Neural Science for Engineers

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Lecture - 22
Basics of Brain Imaging Techniques

Hi, we will continue with our anatomy classes to understand the brain structure. I am emphasizing and spending a lot of time on this topic because one it is as I told you difficult to understand especially for somebody not from a medical background to know the technical nomenclature and be familiar.

Second thing is it is the starting point of quite some of your work, many people would be foraying into various areas of neuro scientific research and the analysis of the brain is a something which is core whether it be image processing, whether it be neural networks.

So, to be more familiar with topic I am using a strategy of I tried showing the 3D part of the story first because I feel that it is the 3D part which you need to understand, but having said that the pace at which I will may have thought taught the material may not be the most ideal and, may be difficult to comprehend also due to various reasons. So, what I have thought about is to give you different perspectives of the whole perspectives of the same thing.

So, what I taught you in 3D, I would like to teach you in different ways with the ultimate goal that you relate each of these and have a comprehensive understanding of brain anatomy. So, that is the purpose. So, how I would go about it is I have finished on modelling clay the structures and what you need to keep in your mind; now I would jump a little bit into imaging, for the simple reason that when you see imaging that is how you most of you would be directly interacting with the brain.

So, the third part I would try to show you operative photographs videos which sort of give you a sense of how it actually looks like. So, that is the other idea. So, pictures have their relevance it is fairly easy nowadays to find atlases of the brain online and there are very good atlases which I would invite you to go and see.

But before you see I would request you that you go through this at least the anatomy part of the story completely because I have put the material in a fashion. So, that it may look intimidating in the beginning, but I hope that you would get a good understanding of the material by the time I am finished.

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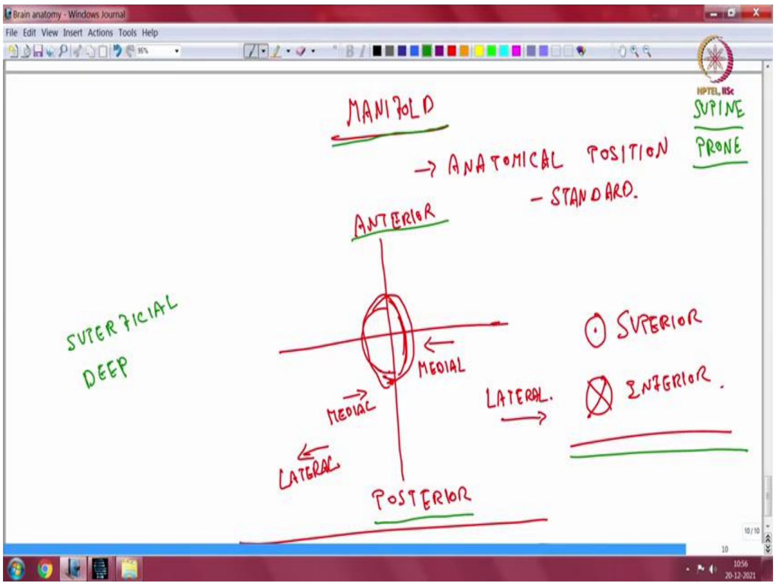

So, I restart my class with the manifold, which is what I would want you to remember because the next part of the discussion has a lot more to do with the manifold. So, anterior and posterior refers to the front and back, there are there is another nomenclature of supine and prone which basically refers to the position as such.

So, please be familiar with these terms it may not be relevant here, but supine is face side, prone is on the back side that is just about it. Anterior is front, posterior, medial towards the center, lateral away from the center, and superior is towards the head, inferior is towards the leg. So, this is what you need to first understand.

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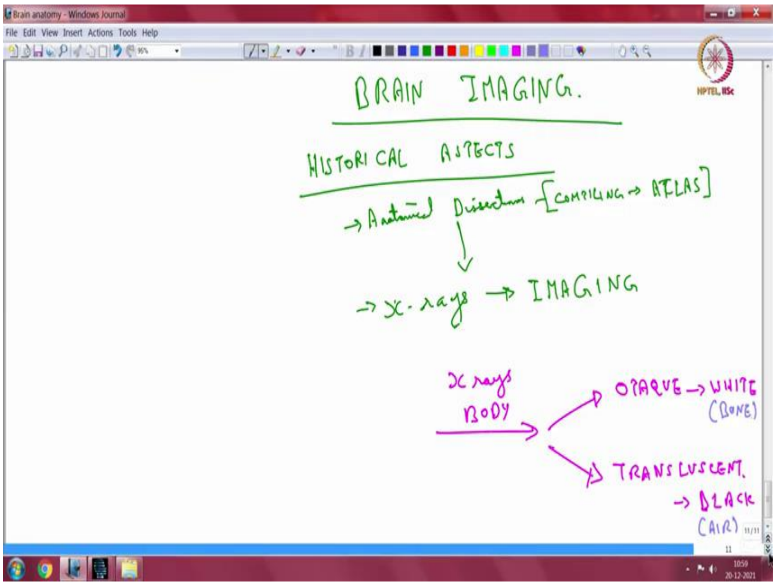

