Bioengineering: An Interface with Biology and Medicine

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Lecture - 05
Clinician's Perspective-I

Welcome to the MOOC NPTEL course on bioengineering an interface with biology and medicine. Today, we are going to have an interactive session with clinician to share their perspective.

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In first-of-its-kind initiative today we are going to introduce you to Dr. Aliasgar Moiyadi. Dr. Moiyadi is a professor and consultant and an accomplished neurosurgeon at The Tata Memorial Hospital and ACTREC in Mumbai.

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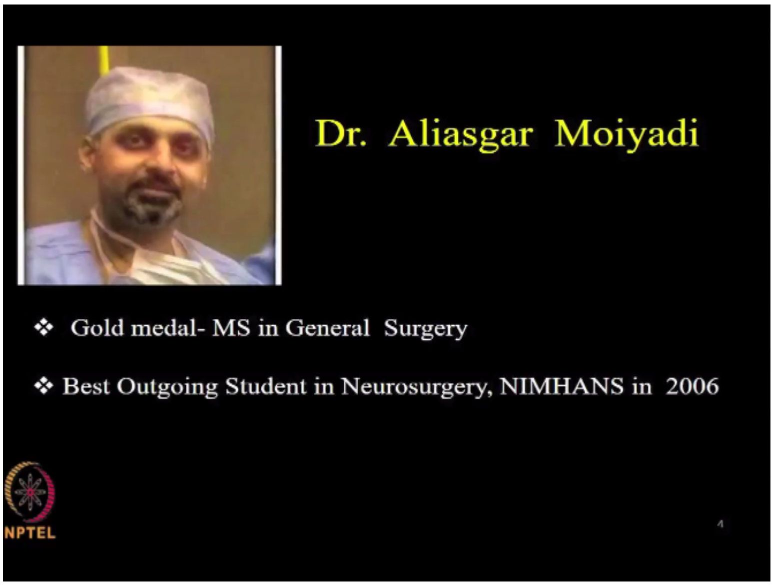

He was awarded with the gold medal for his accomplishments in MS in General Surgery. Dr. Ali was also awarded the best outgoing student in Neurosurgery at NIMHANS in 2006.

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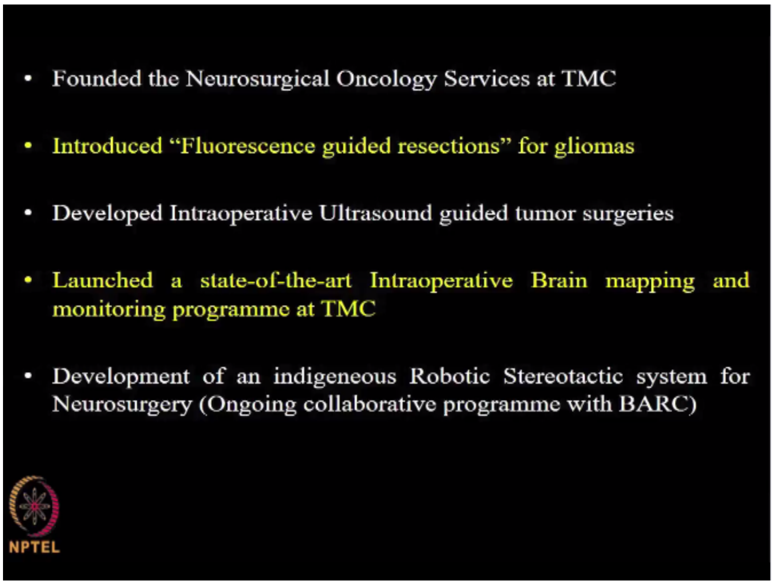

Dr. Ali founded the Neurosurgical Oncology Services at TMC one of its kind dedicated unit in the country. He introduced fluorescence guided resections for gliomas. One of the first neurosurgical services in India to offer of this kind. He developed intraoperative ultrasound-guided tumor surgeries which are recognized as a global leader in this area. He launched a state-of-the-art Intraoperative Brain Mapping and monitoring program at Tata Memorial Center.

He also developed an indigenous robotic stereotactic system for Neurosurgery which is an ongoing collaborative programme with BARC. Dr. Ali has been awarded with several distinguished awards.

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He obtained Indian Society of Neuro-oncology President Award for best Clinician Researcher in 2015.

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He also awarded DAE Scientific Research Council Government of India Award for the Outstanding Scientist in 2015. He is recipient of numerous other national and international grants and awards. He secured participation in the prestigious brain tumor course conducted by the Cold Spring Harbor Laboratory in New York in June 2010.

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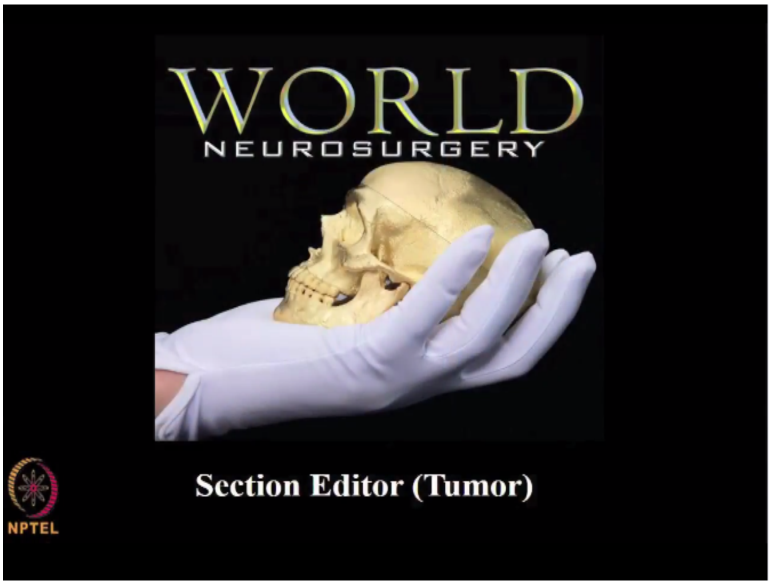

He serves as Section Editor Tumor for the prestigious journal World Neurosurgery. Dr. Ali has published over 70 research publications in national and international peer review journals. His research interests include novel, intraoperative imaging tools, complex skull based surgery, tumor biology and therapeutic strategies. So in order to illustrate how advances in technology has bridged the gap between clinicians and research.

