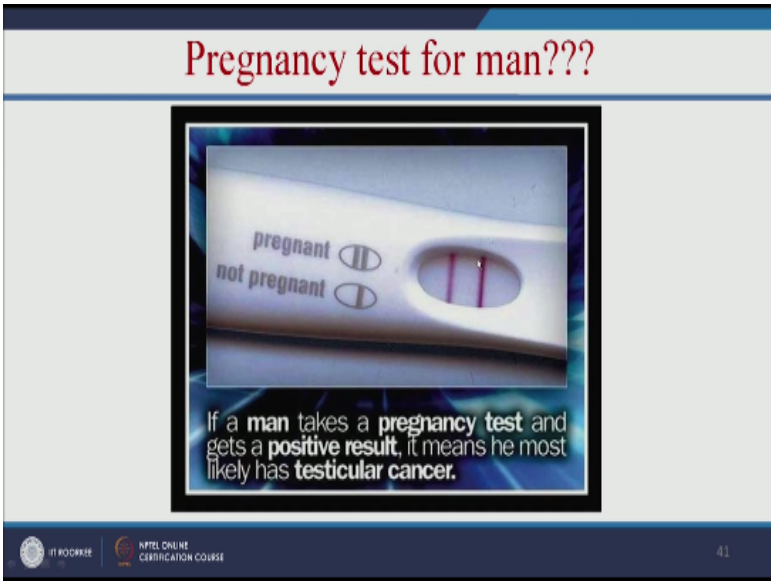

And another example is like a we thought that pregnancy test kit is only for the female so we can see here so the person is pregnant there will be two lines and the person is not pregnant there will be one line so this is the simple pregnancy test kit, we thought this pregnancy test kit is only for female so recently they found this if a man takes a pregnancy test kit and if it get positive result it means he is most likely to have testicular cancer.

So if the person the man is getting a positive for pregnancy test kit that means he has higher chance for testicular cancer, so there are several methods available for cancer diagnosis okay and everyday some new discoveries that coming in this field for advance thing that early diagnose of cancer. So as a summary this lecture we have learnt what is cancer and what are the various nano materials available for cancer diagnosis and we have also leant what is condom dots and carbon dots and how we cann improve the CT scan as well as MRI using this nano materials okay.

Si I will end the lecture here I thank you all for listening, I will see you in another interesting lecture.

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