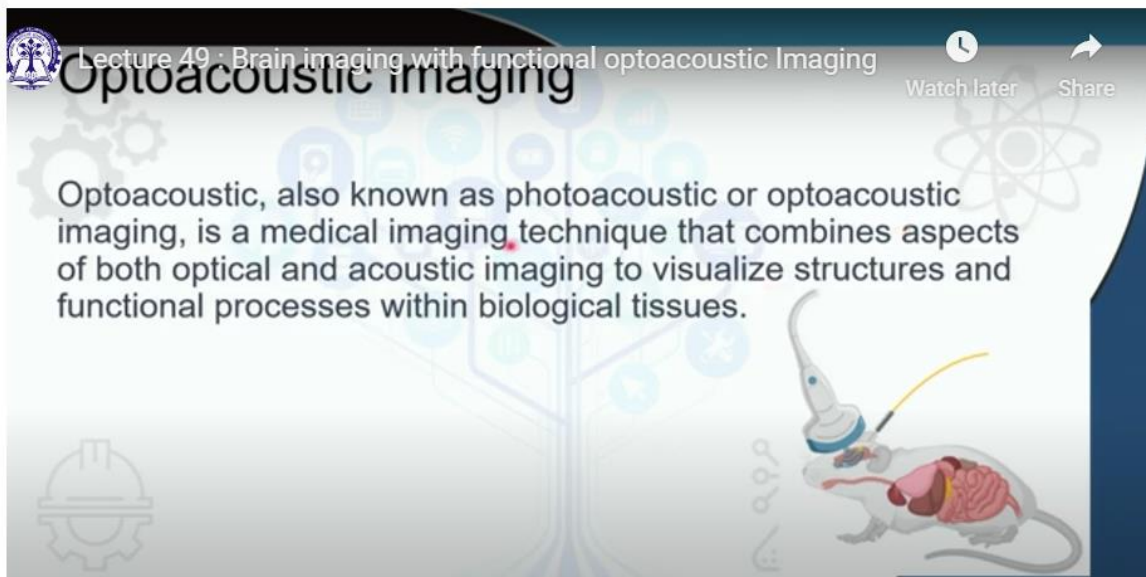


**Nanobiophotonics: Touching Our Daily Life**  
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**Indian Institute of Technology, Kharagpur**  
**Lecture No. 49**  
**Brain imaging with functional optoacoustic Imaging**

Welcome back. We are discussing about brain, specifically neuro-photonics. And in this lecture as well, I am going to talk about how to image the brain using Octo-Acoustic imaging. Photo-acoustic or Octo-acoustic are similar terms that are being used interchangeably. Now acoustic has something to do with sound. So, you must be wondering what exactly is it and it is something very very clever and literally very cool in which they have combined sound and light.

So, Octo-acoustic can literally mean the sound that is produced by light. Think about it. You know about ultrasonography. This ultrasonography is a very very useful technique used in medicine for especially for you know imaging fetus in pregnant women as well as if you have some sort of kidney stone etcetera, some kind of a trouble with your bladder.

They use ultrasonography. Yes, any kidney related problem they generally ask you for ultrasonography. Here and we do not discuss ultrasonography because it is sound and we are discussing about light, but here is the exception where we use light to create sound and that sound is measured. So, input is light, output is sound and we measure the sound and thereby try to image specifically in brain. So, this is something that I found quite interesting.


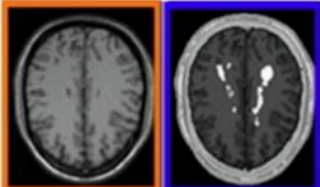


So, what exactly is Octo-acoustic imaging or Photo-acoustic imaging? Also known as

photo acoustic or Octo-acoustic imaging is a medical imaging technique that combines aspect as I said both optical and acoustic imaging to visualize structures and functional processes within the biological tissue. So, this is the mice brain. The mice brain is excited by a laser light that is penetrating that is penetrating through its skull and illuminating certain portion of the brain and because of the presence of the laser it creates some sort of a sound some sort of a pressure wave which is then measured by this sound detection system and it then tries to detect the various areas of the brain that is producing that is producing this sound and thereby try to map the different regions of the brain according to the sound that it is getting.