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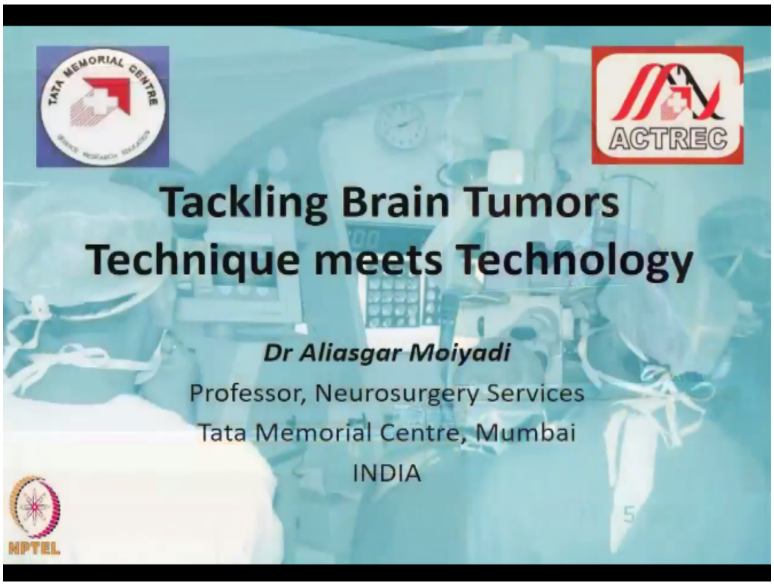

Today, you are going to listen perspective by Dr. Aliasgar Moiyadi who is going to illustrate you his research on the brain tumor and also going to post several challenges and questions for you that how engineering solutions are required in this area. So let us welcome Dr. Aliasgar Moiyadi. I am a neurosurgeon, so what I am going to be talking about is what I do. So just to give you an overview, brain tumors is what I deal with.

And brain tumors can be of many types, many varieties, you do not need to know all of that, you do not need to get bored with that but they come in different sizes, different shapes. They are the commonest brain tumor, the primary brain tumor which arises from the substance of the brain is called the glioma and that is because if probably at some point of time you will have read the glial cells are a type of cells present in the brain.

So mind you the functioning cells in the brain is the neurons that is where you have the synaptic connections but these tumors and these are the commonest tumors arise from the supporting cells glial cells and they are called gliomas. Anyways, irrespective of what kind of tumor it is the strategy is surgically more or less are same. The biggest challenge we face as neurosurgeons when operating on such tumors is that these are usually located within the deep substance of the brain.

And how to reach the tumor, how to localize it without doing any harm to the rest of the brain remains the most important challenge.

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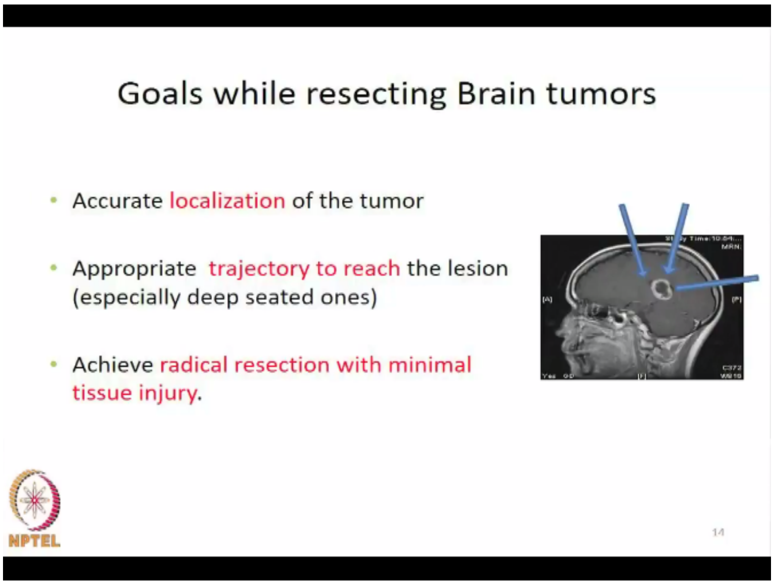

We know that we have to be very careful because brain and other parts of our nervous system are very, very critical, very delicate. They are what we call eloquent areas where they function. There are certain parts of the brain which are less eloquent, certain which are more, certain which can be sacrificed, certain which cannot be, you need to know all that. At the same time, you need to be able to remove the tumor completely.

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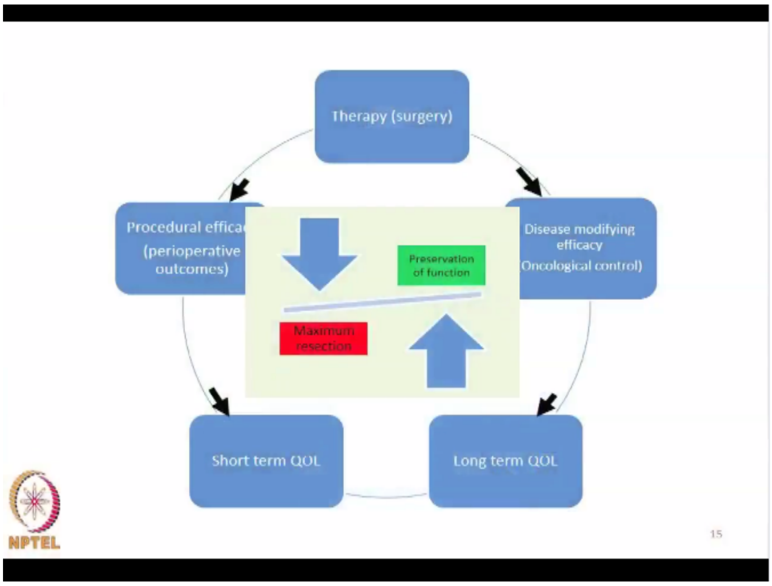

And this is because you have to maintain what we call short-term outcomes. Short-term outcomes is what dictates the recovery of the patient immediately after surgery. There is no point having a patient with the tumor removed but having a significant neurological problem because of your surgery. At the same time, you have to try and maximize the removal because you have to maintain a long-term outcome which is the oncological outcome.

That is removal of more tumor helps the patient long-term survival but doing harm to him and trying to be heroic and radical will do him a lot of harm in the short-term, so you have to balance the two end.

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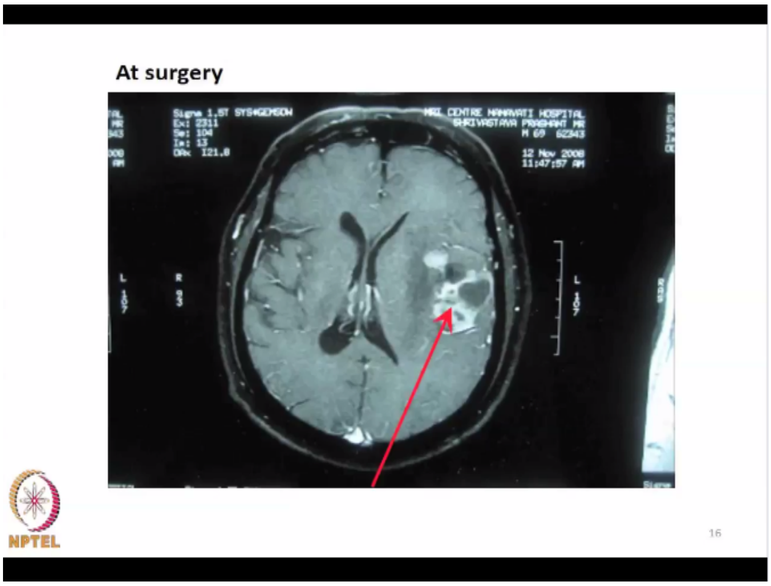

That is the entire game. Now why is it so challenging? Now what I have shown here is this is an MRI picture. MRI is a scan of the brain and this has been cut like this, so you are seeing it from top and what you see that white over there is the brain tumor. That is a tumor, it is seen very well there.