Now, I proceed from there to an introduction on Brain Imaging.

So, I am not taking a separate class on, how to image the brain because lot of material goes out of context. So, here what I am trying to do is I am trying to explain anatomy through imaging for which reason you need to know something about a brain imaging and then we proceed from there.

So, brain imaging a bit of historical aspects it is you know the first idea that the brain has a structure is from anatomical dissections and many of you would have understood that anatomical dissections were serious anatomical dissections and compilation.

See people had been doing dissections way before but compiling the material to atlases and writing textbooks on the stuff started along with the renaissance when there was this idea that the human body is dissectible, had to be dissected to understand both its structure and function. For nearly four centuries nothing much happened until we got x-rays by which you could actually see through the living human body.

So, that was a that was the basis or the first step in imaging. So, most of us at some point of time in our lives or would have either seen or undergone an x-ray for various reasons; the commonest place where x-rays are now used is in dental work and anybody who is undergone any kind of dental work would definitely have had an x-ray. Of course, x-rays are used for several other purposes, but the principles remain the same, x-rays go through the body and give two outputs in the image, either it can be opaque a translucent.

So, opaque would become white, and translucent would be a various shades of grey and black. So, black could indicate air, fully white would indicate bone and this is the contrast by which you interpret x-ray images. We are not about to discuss x-ray to any extent.

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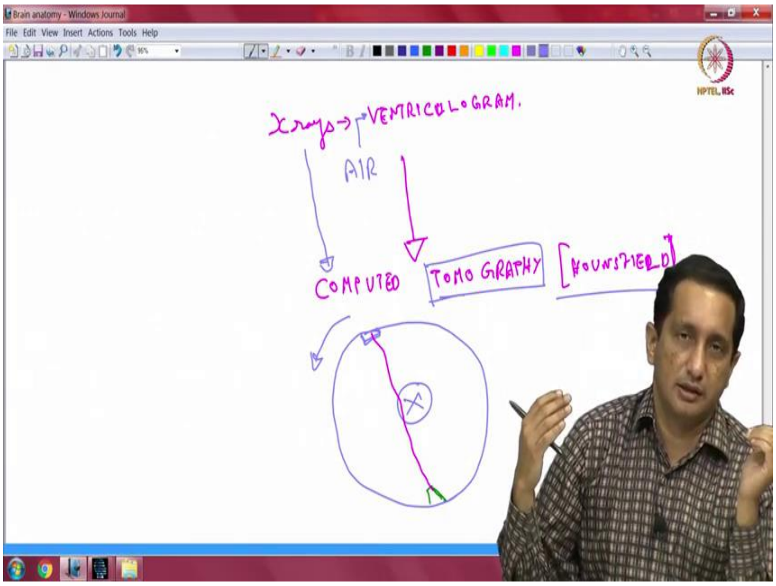

Even in brain imaging x-rays played a fundamental role because, x-rays a resulted in something called as a ventriculogram. So, the so these were the only two differentiating features.

So, you have got black and white, and you got air which acts as a contrast medium and so, how do you; how do you do that? You introduce air into the ventricles, I showed you about something about ventricles earlier in my classes and explained that ventricles contain CSF, normal part of brain anatomy, ventricles similar to the heart, but in the brain functions are completely different they have no whatsoever relations excepting for the name.

So, you would put air into the ventricles and then based on that you can infer several things; you can infer whether there is a tumour sitting which is distorting the ventricle, whether the ventricles are big, whether the ventricles are there is a shift. So, by which you could infer and maybe treat people.

Now the next major advancement is computer tomography all of these are Nobel Prizes, basically imaging in the brain is a Nobel Prize; you do something good in the brain you are guaranteed to get a Nobel Prize from 30 years down the line.

So, computer tomography basically you know in a data science terms it is a pretty logical understanding that somebody should have thought about it earlier then wait for nearly 50 years to get it done.

