

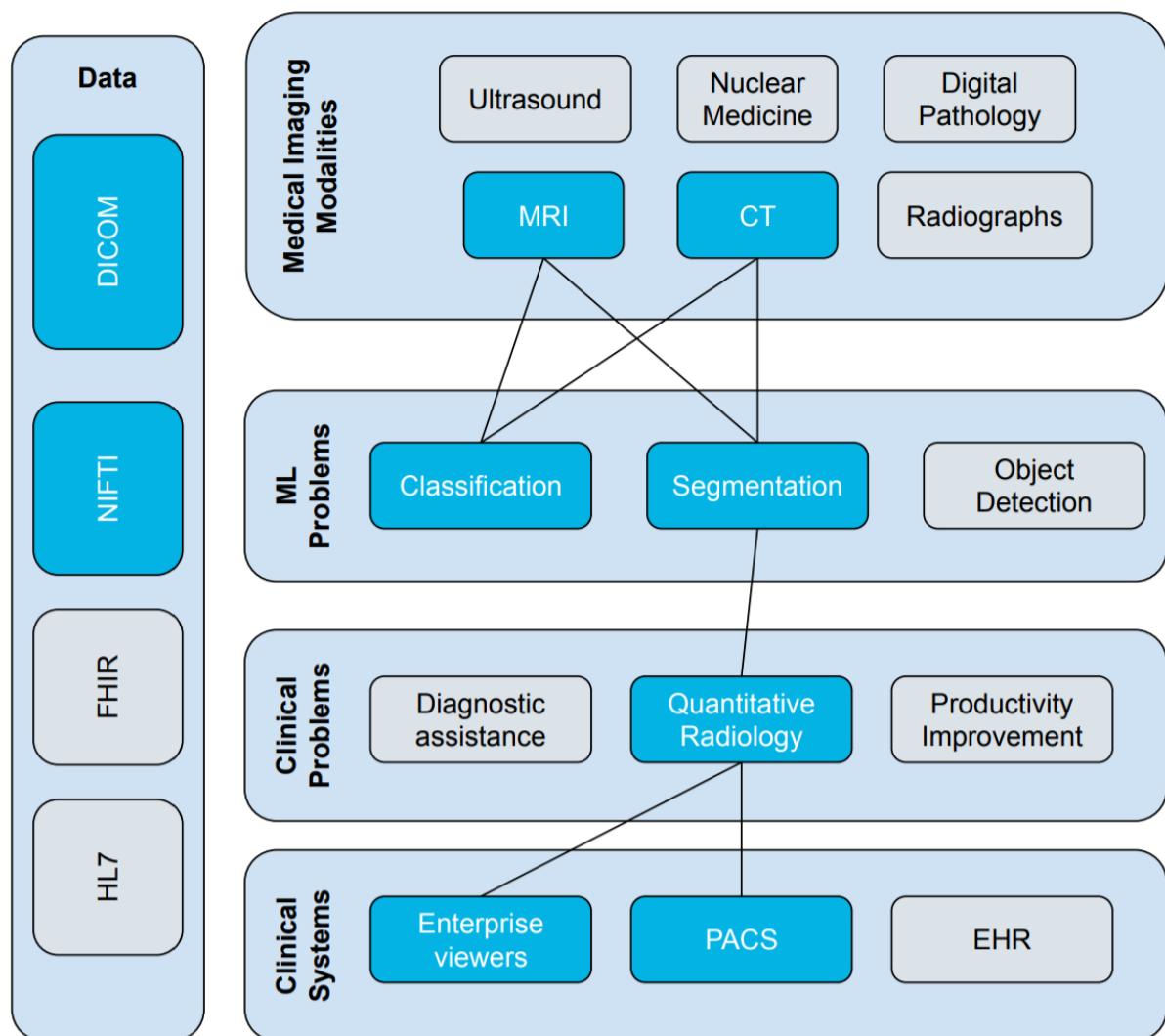


2

Applying AI to 3D Medical Imaging

Course Concepts

We will be touching upon many concepts throughout this course, that span multiple fields. Here is a diagram that may help you build a mental picture as we dive deeper into these concepts and how they play together.