## Importance in brain imaging

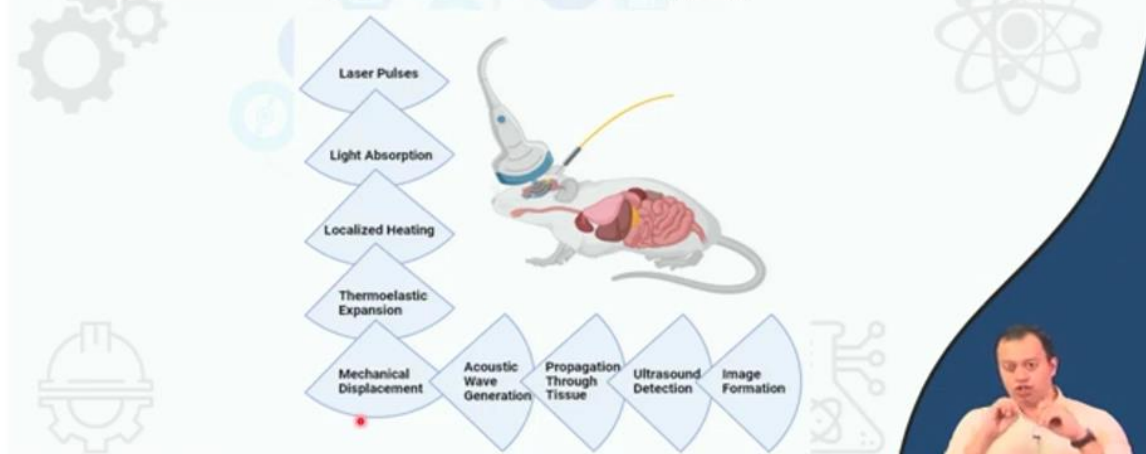
- Optoacoustic imaging can provide both functional and structural information about the brain.
- Optoacoustic imaging allows non-invasive monitoring of cerebral hemodynamics, such as changes in blood volume and oxygenation. This is crucial for understanding brain responses during tasks, cognitive processes, and diseases.
- Optoacoustic imaging is non-invasive and does not involve ionizing radiation, making it safer for repeated studies and suitable for various patient populations.
- Optoacoustic imaging has the potential to advance research in neuroscience, providing new insights into brain disorders like stroke, epilepsy, brain tumors, and neurodegenerative diseases.



So, obviously well first let us go through the reason why we go through it, what are the important aspect, but I know you all are waiting for how light produces sound I am coming to that, but let us go through this. So, Octo-acoustic imaging can provide both functional and structural information of the brain, it allows non-invasive monitoring, the hemodynamics blood dynamics such as changes in blood volume.

Octo-acoustic imaging is non-invasive and does not involve ionizing radiation like you know CT scan and what not PET positron emission tomography. Octo-acoustic imaging has potential to advance research in neuroscience etcetera etcetera.

# Principle of Optoacoustic imaging



So, how does light produce sound? Yeah this is the most important thing. So, this is this is something very nicely done very nicely the slide has been done and I thank my TA Subhanita Roy Paul for doing this I absolutely loved it how she has beautifully designed the slide. So, I will try to tell you.

You are sending a particular set of photons suppose these photons are absorbing. So, we are now away from the non-absorbing window of 600 to 950 nanometer. Now, we are talking about a particular set of light, particular set of photons which are indeed absorbed which are indeed absorbed by the brain right any other frequency other than 600 to 650 to 900 nanometers. So, this particular frequency of the brain of the light is absorbed by the brain. So, when there is an absorption by certain area of the brain tissue it absorbs the light slightly swells up right any absorption any absorption any absorption reader produces some sort of a heat localized heating happens localized heating because of the absorption of light.