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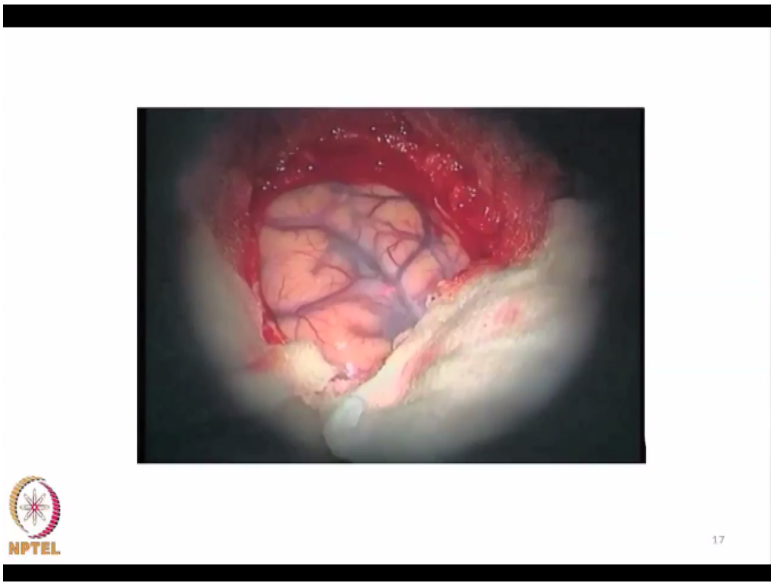

But when we open the brain, this is how it looks. This is just a normal brain. The tumor does very little to change the surface appearance of the brain and therefore you have to be very careful where you enter because there may be certain areas which are very critical, certain areas which are normal which you have no right to mess around with and you do not want to make a mistake here because you may land up with a deficit or a neurological problem which can be life-threatening and will be irreversible.

So technology has helped us over the years in 1970s and 80s assured in the era of microneurosurgery.

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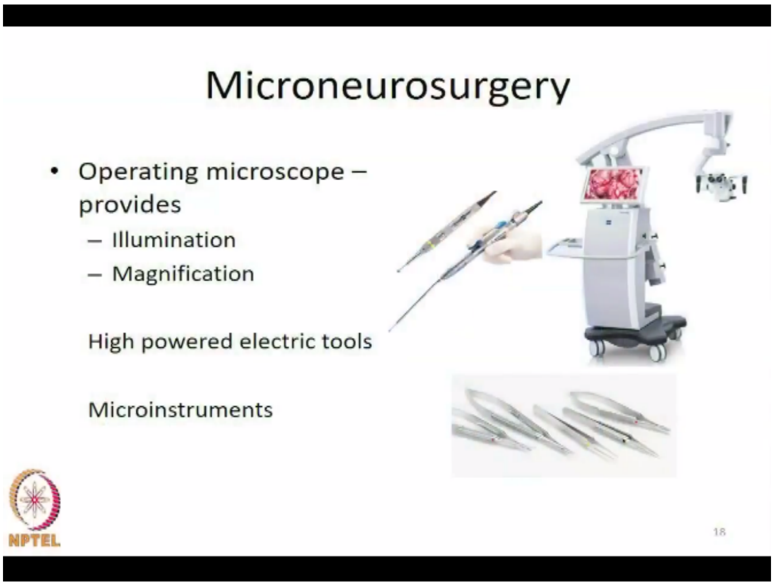

So we have the operating microscope surgical microscope that is how it looks like. We have high-powered instruments which help us do safe surgeries open the skull. We have fine microinstruments again all marvels of engineering which help us do very delicate surgery in a very precise manner.

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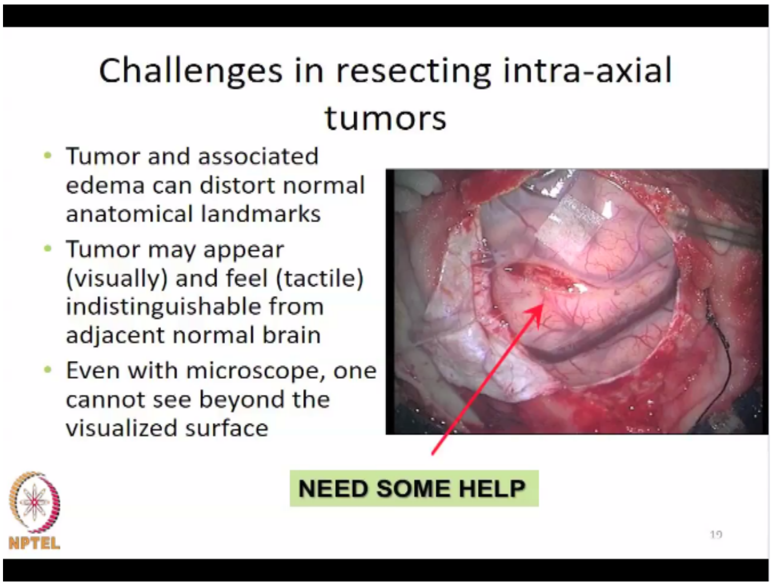

Still there are a lot of limitations because of the inherent nature of these tumors and this video is not running. So the problem with these brain tumors is that you cannot distinguish where the tumor ends and where the normal brain starts. In this video, this is the normal brain and this I have put a small piece of sterile paper there during the surgery because we are mapping the brain and I will tell you what that means.

That is the motor area of the brain that means that is the area which is controlling the half of your body. So in the brain again if you remember neuroanatomy or when you read it for general knowledge sake that there is usually a crossed connection. Your right half of your brain controls the left half of your body and the left half of your brain controls the right half.

So we are operating on the left brain and there is a part in the brain which is the motor area which is controlling the entire half of the body's motor function that is your movements. We have to be very careful that that should not be damaged. The tumor is sitting here in this part which I have already slightly opened up. There is no way to know what is tumor, what is normal brain.

We need to use certain tools and I will show you what we do and that is the reason we need this help. This is technical help. This is where technology has gone a long way in making safe and radical surgeries possible.