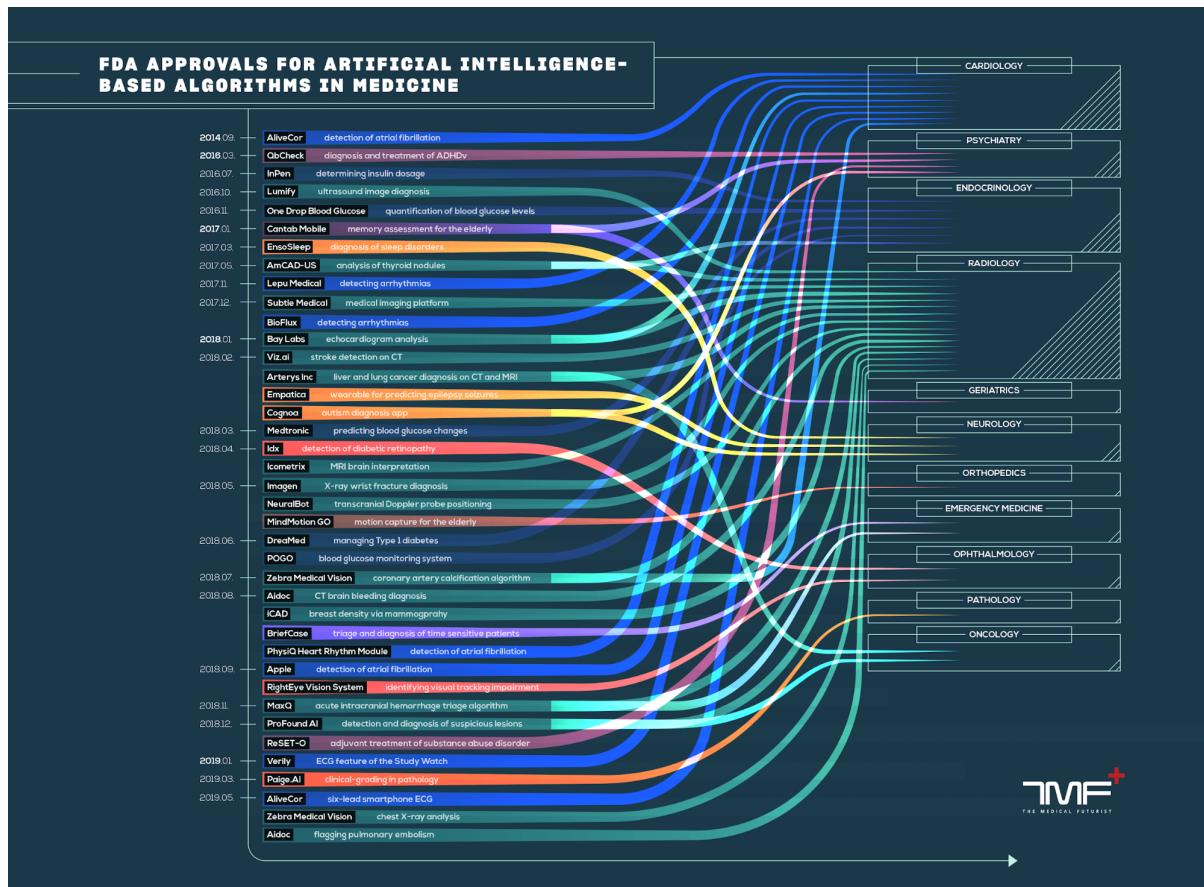


The dark blue color is used for those concepts which we spend more time on, while gray ones are mentioned and are relevant, but are not discussed in detail.

Some of these may be familiar to you, and some may be new. We will try to provide links at the end of each lesson to help you explore these in further detail.