But of course, I think data sciences were not very popular at that point of time. So, in computer tomography you have the same notion of x-rays, but you do it in a circle. So, you have the person sitting in the circle and in the circle and you have a source and a sensor situated on opposite side. So, you would have a beam of x-rays traversing to the person to the opposite side and then you can move this thing across.

So, you would get a tomography. So, that is the key term tomography. Tomography in the sense that you get points on a circle where you get density measurements of these x-rays and by which you reconstruct the material. So, the algorithm which is used for reconstruction basically got the Nobel Prize and that is in very brief terms what a CTE does.

So, CTE is basically extension of x-ray, x-rays pass through the body across the curvature and in the curvature, you get the density values collected on the opposite side and based on the density values you infer what is the density in the center. So, that algorithm is put on a grey scale, is what a CT image is all about, but there was a profound difference. So, imaging changed with CT. CT changed the way in which we look at the human body and that is something which is remarkable in its own way.

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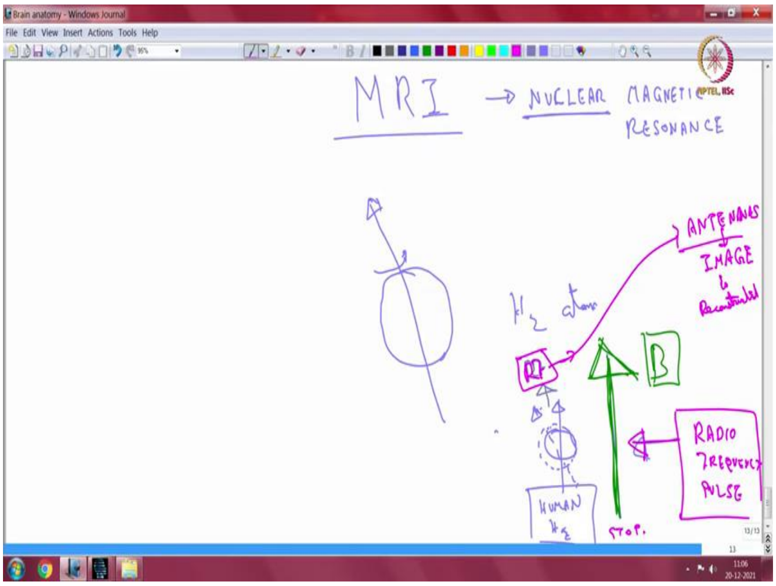

But unrelated physics subject of nuclear magnetic resonance, NMR, is what we called as magnetic resonance imaging. So, apparently nuclear was taboo even then and then that is why you got a very decent sounding name of magnetic resonance imaging. So, the magnetic resonance imaging uses different principles, it is based on the spin of a hydrogen atom. So, you have two kinds of spins of a hydrogen atom, you ensure that the entire hydrogen atoms are brought into alignment with a very big magnetic field.

Then, this is a big magnetic field B and this is the human hydrogen. So, human hydrogen protons basically are brought into alignment with the magnetic field then you give a radio frequency pulse. So, radio frequency pulse, magnetic field, you stop the magnetic field and then you see what happens to this. So, what happens to the hydrogen proton is that it goes back to its native configuration.

So, it is somewhat like this, and that process actually results in a RF signal. So, the RF signal is picked by antennas and the image is reconstructed too simple an explanation. So, where does the hydrogen come from; hydrogen comes from water. Most of us who are sitting at least for this class should be aware that we contain a lot of water. I spoke to you about the importance of ionic medium in everything starting from cell dynamics to cell information, transmission, to transport recycles, everything there is in a water medium. So, protons come from there.

So, basically the proton forms the key entity. So, find out the signal from every single hydrogen atom and the by this method. So, you ensure that they all get aligned in this particular magnetic field. So, it is from top to bottom and then that would ensure that these atoms come to a one single magnetic field and when you relax the switch off the field with a radio frequency.

The radio frequency is taken up by the hydrogen atoms and based on their original position, when it comes back to the original position you get an output radio frequency, a lot depends upon input radio frequency and the nature of that tissue.