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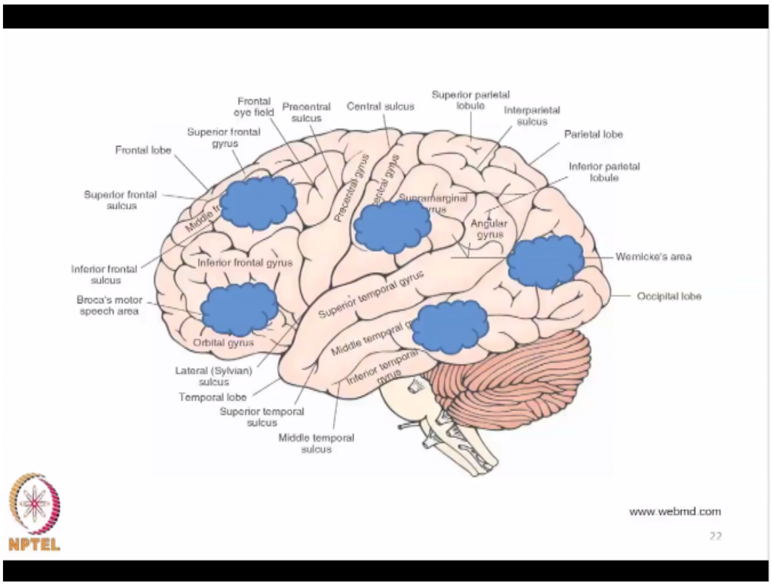

This is how the picture in the book of the brain looks like. You have different functioning areas. This is what I was showing you, so this precentral gyrus if you read that that is the motor area that is where we were operating. Now brain tumors may be located anywhere over here. They do not respect areas, they do not even read the book, so they do not know where they should not be and where they should be, they just grow anywhere.

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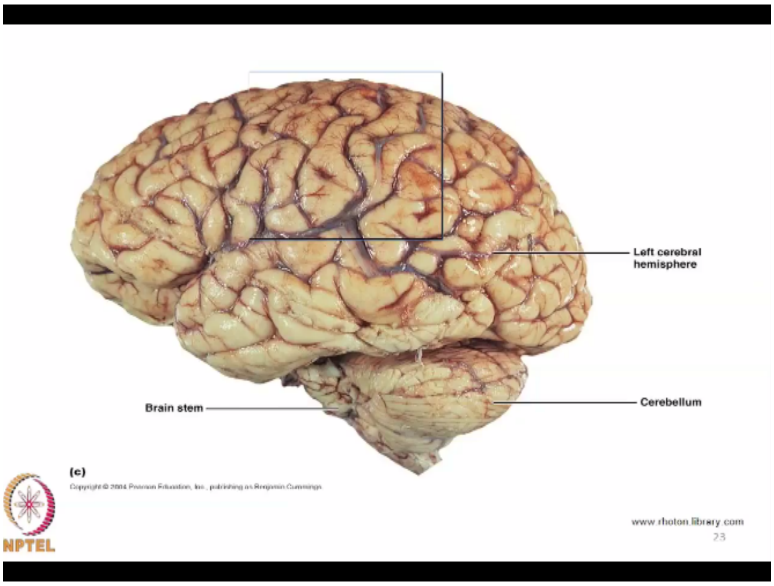

The problem is when you are operating this is how the brain looks.

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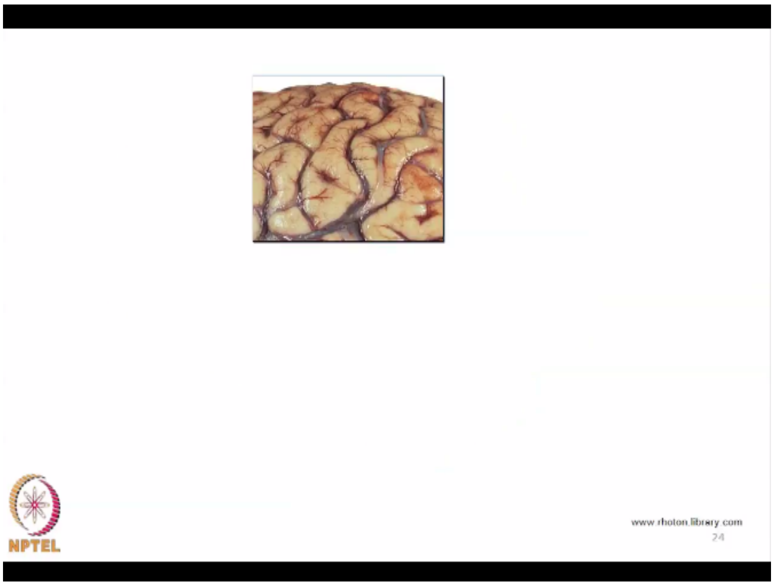

This is how it looks and in fact this is how your surgical field looks because you do not have the whole brain exposed in front of you and when this is what is happening it is very difficult for you to know where you have to enter, what areas you have to spare and what areas you have to remove. Now these constraints put a lot of limitations on the optimal outcomes and this is where technology comes to help. There are various ways this can be done.

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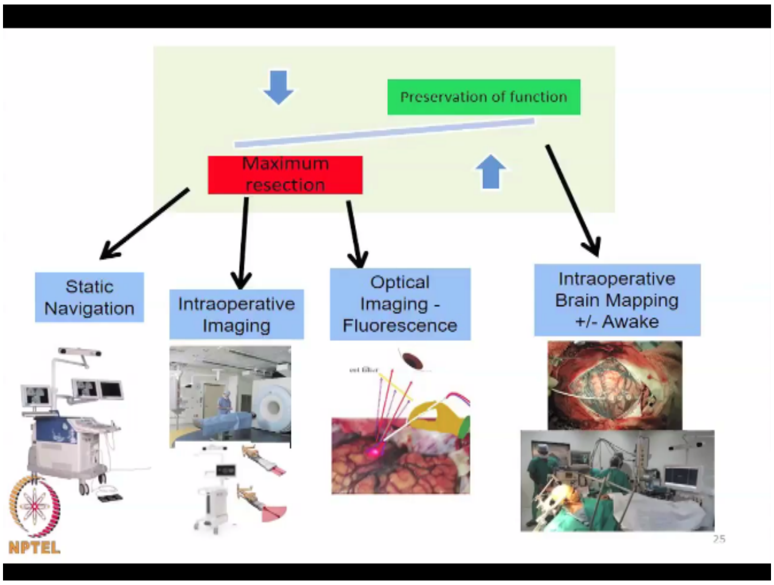

As I said you need to balance your heroism with safety. There are tools which help you do that, you call it navigation, I will tell you what that is. They have intraoperative imaging. We have optical imaging visualization and at the same time we have to maintain functional integrity by doing what we call brain mapping.

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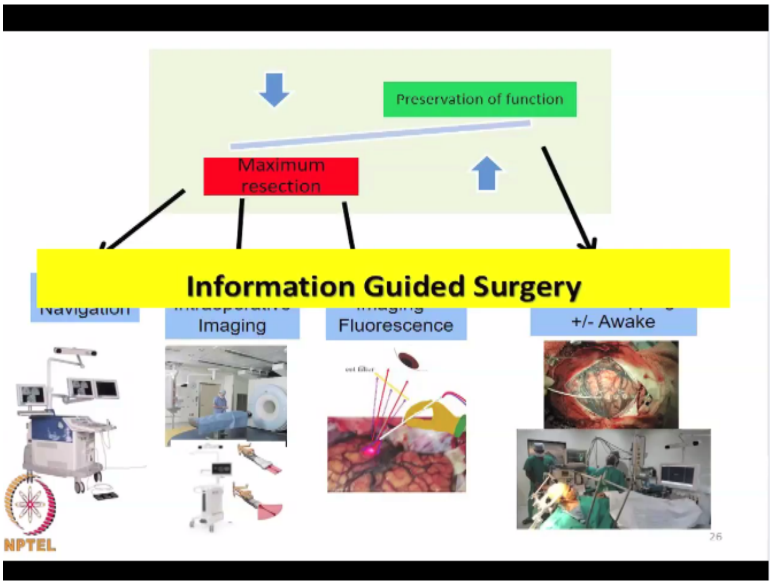

Now if you use all of it together, you get the maximum information that is what I call information guided surgery.