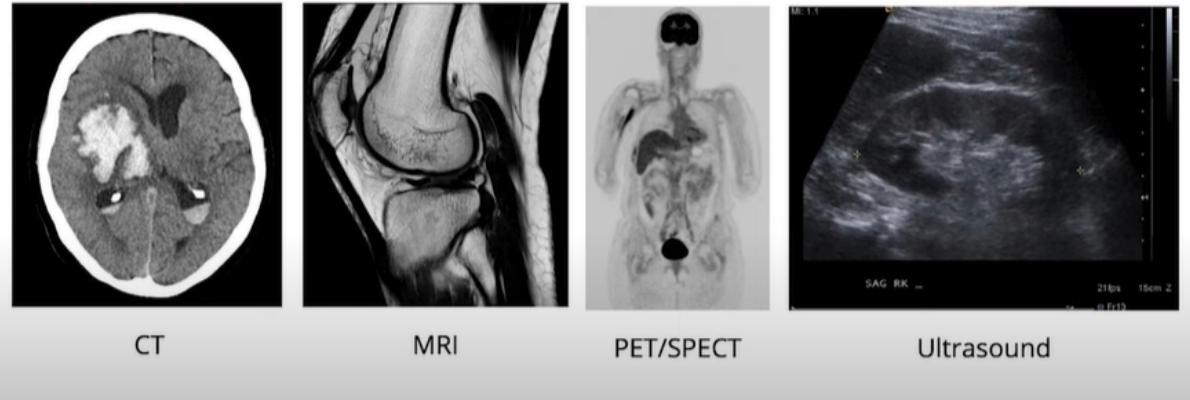
Medical imaging has been around for quite a while now, but not until recently have automated analysis techniques seen a lot of success.

Perspective



What are 3D Medical Images?

3D Medical Imaging Examples



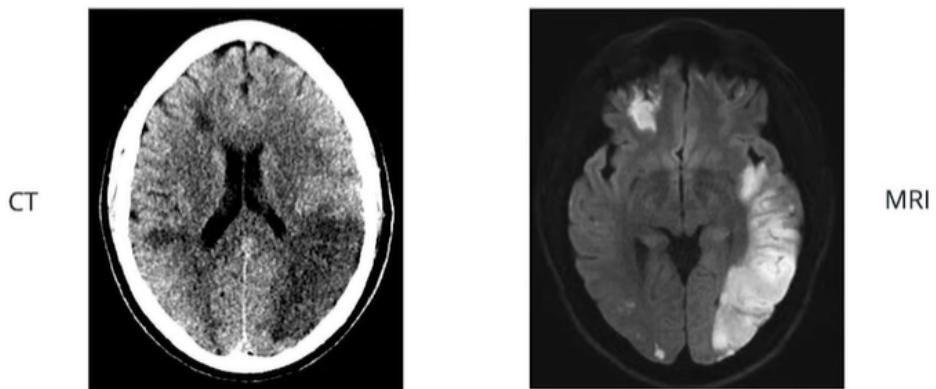
Why 3D?

- Often, increases sensitivity (**IS** there a finding ?)
- Better localization in 3D space (**WHERE** is the finding?)
- In most cases, a better delineation between tissue types (**WHAT** is the abnormality potentially?)
- Anytime a medical imaging study is chosen, we must take into consideration:
 - Contrast Resolution
 - Spatial Resolution
 - Invasiveness
 - Radiation Dose

Contrast Resolution

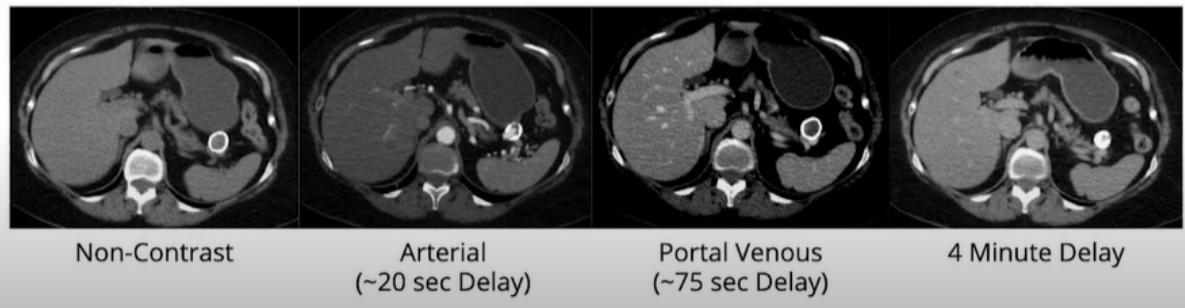
- Refers to the ability of any imaging modality to distinguish between differences in image intensity.