Light is converting photon is converting into phonon, phonon is vibration I gave it away right vibration is sound. So, anyways localized heating localized heating is happening heat is dissipating. So, the area of the tissue is bad habit area of the tissue is simply expanding its habit and there is a mechanical change here you know about Frank Gordon principle. There is a mechanical change in that region of the tissue that has absorbed the light it has absorbed the light heated up swollen heated up and the heat is now dissipating. So, the surrounding area the surrounding area of the brain surrounding area of that tissue contains several different types of fluids.

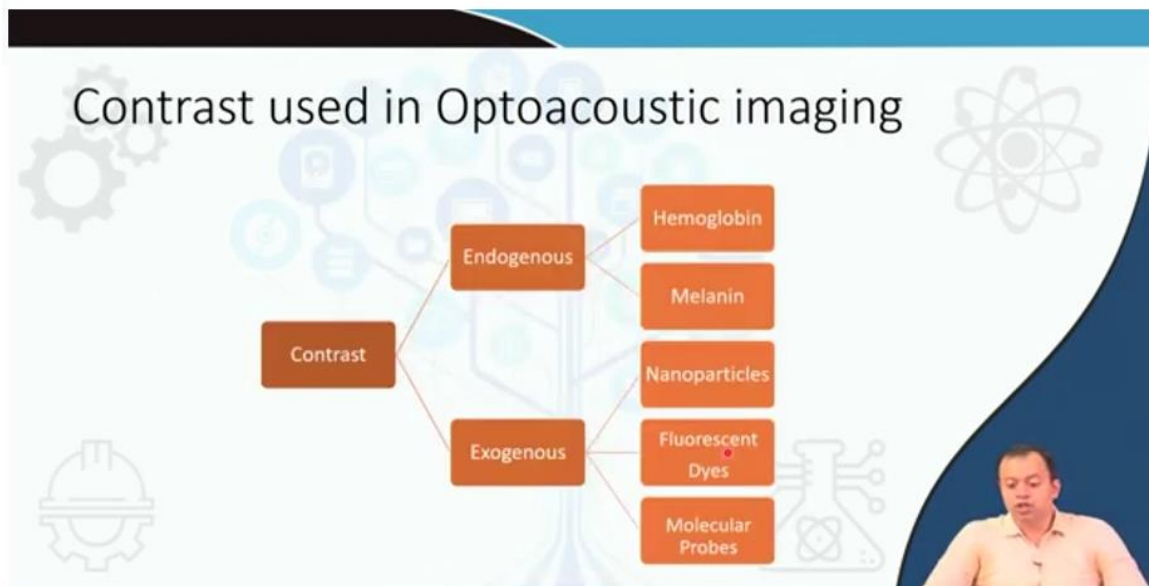
Cerebrospinal fluid this fluid that fluid overall that fluid contains huge amount of water yeah bound water and what not these waters absorb the frequency these these these water

can absorb the heat and turn into steam and they can propagate the steam or so called if not if you are uncomfortable with using the term steam because I am also uncomfortable steam is directly connected with water and if not it is not exactly water water H<sub>2</sub>O it is it is a fluidic environments it is a fluid type thing. So, let us start again the brain tissue a portion of the brain tissue has absorbed light that light has been absorbed and it has resulted in generation of localized heating. The localized heating has resulted in mechanical expansion of a certain area certain area of the tissue which has absorbed this has resulted in formation of pressure waves. This has resulted in formation of pressure waves it is the heat is dissipating what does this means that a thermal wave a thermal wave is passing through a thermal wave is simply passing through the surrounding area the heat is getting dissipated the heat is getting dissipated light comes it absorbs it swells up and the heat is dissipating. In a localized way the heat is dissipating the heat can be considered as a thermal wave.