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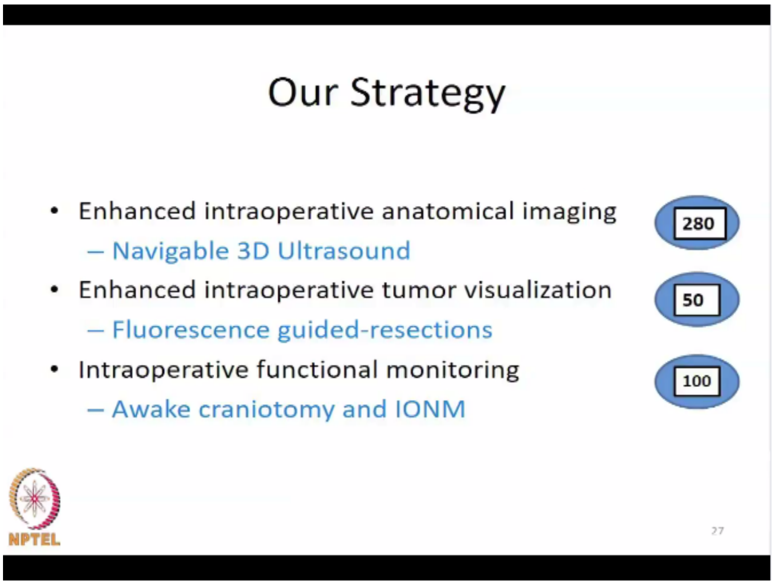

At our center what we use and what we have been good at is what we call intraoperative navigated three-dimensional ultrasound. We use something called fluorescence and we use of course a lot of functional mapping techniques. Now just to give you a brief of each of these, what is navigation? So it is nothing but it is a GPS system. So all of you know what GPS is okay, everybody of you are smart, you all have smart phones, you all have used maps, you all know what GPS is.

So essentially what GPS does is it has pre-fed maps and you follow that because of some kind of complex triangulation, I do not know, you all would know better how that works but that is how you guided. If I want to get out from here over there, I just put it on to my smartphone and it tells me how I have to go, that is exactly what navigation does. It is image-guided navigation.

So we work with images which are fed into the computer in the navigation system.

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This system here and it is the preoperative MRI of the patient. It is co-registered with the patient's anatomy and during surgery you saw we had a restricted field but using this device we are able to exactly see beyond what is seen on the surface, we are able to plan and execute. That is a basic problem with GPS and navigation and that is that it is as good and reliable as long as the maps which are fed in are accurate.

The moment a route changes or a new road comes and you have old maps you will fail, you will go on to the wrong way or you will be led to a dead end and that is what happens during surgery also. That the maps that are fed in are the preoperative, now the brain is a very semisolid fluid dynamic system, when you open the brain there are changes. There is sag, there is some deformation.

And then your preoperative anatomy becomes null and void. So you need to update your maps intraoperatively and we do that using some kind of intraoperative imaging. If you have ever seen an MRI or anybody of you has had a CT scan on MR they are huge machines, you cannot have that intra-op, it is possible and it is there where these systems available but they are too logistically challenging. What is alternatively available is a very simple intraoperative ultrasound.

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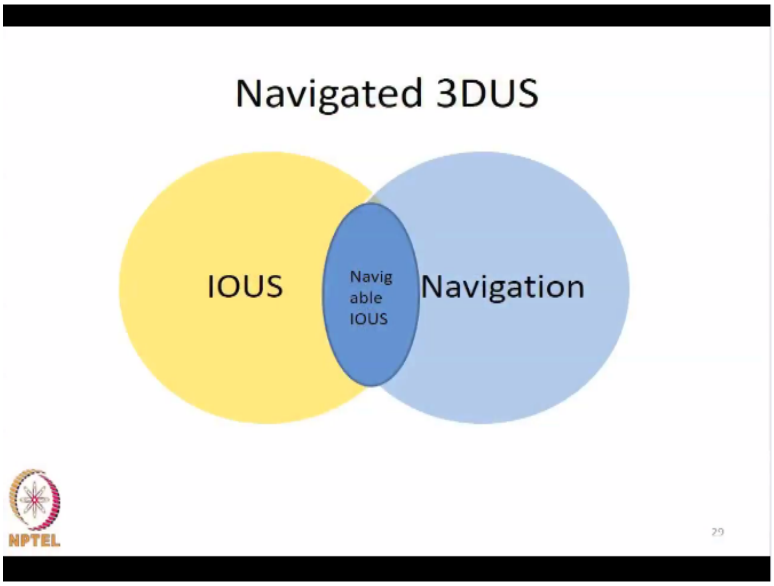

You combine that with navigation, you get navigated ultrasound and it helps you re-scan the patient's anatomy repeatedly and to get a real-time update of where you are.

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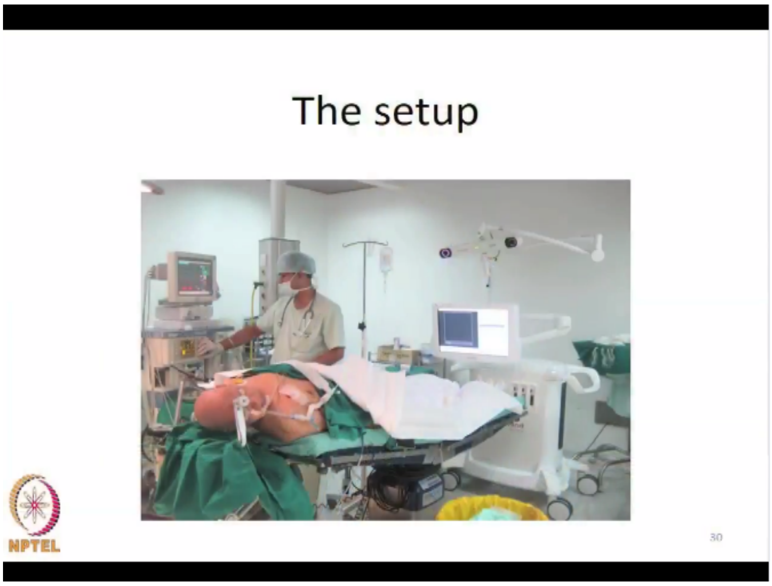

This is what we call navigated ultrasound and this is how it looks.