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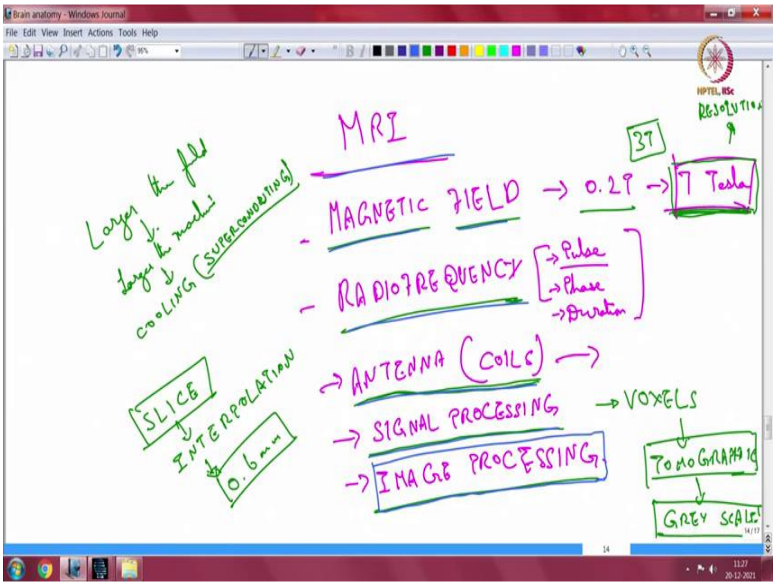

So, what are the variables under consideration you have a magnetic field that is anywhere between 0.2 Tesla to 7 Tesla; Tesla has nothing to do with the car, it is the magnetic field strength, then you have radio frequency. So, you can do a lot of stuff with the radio frequency, you can pulse it, then you can phase it and you can duration. So, there are various methodologies adapted to change this radio frequency again I am not an expert in any of this stuff. I am just conveying it is interesting to note this stuff.

But you need to know these things as a basic stuff. So, you have a magnetic field you have radio frequency and then you have got obviously antennas. Now antennas are basically coils and they are placed in close proximity with the body part which is being imaged. Now after that is signal processing and after that is image processing. We will analyze a little bit of this stuff before we actually go into the details.

So, small magnetic field to higher magnetic field. So, as the magnetic field increases resolution increases, increase resolution. So, resolution is how fine you can interpret between two closely placed structures and the larger the magnetic field the better. So, why not 140 Tesla's. So, human beings we have been so far, I have been able to test only at up to 7 Tesla's, machines up to 14 Tesla's I understand I have been built, but they are not available for commercial purposes.

Generally, when you go to a hospital and get most hospitals now have 3 Tesla machines which is the same amount of Tesla which machines you know in the hospital where in the NIMHANS where I work have. So, most of our machines are 3 Tesla. There are several nitty-gritties. So, the larger the field, larger is the machine and more cooling issues.

So, cooling is for ensuring that you have superconducting magnets ok. So, this is one of these applications in which you crack what is that super conducting at room temperatures you would have a big breakthrough in MRI technology.

So, a larger the machine basically it is the weight. So, there are weight issues you cannot have very high magnetic fields in random locations say for example, hospitals are very interesting incidents in which things have happened, especially with the 7 Tesla machines even with the 3 Tesla machine there is a lot of restriction on the surroundings of a magnetic resonance machine.

It is a big infrastructure to build its not very easy. So, that is something about magnetic field. So, the larger the magnetic field the better the hydrogen ions protons get aligned to the magnetic field and that is the key of the issue.

Radio frequency is the second part. So, you insulate these protons with radio frequency; you give radio frequency to these protons they shift in the field, and they give back the radiation radio frequency when they come back to orientation. So, that output radio frequency as I told you depends upon the input parameters of the radio frequency they are in terms of pulses. So, what is the duration of the pulse? What is the face of a pulse? So, all these parameters, again I am not an expert we can do definitely go up and read up this stuff.

But do have an understanding, it is the radio frequency parameters which are the key to tuning the image and as I understand these are more like you know the protocols have been developed and by consensus. It is different machines give you different radio frequency settings and operator basically only uses certain things. It is like having gears in a car, you know you can have better transmission ratios in a car, but you have only about 5 or 6 gears in a car which you can actually shift between.

So, the radio frequency is like the gear ratios, you do not have a infinite gear ratios to run your car. You got very fixed gear ratios which are based basically given by the manufacturer and similarly radio frequency settings are with the manufacturer, magnetic field is also with the manufacturer.

So, antenna and coils there are lot of developments happening in each of this space. So, there is a lot of stuff happening in 3 D coils. What is generally, what I have understood is that you have coils which are placed more closer to the region of interest you would have better imaging acquisition and better images as a consequence of that. So, that is about that is something about antennas.