The thermal wave the thermal wave passes through the surrounding area making the surrounding fluids the surrounding fluids expand and contract expand and contract you know where the heat is present the heat is travelling a thermal wave is travelling the heat is travelling wherever the heat is present at this moment these areas have expanded the pressure wave the fluid media which is there has expanded then the heat has moved to this direction. So, this has contracted this has expanded now this has contracted the next area has expanded. So, basically the thermal wave results in a pressure wave results in a pressure wave passing through in a very very small localized area few microns few nanometers few microns area as such. Again, light is absorbed by the area of the tissue the tissue is expanding the heat finally, dissipates. So, the tissue can contract and return back to its original position, but the heat is dissipated in the form of a thermal wave in the form of a heat wave not atmospheric heat wave that is a separate thing heat wave and it is moving as the heat wave moves it makes the surrounding fluids expand and contract expand and contract because the wave is moving like this.

This is by definition contraction and rarefaction contraction and rarefaction is how sound moves sounds are not sound waves are not EM waves or transverse transverse wave remember your high school physics its longitudinal waves you know contraction rarefaction contraction rarefaction. So, the heat that is travelling the dissipative heat because of the localized heating localized heating produces contraction rarefaction contraction rarefaction that basically is the sound that this detector is detecting right this heat wave this pressure wave thermo mechanical wave propagates through the tissue it is detected by the ultrasound detector and the image is formation where exactly is the vibration where exactly is the propagating wave now and how is it propagating due to which area of the brain tissue absorbing what light simple as that. Obviously, this sound is ultrasound you would not be able to hear it you only hear what 20 hertz to 20 kilohertz

or something like that. So, they are ultrasound you do not hear that, but this by definition is sound by definition is acoustics again laser pulse light absorption localized heating results in expansion, expansion results in mechanical displacement, this displacement results in acoustic wave generation mechanical displacement as in the sense that the tissue contract return back to its original position by expelling by throwing away the heat it has it was like this it swelled up because it has absorbed heat, but now it has it is expelling the heat and coming back to its original position this all happened in few microsecond nanosecond time the heat generated a few Kelvin maximum and also the wave generation is also of minimum minimum the pressure wave the localized pressure wave the localized thermo mechanical wave that passes through the heat dissipation is basically the wave is something of a very low frequency or I do not know very high frequency in can also happen and it is absorbed it is detected by the ultra ultrasound detector and you get the images out of it.



So, the contrast using optoacoustic imaging how do you get the contrast endogenous and exogenous inside or outside endogenous is where hemoglobin and melanin these are the proteins and hemoglobin is also the protein they can absorb heat and they can produce different sorts of pressure waves thermo mechanical waves that produces different types of contrast different types of you know imaging imaging part and you can detect it or if you have the capacity if you are not dealing with a human being directly you can utilize nanoparticles fluorescence dyes or molecular probes which will behave differently upon absorption with different lights and thereby will be producing different types of thermo mechanical waves these thermo mechanical waves are then detected and you image it as the wave is propagating you are trying to just like ultrasonography you are trying to detect how the wave is propagating at different areas of the brain and thereby get a three dimensional structure of the brain just like ultrasonography but ultrasonography of the

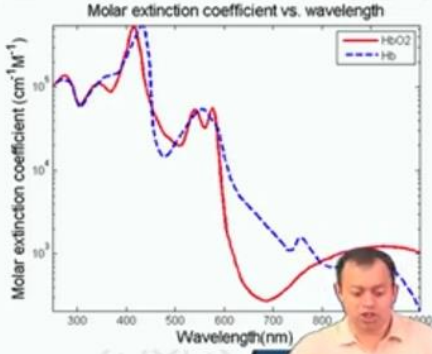


brain at a very localized level and the input here is laser light.

## Applications

Photoacoustic imaging can be used *in vivo* for

- Tumor angiogenesis monitoring,
- Blood oxygenation mapping,
- Functional brain imaging,
- Skin melanoma detection,
- Methemoglobin (hemoglobin in the form of metalloprotein means the iron in the heme group is in the Fe<sup>3+</sup> (ferric) form rather than Fe<sup>2+</sup> state) measurement.