Refers to the ability of any imaging modality to distinguish between differences in image intensity.



- An imaging modalities' intrinsic contrast resolution can be further modified by the use of administered contrast media. most commonly intravenously and/or orally, depending on the study.

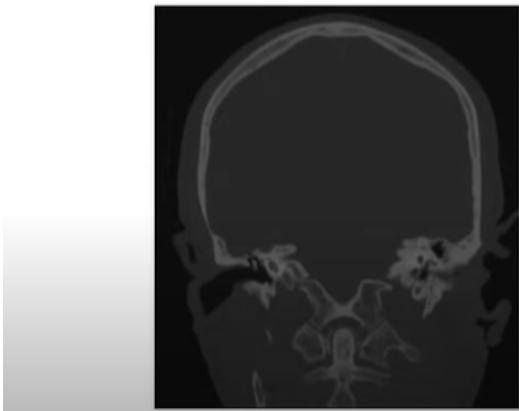
An imaging modalities' intrinsic contrast resolution can be further modified by the use of administered contrast media, most commonly intravenously and/or orally, depending on the study.



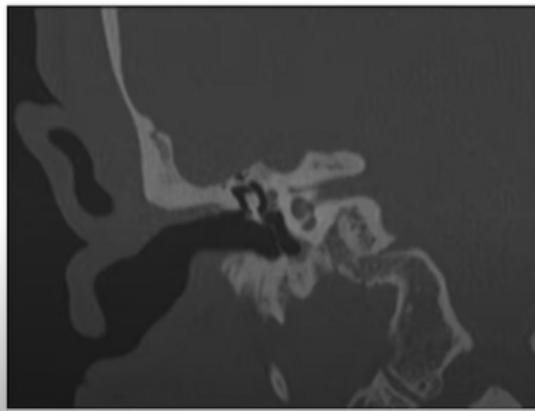
Spatial Resolution

- Refers to the ability of the imaging modality to differentiate two objects

CT - Face



CT - Temporal Bone



Why 3D?



Who uses 3D Medical Images?