Now the whole data in terms of is in terms of voxels and then you need to generate tomographic information. So, tomographic information is you convert this 3D data which you have acquired through the radio frequency antenna and from that you build greyscale images. So, somehow most of the imaging has been very grey in color. So, you know x-rays had only 2 colors and then the grey in between and CTE by being a follower of x-ray also had grey.

So, MR also has the tradition of being grey. So, you have a grey scale in which the tomographic information is being represented and that is what is happening from the signals which are acquired from the radio frequency antenna; your radio frequency antenna takes in the radio frequency signals which are a function of the input radio frequency which goes when the patient is oriented in the magnetic field.

So, that is what is happening. Image processing is the last part of the story. So, what happens in MR is you interrogate a slice of tissue.

So, you interrogate a slice of tissue across the brain. So, you interrogate tissue within that and then you interrogate another tissue within the next slice. So, you have something like 2 slices and there are definitive multiple slices.

So, you can have parameters such as slice thickness, time duration taken for the slice thickness, how do you bridge the gap between the slices, how do you interpolate data, I think that is the correct term. So, there are gaps, and you need to do interpolation to accommodate for the data which is there between the 2 slices and thicker the slice obviously, lower the resolution. See remember this resolution is a very funny business it is not just a single, it is not a function of one single entity, it is a function of multiple entities.

So, you have field as one of the parameters which affect the resolution magnetic field strength. So, the larger the field strength you get this one, even in radio frequency there would be parameters which change the amount of resolution, the slice thickness changes the amount of resolution. There is another issue in slice thickness slice which is how the tissue is interrogated.

So, the resolution of tissue is non uniform, what I mean is in a slice you have very good resolution, but in between slices you have lesser resolution. Now you can go read up this material in greater detail in a in some imaging textbooks, but I would require you to remember that slices, how the slicing is done sort of determines the overall picture resolution.

Now, the output resolution of MR images that are 0.6 mm; now you should remember that when we speak about radio frequency waves or this discrepancy is important to be understood.

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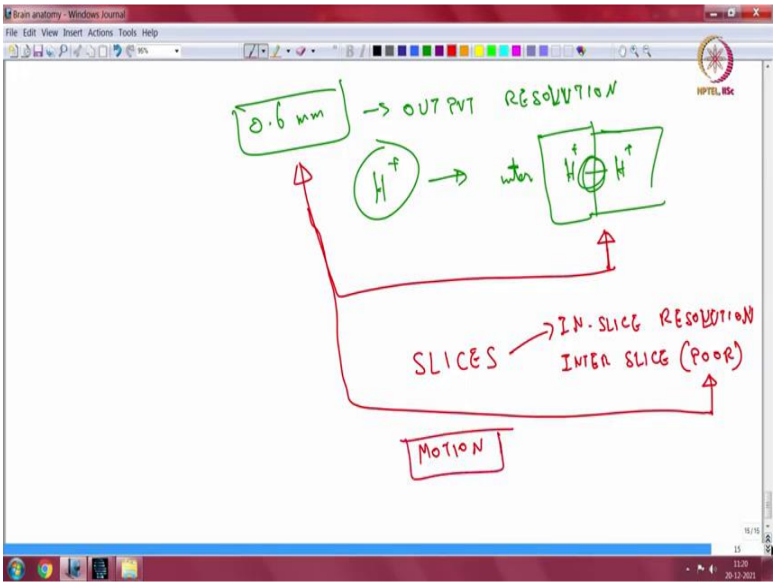

So, 0.6 mm is our output resolution practical. See practical in the sense imaging, you get an image you ask for resolution greater than meaning lesser than 0.6 mm it is not you do not get it.

But if we look at the dimensions of the other material say proton. So, proton basically if you are interrogating every single proton, you are looking at inter bond level stuff I do not know what bond it is, but anyway we have we should be able to resolve between two closely placed hydrogen atoms. If we go by the theory that MR technology is based upon protons and all this stuff is because the individual protons move in a magnetic field with the radio frequency pulse.

So, theoretical limit of magnetic resonance imaging should be the space between two hydrogen atoms, but that is completely out way beyond. So, this is one of the limits. The other limit is between slices. So, in slice resolution is high, in slice resolution. So, in a given slice you can have a very good resolution between two structures, but if we go look at inter slice, this is poor.

So, this poor business is one of the other things why you have this 0.6 mm and why you do not have better than 0.6 mm. Now the other issue which would actually influence is a motion.