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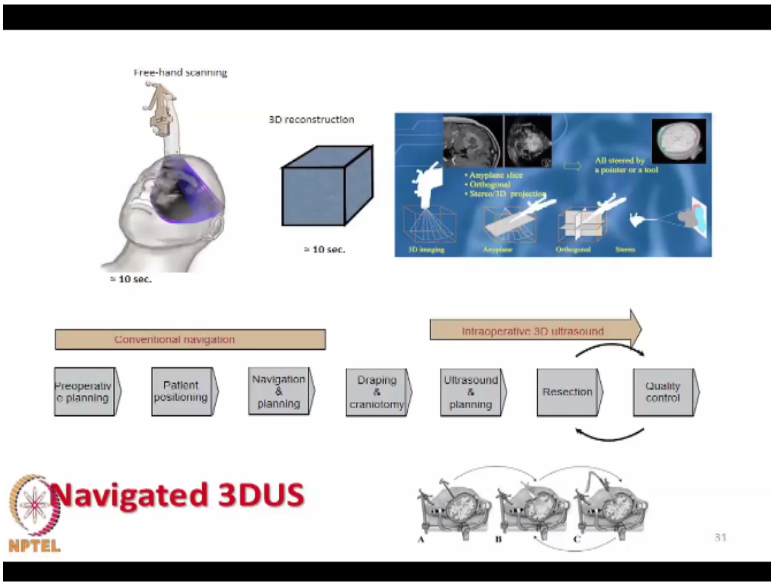

You do a 3D sweep of the ultrasound wherever you are operating, after opening the brain you compute a 3D volume that is a lot of computational computer science involved in that different algorithms, you fuse all the images and then you can re-slice them to see it the way you want it and when you do that you can keep doing it again and again to update your images and know exactly where you have reached, how much of tumor you have removed, where you have to stop and whether you have achieved what you set out to do.

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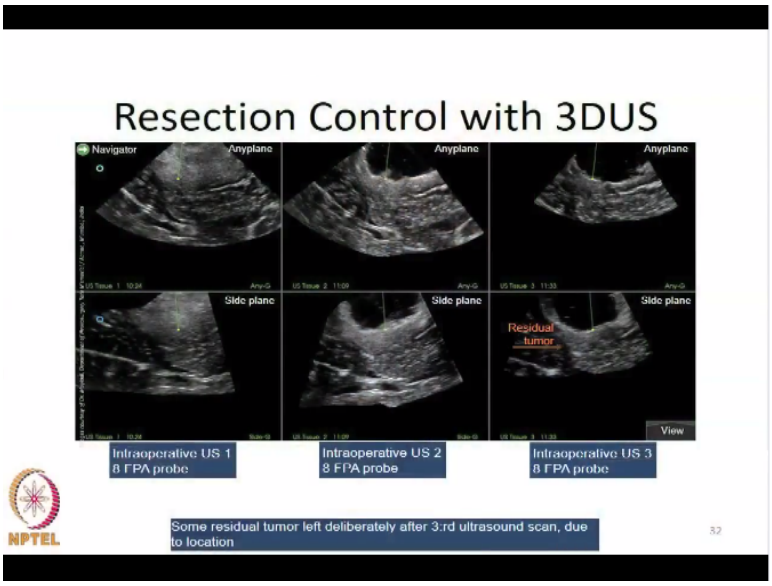

This is just an example of how the ultrasound looks. It is not coming too well on the screen but that is how it looks. The other modality we use to help ourselves is that our eyes are limited by what they see. Ultrasound shows you the anatomy but sometimes it also fails. What you need to do is enhance that visualization, so as I said tumor sometimes looks the same like normal brain but there are certain properties of tumors which can be exploited and incorporated into surgical tools in order to enhance and augment your visualization.

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This is one such property. Again maybe this is a little complex. This is the Krebs cycle that it is the heme cycle. Hemoglobin as you all know is something which is present in our blood and heme which is the important component is made from a particular substance called ALA, aminolevulinic acid.

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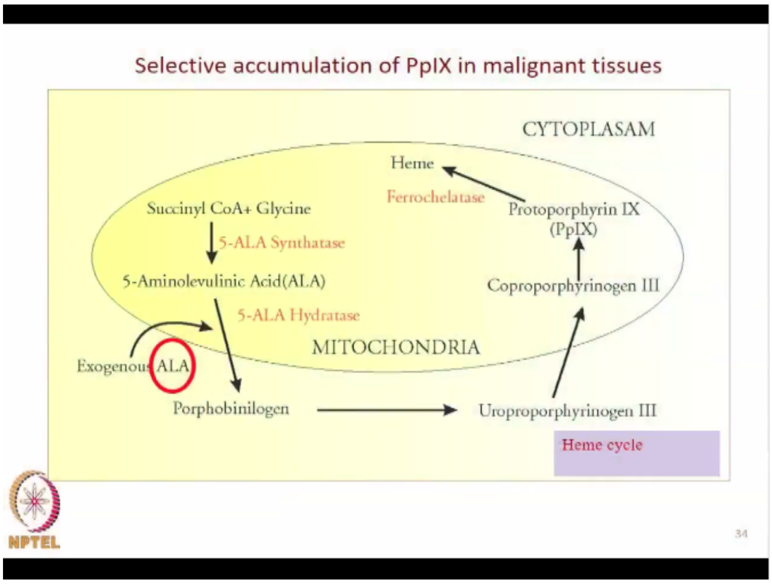

Aminolevulinic acid enters the cycle and eventually forms heme which is important for the body that is all you need to know. What happens in these brain tumors especially the gliomas is when you give ALA it is a very simple available chemical substance, you give the patient

ALA, it enters this cycle but it overrides the negative feedback and it starts producing more and more of these metabolites.

On top of that this particular last enzyme ferrochelatase which is going to convert all those metabolites into heme is deficient. So therefore on the one hand there is an overdrive of the system, second that there is cut off at the topmost level which means that a lot more of this particular metabolite accumulates in the glioma cell and this is exploited because Protoporphyrin IX. PP9 is an fluorophore, it fluoresces.

Now what is fluorescence? Fluorescence is I have a slide there, I will show you but it is nothing but it just it comes out in a different color.

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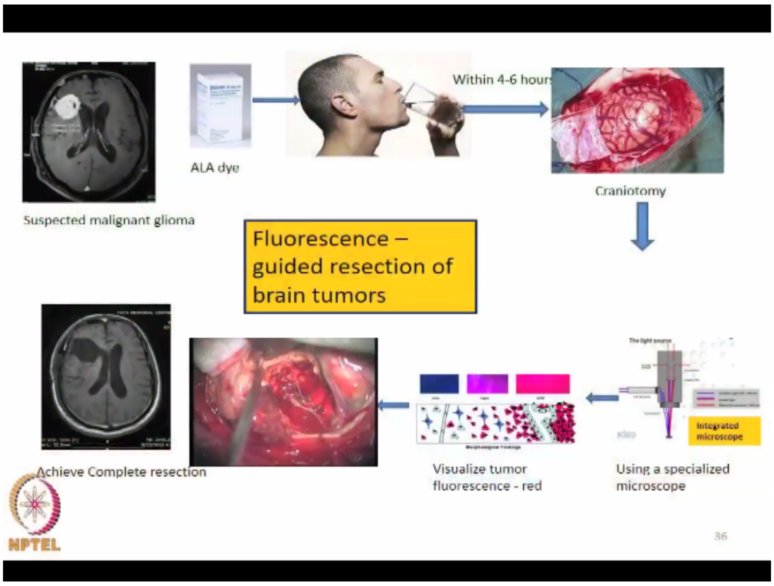

And how does it work clinically, what we do is that the patient is given this particular dye. He drinks it few hours before surgery. When you open the brain, again this was a video which I think I should run yeah.