User Archetypes

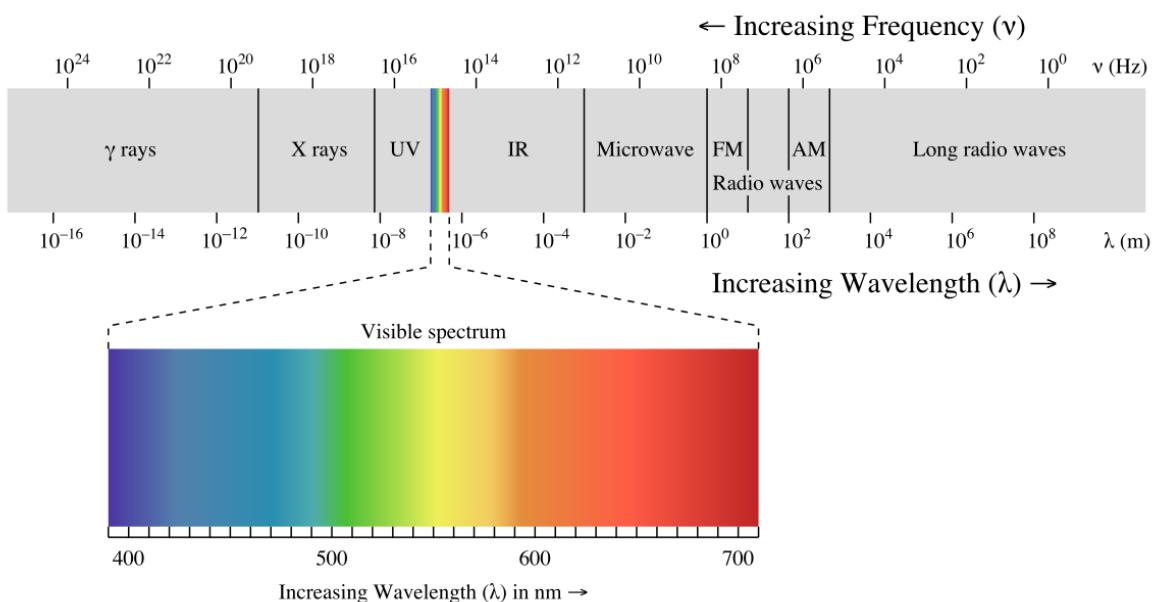


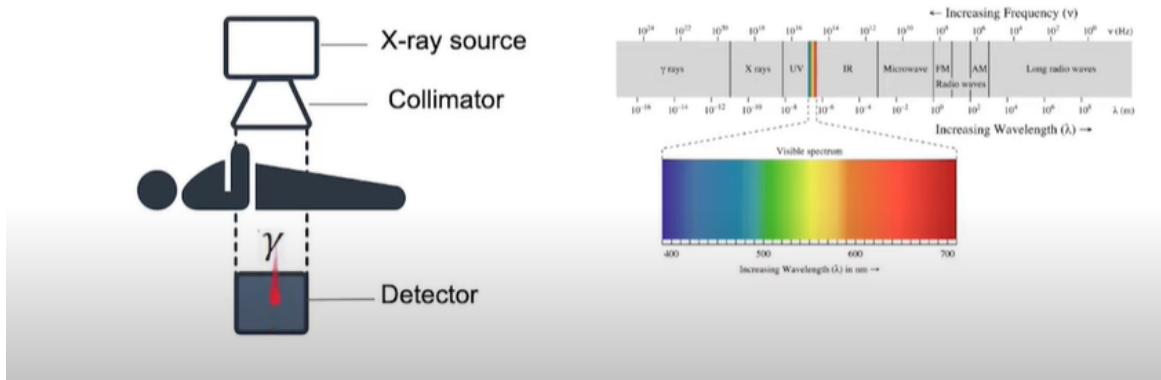
<https://youtu.be/BA7IAQiDA6k>

Physical Principles of operation of a CT scanner

X-rays

The main operating agents of a CT scanner are X-rays, which are a form of electromagnetic radiation. A reminder on electromagnetic spectrum below:





X-rays are a form of ionizing radiation, which means that they carry enough energy to detach electrons from atoms. This presents certain health risks, but the short wavelength of this part of the electromagnetic spectrum allows the radiation to interact with the many structures that compose a human body, thus allowing us to measure the amount of photons that reach detectors and make deductions about the structures that were in the way of photons as they were traveling from the source to the detector, with a high precision.