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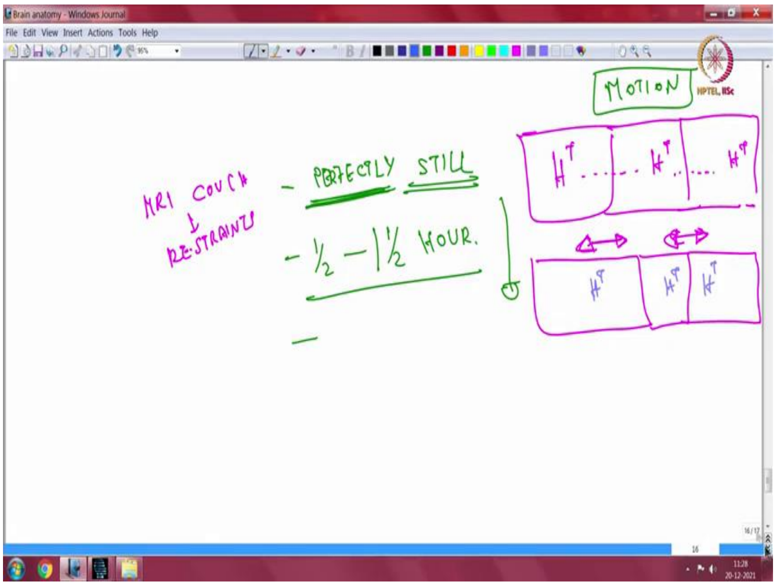

So, though we have theoretical limits of H^+, H^+, H^+. So, this is the theoretical resolution which you should have, but if there is motion between 2 H^+, H^+, H^+, H^+. So, what would be the effective resolution.

So, you have something like this, you have something like this, and you have something like this. So, this what happens with motion. Now logic is you stop motion and do that. Which is why I do not know how many of you would have actually undergone an MR. So, what instructions are given is you have to remain perfectly still, for how long?

So, you have to remain perfectly still for one to one and half hours. So, most of us would find it difficult to remain perfectly still, see perfectly still is a loaded term. Perfectly still is absolutely no movement in any part of your body for a duration of half an hour to one and a half hours. So, you cannot even blink. You are not supposed to look in any direction, we close our eyes, you keep your hands and the MR couch has restraints and it all looks quite rosy.

But remember what kind of distances we are speaking of; we are speaking of distances between two hydrogen ions. Now where does maximum moment happen with the body it is with 2 very interesting problems.

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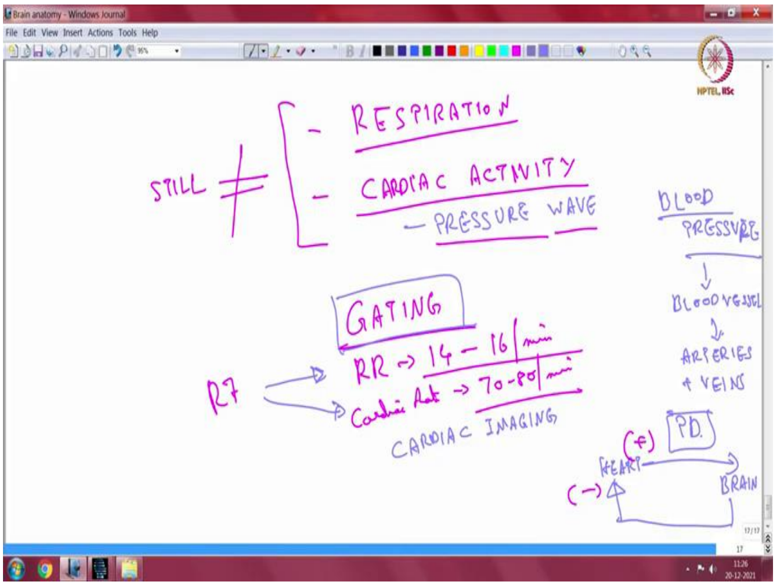

One is respiration, cardiac activity, and in relation to cardiac activity, the pressure wave.

When we understand the phenomenon of blood pressure all of us have heard this term, it is a very common term, known as a high blood pressure is a disease, low blood pressure is also a disease. So, what does the term blood pressure mean? Pressure means that the pressure of blood within the within blood vessels.

Blood vessels is both arteries plus veins, pressure is basically equivalent to potential difference. So, potential differences between heart and in for us we need to look at brain and also vice versa. So, you need to have negative pressure here, negative pressure here and positive pressure here for the circulation to be maintained, but what it also means that a blood pressure is not a static entity and what you should look at is it is a pressure wave.