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So what this is? See this is the live surgery going on under the microscope. We are trying to remove tumor and as you see what I am trying to remove is not very different from what I am seeing normally around but when I switch the filter, this is fluorescence, what is blue is the normal brain, what is red is the tumor.

This is all integrated into the surgical microscope and when you are removing it, you can really see what is the tumor and what is not and therefore remove it even though you are normalized under the microscope fail to see it. You have to however realize that you cannot keep removing everything that is red. You have to combine with functional techniques. That means you have to respect functional areas.

So where there are important functioning areas in the brain, you do not want to damage them. It is very important to understand the function of the brain. Now how do you understand the function of the brain? It is not written on the brain surface when you open that this particular gyrus or this particular part of the brain is sub-serving this function and there can be tremendous heterogeneity between different people.

Somebody's some areas are well-developed, others are better developed, how do you do that? The best way to study it is to keep the patient awake during surgery and this is what we call awake surgery. You all might have come across this terminology at some point of time or you might have seen it and it is not something which is new. This is very old but it is something which is very important.

And this is very crucial when you are operating. So this is just an example to show you the operative setup when we are doing an awake surgery.

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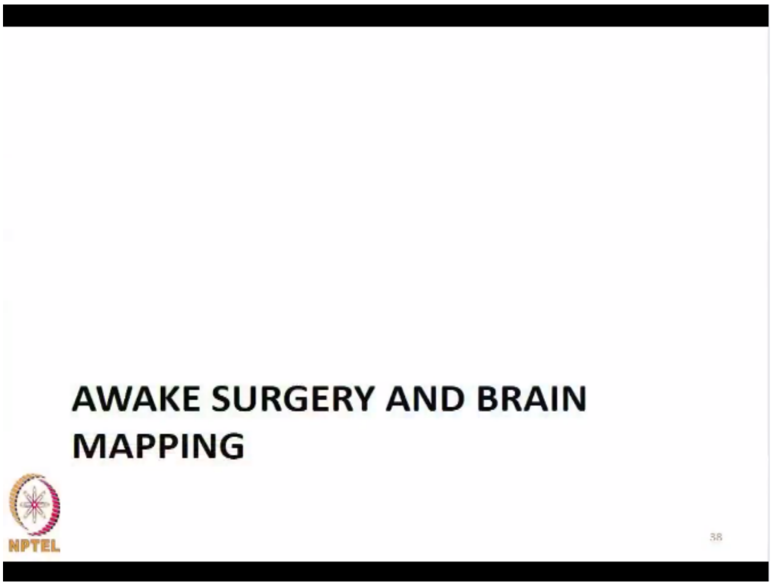

That is on a navigation system behind there, we have kept that navigation and this is the general setup. So the patient is all ready to be operated.

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He is already fixed on the head clamp. We always use head clamps to fix the head because you do not have to move during surgery and the patient is awake. If you can make out he is awake, he is responding to your commands. He will respond throughout the surgery. It is painless mind you because you give local anesthesia. The brain if you touch a normal person's brain has no sensation. It is amazing.

The brain senses sensations from the whole body but when you touch the brain you will not perceive any sense because the brain has no nerve endings on it by itself. So the brain is absolutely painless. So you can operate on the brain but you have to make sure the rest of your surgical area is pain-free. Now why this is important is because when you are operating you have to keep the patient awake to ask him to do different functions.

So that you can continuously monitor what parts of the brain are going to be at risk and what are not and that will help you execute your surgery well. This is important, it has to be combined with whatever I talked about ultrasound, MRI, fluorescence. There are many things. All these tools have to be combined together in order to get your best optimal result and this is obviously possible only if you got the right technology at your disposable.

It is just a caution that surgery is not always enough. There are other forms of treatment in brain tumors which are sometimes very necessary especially for the more malignant ones including radiation, chemotherapy and other forms of treatment. Sometimes all of this also fails and therefore a very important part of our job is to try and understand why that happens and that is because of tumor biology.

There are various ways of studying tumor biology and there are various strategies and Sanjeeva and we have been involved in a lot of these proteomic based research.

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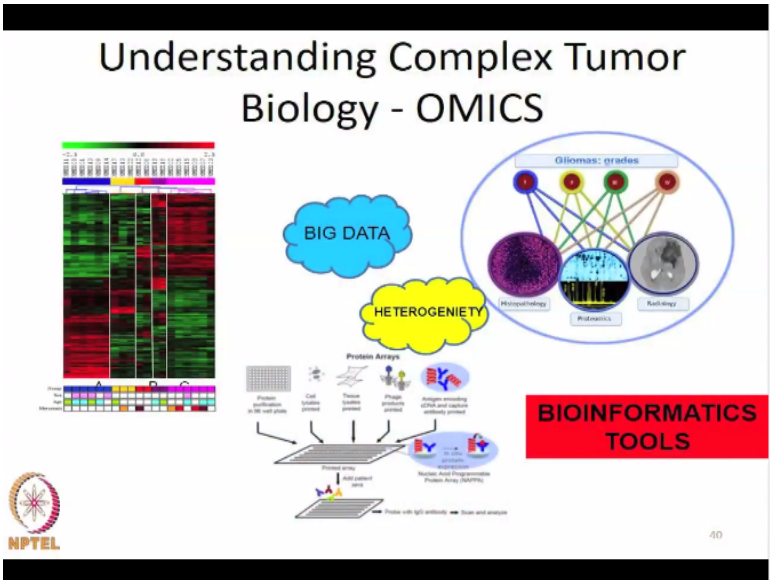

Besides the intraoperative novel imaging techniques, which is something which is again close to my heart. Now the purpose of this whole talk is to sensitize you all that this is just neurosurgery but in each field of surgery there are different aspects which probably are important and cannot be achieved without appropriate technological advances. So as I said the purpose was and the idea was to sensitize you guys about what is possible.

But also what needs to be done beyond what is already being made possible by technology. So for me and for a lot of surgeons, it is most importantly trying to be able to correctly identify the extent of tumor and to be able to delineate it reliably and to achieve the resection or the removal without having too many problems. It also means augmenting human capability. Human capability has a limit and you have to augment that.

How can we do it? There are various ways augmenting vision as I showed you with you know optical imaging. It is not just fluorescence but there are many other things which can be done to augment the visualization I mean and you know you can have a wild imagination as to what is possible and it can be done. The other augmentation required is for skills, technical skills and that is where robotics comes in.