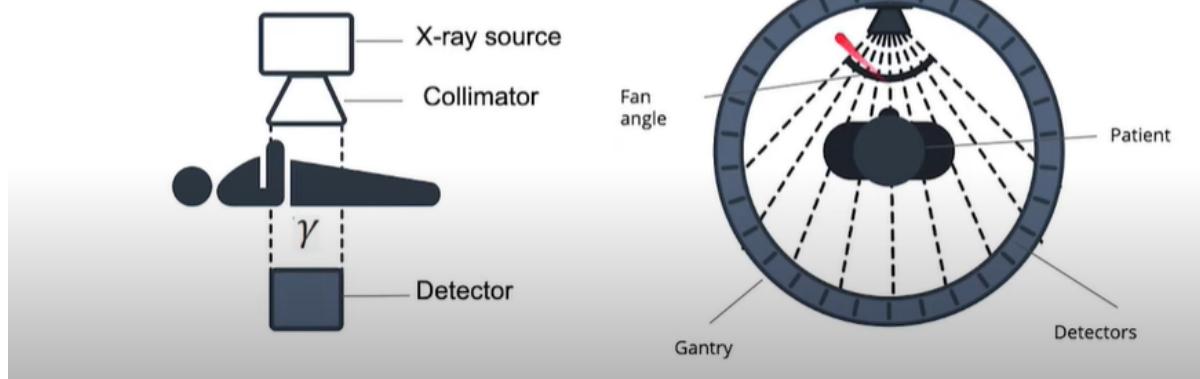
CT scanners

As you have seen, the CT scanner operates by projecting X-rays through the subject's body.

X-rays get absorbed or scattered by the anatomy and thus detectors measure the amount of this attenuation that happens along each path that the ray is taking. A collimator shapes the beam and ensures that the X-rays only pass through a narrow slice of the object being imaged. Rotation of a source inside a gantry makes sure that projections happen from different angles so that we can get a good 2D representation of the slice. The moving table ensures that multiple such slices are imaged. A collection of slices makes up a 3-dimensional CT image.

Tomography

Tomography = "cross sectional imaging"



Going 3D

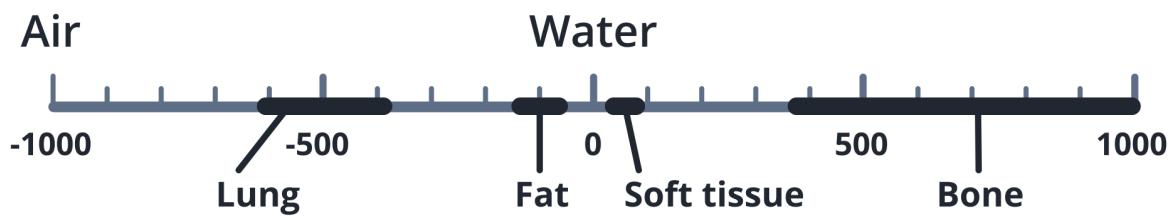


In this module, we have covered the basics of the operation of CT scanner and have gone through an exercise that lets us take a glimpse at what is actually happening when a CT scanner is reconstructing an image.

You have seen how the nature of CT data acquisition - the fact that we are effectively measuring *radiodensity* of biological material - allows us to define a consistent way of associating intensities of pixels in a CT scan slice with the physical density of a structure that is being imaged.

This allows us to guarantee a great degree of consistency among all CT scanners, and thus allow us to have the Hounsfield Scale, named after Sir Godfrey Hounsfield who invented modern CT scanners in the 1970s.

Hounsfield Scale maps tissue types to pixel values of CT scans and is essential to understanding CT scans.



Bone	$+400 \rightarrow +1000$
Soft Tissue	$+400 \rightarrow +80$
Water	0
Fat	$-60 \rightarrow -100$
Lung	$-400 \rightarrow -600$
Air	-1000

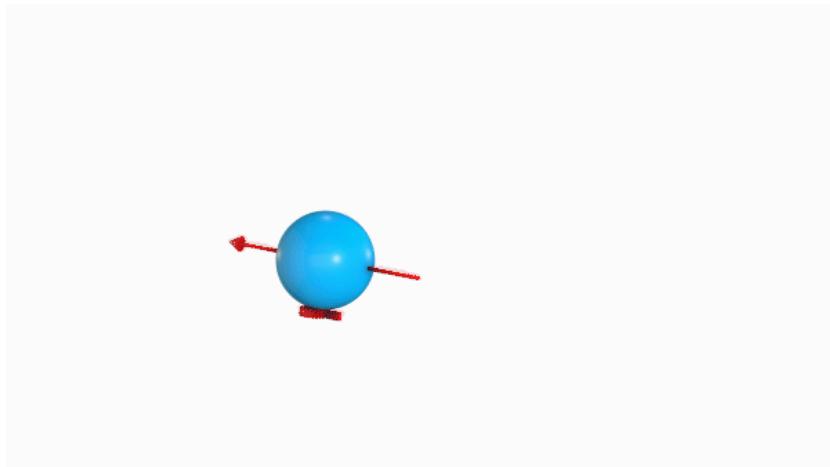
MRI - Magnetic Resonance Imaging

MRI Measurement

- Protons in hydrogen atom align themselves in strong magnetic fields, precessing at frequency proportional to the field strength.
- Field Gradients are added to vary resonant frequencies, spatially
- An RF pulse of resonant frequency is applied to flip the protons