The pressure wave which is generated in the heart moves across all these blood vessels, these blood vessels are not rigid pipes, they are flexible pipes. So, the wave goes across every single blood vessel in the body and if you remember earlier, I spoke to you that the brain is richly supplied with blood vessels. So, what it means is that this pressure wave, the small parts of these pressure wave impinge on various parts of the body and basically if you want somebody to be perfectly still, it is just not possible.

So, you should understand that the theoretical limits of MR cannot be realized, theoretical resolution of MR imaging can never be realized in a live human being for the very simple reason you have got respiratory and cardiac activity. There are things which they do and that is the phenomena called gating.

So, you have respiration respiratory rate is about 14 to 16 per minute and heart rate cardiac rate is about 70 to 80 per minute and you can ensure that the signal is the RF signal can be synchronized to these things and you have cardiac imaging. Respiratory we do not because air is a bad medium for MR imaging in general.

So, I have tried to explain a lot of the background in a very short duration of time. Each of these are research topics in themselves, have a lot of scope opportunity to do. So, people who are looking at MR imaging's, they are images which are fairly different from MR imaging and that is what I have tried to highlight over here. So, MRI is about magnetic fields, radio frequency, the coils, the signal processing which happens from the coils and then at the end of it is image processing.

So, most people who are working in fields are only working in the last part of a very predetermined sequence of events, you cannot, you do not have options to tune all of this stuff. So, understanding brain structure function through imaging has this caveats which are listed over here.

So, it is important to know that image processing is the last step of a very long series of data acquisition which is happening in the MRI machine and you have very finite limits of tweaking signals to do image processing and get meaningful outputs.

So, please do remember this stuff when we look at MR images and try to interpret that. So, there are limits to MR imaging and another issue is as the Tesla increases resolution actually sort of comes down, there are several other issues which creep up including heating and various other kinds of things which I am not going to speak now.

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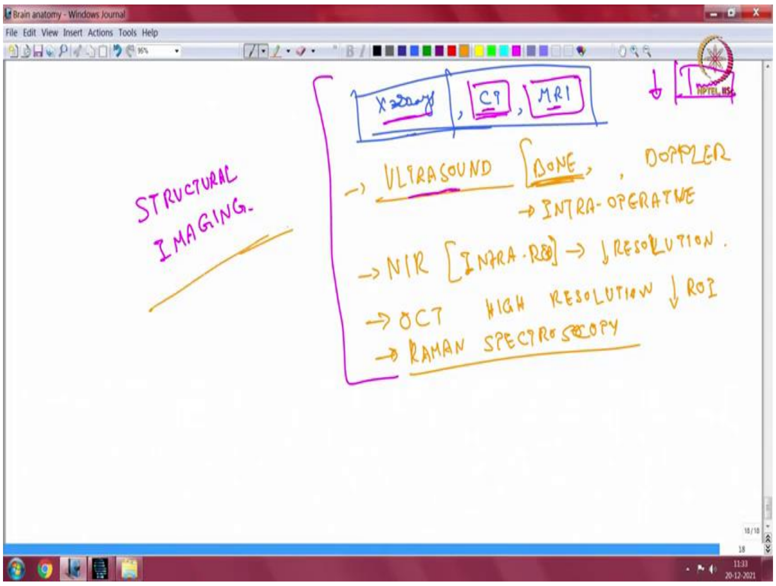

So, far we have been looking at x-rays, CT and MRI which are the benchmark imaging systems CT and MRI are the most important parts of the story.

But there are several other kinds of imaging modalities which you should know, one is ultrasound. So, the problem is bone. So, I have shown you skull and how the skull covers all of the brain and then it is not possible for the brain to be insulated without tackling bone issues. So, ultrasound is popular intraoperatively we use. I use fair amount of ultrasound to do located stuff which is within the head and after taking out the skull.

So, intra operative. There are multiple issues with ultrasound, ultrasound is generally not popular. Then you also got near infrared imaging, which also has issues of poor resolution, but it allows you to find out some other things. So, that is the reason optical computerized tomography high resolution.

But region of interest is very low, depth of penetration of the OCT is very low. So, there are multitudes of imaging modalities which help you to have ultrasound there is also the advantage of Doppler I have not included. So, the whole of this things is something called as structural imaging.

So, structural imaging is you see this structure without actually seeing something in action and structural imaging is decent enough for most medical stuff because it is not that we as physicians surgeons do not like to know the function.