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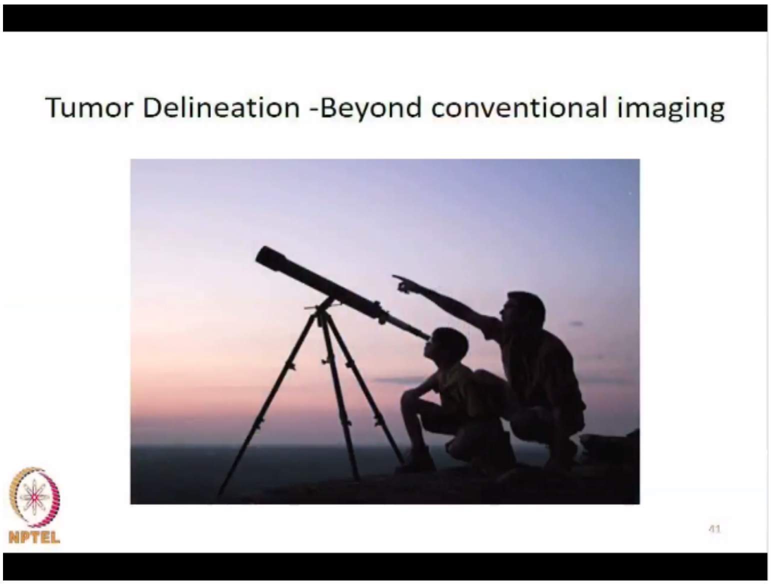

Robotics is a big, big component. In the next 5 to 10 years, there is going to be a lot of advances in robotic technology and its application into medicine. I mean robotics for you all is widely applied in engineering and in probably manufacturing and other fields but it is also applied in a lot of medical fields.

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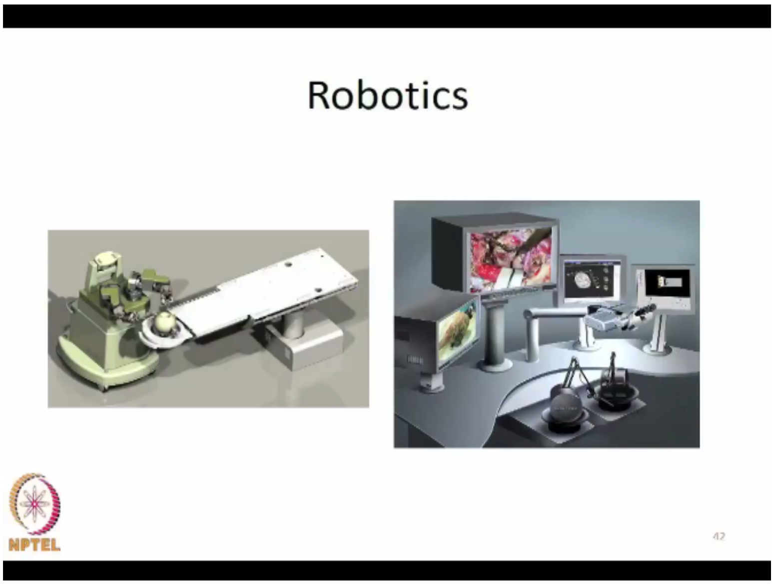

In the last 5 years, I have seen a lot of development and this is the future. There can be different solutions for robotics in different parts of the surgery but that is where a dialogue and the close interaction becomes very important and of course understanding a lot of the basic science information of the data which emerges from techniques like proteomics, genomics and other forms of tissue.

Studying the tissue and the cells is important because it throws up a lot of data which can be meaningless unless somebody smart sits down and computes it well. So this according to me are some of the areas where they can be tremendous contribution from guys like you and I hope this stimulates some of you at least to put your minds to it, maybe not now sometime in the future and you never know what you have in a few years down the line. Thank you very much you.

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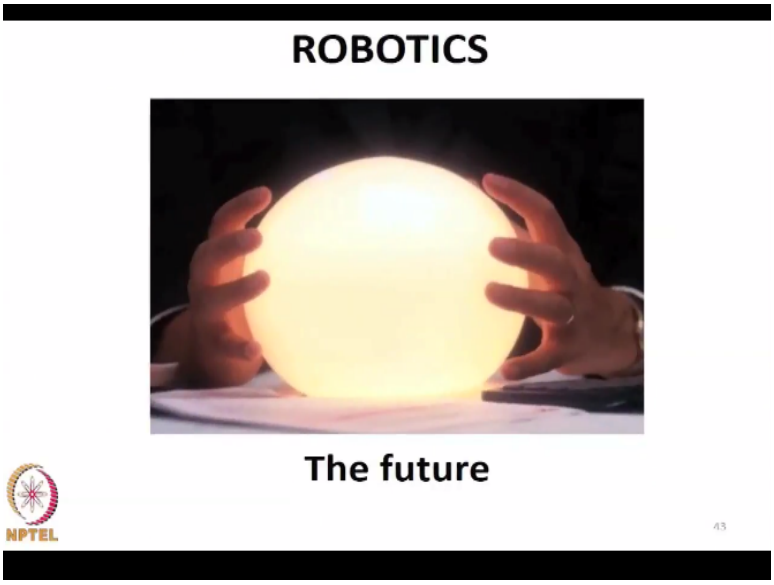

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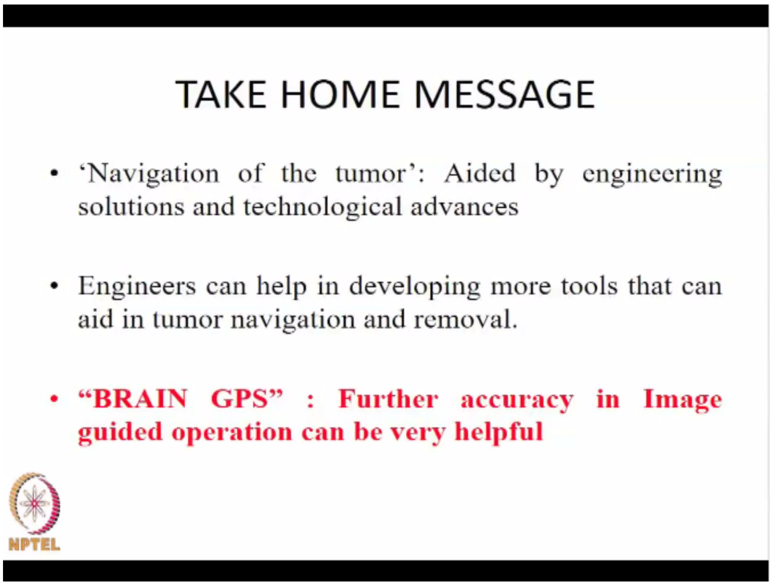

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POINTS TO PONDER

- Enhancing Tumor Delineation
- Augmenting Human capability – technical skills
- Understanding big data

NPTEL