Molar extinction coefficient vs. wavelength

Molar extinction coefficient (cm<sup>2</sup>M<sup>-1</sup>)

Wavelength (nm)

HbO<sub>2</sub>

Hb

So there are several applications photo acoustic imaging can be used in life for tumor agenesis tumor monitoring blood oxygen mapping functional brain imaging skin melanoma detection and all of these things. So, this is the difference between the oxygenated blood and non-oxygenated blood as measured using photo acoustics. There are of course several limitations. Octocoustic imaging phases limitation in imaging depth

## Limitations


- 1. Imaging Depth and Sensitivity:**
  - Optoacoustic imaging faces limitations in imaging depth due to light attenuation in tissues.
  - Increasing laser energy can compensate for this, but safety standards restrict high laser exposure on the skin.
- 2. Contrast Agent Considerations:**
  - Choosing contrast agents for optoacoustic neuroimaging, factors like photostability under pulsed radiation and *in vivo* toxicity must be carefully evaluated.
  - Photobleaching effects differ from fluorescence imaging, and some fluorescent proteins induce phototoxicity.
- 3. Tissue Heterogeneity and Artifacts:**
  - Biological tissues' heterogeneous nature can lead to image artifacts and affect imaging quality and quantification.
- 4. Chromophore Separation:**
  - Hemoglobin's dominance as an intrinsic absorber in tissues can hinder accurate quantification of other neural activity markers.

due to light attenuation in tissues increasing laser energy can compensate for this, but safety standards you damage the brain actually choosing contrast agent for opto acoustics neuro imaging factors like photo stability toxicity has to be evaluated photo bleaching biological tissue are heterogeneous in nature. So, depending on how the wave is traveling the wave is thermal thermo mechanical wave is not traveling through a homogeneous

media. So that will cause its own individual problems and of course presence of hemoglobin and all other artifacts can cause severe problems.

## CONCLUSION

- In conclusion, Optoacoustic imaging harnesses the interaction of light and sound to provide high-resolution, non-invasive images of biological tissues, offering a unique blend of optical and acoustic benefits
- Through light absorption and rapid localized heating, optoacoustic imaging generates acoustic waves that are detected and used to create images.
- Optoacoustic imaging finds growing importance in neuroimaging, offering real-time functional and structural information about brain disorders, hemodynamics, tumors, and neurodegenerative conditions.
- The use of contrast agents, both endogenous and exogenous, is pivotal in optoacoustic imaging to enhance visualization and specificity, enable targeted molecular imaging and facilitating the detection of subtle changes within tissues.



So, in conclusion this is a very cool thing, but like still it has limited application not that I have anything against ultrasonography people they are doing fantastic work, but we can also generate sound with light. Can sound people say that they can generate light with sound? This is a friendly competition friendly banter between us. So, in conclusion optoacoustic imaging harness the interaction of light and sound to provide high resolution non-invasive biological tissues through light absorption and rapid localized heating optoacoustic imaging generates acoustic waves optoacoustic imaging finds growing importance in neuro imaging as such and the use of contrast agent both endogenous and exogenous can help improve the resolution of the tissue.

## Concepts Covered

- Optoacoustic Imagine
- Importance in brain imaging
- Principle
- Contrast used in optoacoustic imaging
- Applications
- Limitations



So, these are the concepts that I covered for today.

Lecture 49 : Brain imaging with functional optoacoustic Imaging

Watch later Share

## REFERENCES

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- Xia J, Yao J, Wang LV. Photoacoustic tomography: principles and advances. *Electromagn Waves (Camb)*. 2014;147:1-22. doi: 10.2528/pier14032303. PMID: 25642127; PMCID: PMC4311576.
- Photoacoustic imaging- Wikipedia

A small video inset in the bottom right corner shows a man in a light-colored shirt speaking.

Please go through some of the references that I have quoted here and I will see you in the next class. Thank you.