But you know, when there is a limitation at least seeing the structure is far better than knowing something dynamically. So, for medical purposes each investigation has a specific role. It is not that like I told ultrasound does not go through the skull, but when you take out the skull it is of use.

So, x-rays say you want to quick check the spine you know spinal cord integrity can be quickly checked with x-rays, CT is the standard for traumatic diseases. You know somebody has an accident, CT acquisition time is an is mostly under a minute.

So, under a minute you can get a CT and so, that is very fast to find out life threatening problems. MR takes about 30 - 40 minutes at the at the minimum. So, it is not a very popular idea. OCT is also useful for stroke in which the golden hour principle exists, and you have to do you have to identify and act upon things.

MR gives you better resolution; MR gives you a lot of very fine details which we will be seeing subsequently, but it has it is limitations in terms of time, availability, infrastructure required and so many other issues. NIR is upcoming technology for very niche areas such as trauma, head injury evaluation and things like that.

OCT is specific for mostly lab kind of stuff. I cannot recollect things in which it is useful for in the operative setting, which is the only place where you can actually see brain at close proximity. Brief mention of Raman also. So, Raman spectroscopy also has some relevance in brain imaging and diagnosis, but Raman if people do know Raman, the equipment is so big that you cannot take it into theatres. So, that is about structural imaging.

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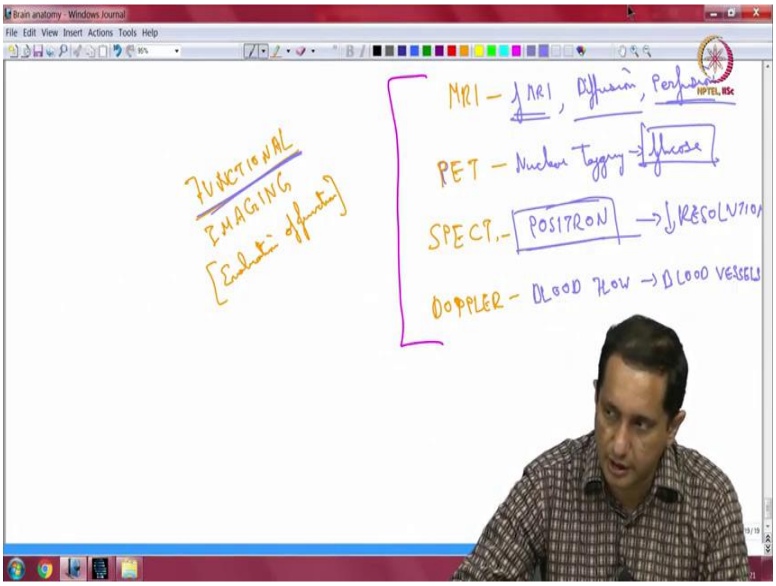

So, functional imaging is evaluation of function. See the engineering notion of function is pretty different from our notion of function. So, functional imaging there are several modalities. So, MRI, FMRI. So, diffusion sort of gives an idea of function and perfusion.

So, these are the general idea by which you can you have some notion of the function of the brain then, you have a positron emission tomography, you have a SPECT, single proton emission computerized tomography, in ultrasound you have Doppler. So, PET is based upon nuclear tagging.

So, there are various kinds, the most popular is glucose. In my class on glycolysis, I have highlighted glycolysis and the power systems of the brain, I have highlighted how glucose is utilized for the complete structural integrity of the brain and signal transmission, signal processing everything a lot of it is energy dependent and glucose is used to process.

So, when you tag with radioactive glucose you find out the areas where increased uptake of glucose is available and then you build inferences out of it. Single positron emission positron emission tomography is again based on positron detection, and you do get a low-resolution tomographic images. Sort of reflex perfusion and FMRI and this one. Doppler gives you only blood flow in blood vessels.

So, these are methods by which you interrogate the brain. So, this is a very brief summary of the stuff which happens within the imaging side. Many of you would be interested in this topic for which reason I thought I should introduce a capsule. It is also necessary for me to explain the next part of the story which is anatomy of brain in imaging.

So, most of you would not in any part of their career both academic and in their work have the necessity of seeing a brain, either live or as the cadaver brain. So, work would be dependent on images which you get and images from live people are basically MR, CT, rarely ultrasound.

So, PET and SPECT of course, So, it is necessary that you understand how these images are generated before actually seeing the images and I need to put the context proper before I go into the imaging part of the story. We will stop here and then we will continue into the next session.

Thank you.