MR scanner leverages a basic physical property of protons (charged elementary particles that make up atoms) to align themselves along the vector of magnetic fields. This effect is particularly pronounced in protons that make up hydrogen atoms. Hydrogen atoms make up water molecules, and water makes up to 50-70% of a human body.

The thing with protons is that they possess a property called spin which could be thought of as spinning around an axis. In a normal environment, the direction of this axis is randomly distributed across different protons. In the presence of a strong magnetic field, though, the proton spins get aligned along the direction of the magnetic field, and start precessing (think of what a spinning top that's lost some of its momentum is doing):



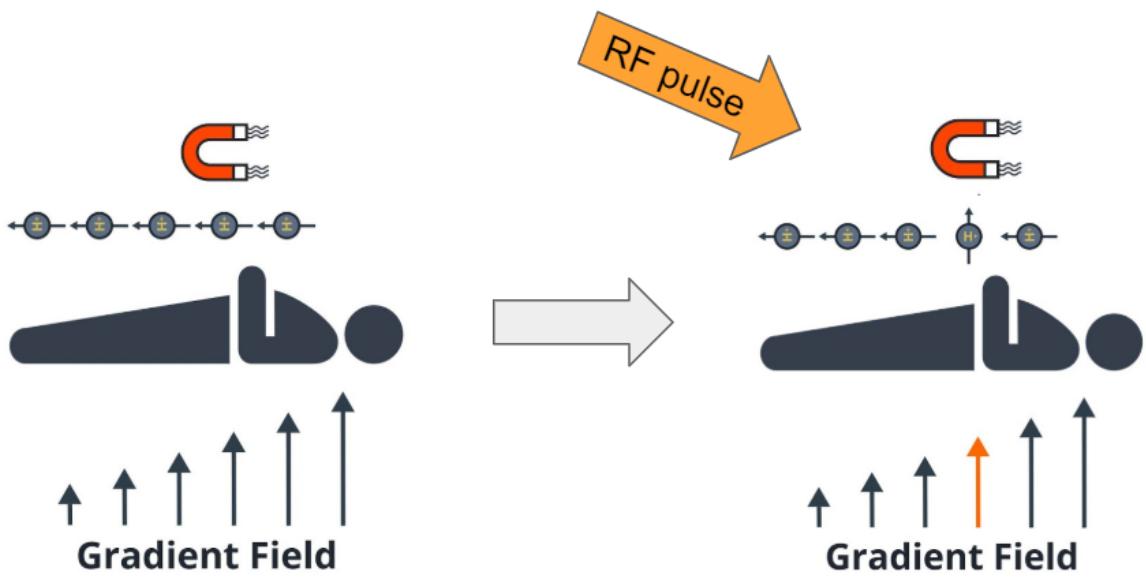
Fun fact: “strong magnetic field” means really strong. Look up “MRI metal chair experiment” on YouTube to get a sense of what that is like. Such a static magnet can rip metal from a patient’s body - that is why anyone going into a scan will get asked if they have any magnetic implants and will be asked to remove any jewelry. That is also why certain patients (e.g. with metal shards left over from a trauma) would not be able to get imaged in an MRI scanner.

When an external radiofrequency pulse is applied, of a frequency proportional to the frequency of precession, the protons respond to this pulse in unison, or **resonate**, and flip the orientation of their spins. Once this pulse is gone, they return to their original orientation (along the static magnetic field).

The way in which protons return to their original orientation is different and depends on the tissue type that protons are a part of.

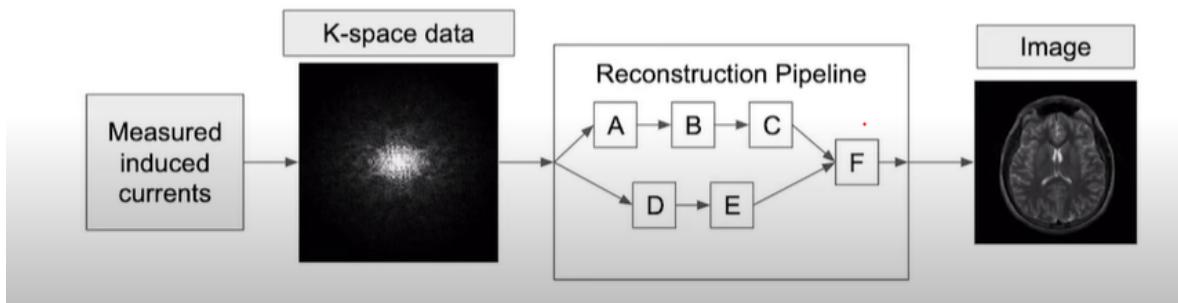
Since many protons are returning to their original orientation at once, they generate electrical currents in the coils that are placed nearby. Due to the resonance effect these currents are not insignificant and can be measured - these measurements constitute the data about the tissue being studied which is collected by the MRI scanner.

Gradient fields are used to vary the static magnetic field, and thus precession frequency, spatially. This allows the MR scanner to isolate a part of the body (i.e. a slice) that is being imaged. Further gradient fields are used to isolate information coming from specific locations within a slice.



MRI Reconstruction

- With known pulse sequence, measured signal is a function of time and EM field magnitude
- This measurement can be represented as data in a spatial frequency space known as "k-space"
- K-space data undergoes reconstruction pipeline to obtain the optical space image

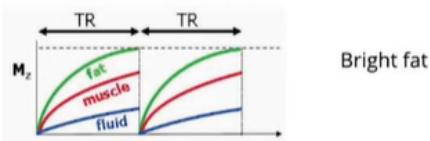


MRI Pulse Sequences

Gradient fields + RF Pulse = Pulse Sequences

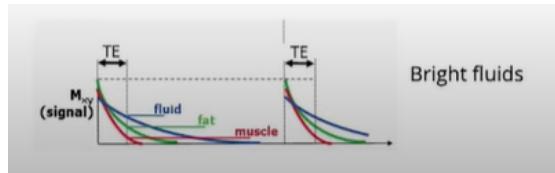
T1 weighted sequence

- Measuring time it takes for protons to return to original orientation.



T2 weighted sequence

- Measuring time it takes for protons to lose synchronization after a pulse.



Gradient fields + RF pulse = Pulse Sequence

T1 weighted sequence



T2 weighted sequence



Summary

K-space and Reconstruction

The currents measured by RF coils get turned into a digital format, and represented as vectors in “**K-space**”. The concept of K-space goes back to the wave theory in physics and basically defines a space of vectors that describe characteristics of electromagnetic waves.

In our case, these wave vectors carry information about the characteristics of the matter in the space that has been measured. Essentially, these vectors record the spatial frequency of signal intensity, and thus, through the process that involves an Inverse Fourier Transform and a lot of de-noising and other optimizations, get turned into a familiar 2D image that represents a slice through a human body with different anatomy having different pixel intensity. This process is referred to as **image reconstruction** in MR physics. Typically, image reconstruction is performed on a computer that is directly embedded into an MR scanner, and the problem of optimizing or scaling image reconstruction alone is a very interesting one.

If you are familiar with Fourier Transforms, but the concept of “spatial frequency” still seems way too mind-boggling - don’t worry, it could be. However, image analysis through FTs is a common technique in image processing. I have a link to some good materials on the subject later which will hopefully help you understand this concept a bit better if you are interested.

Similar to a CT scan, multiple slices imaged with a pre-set spatial interval through a human body are combined to obtain the 3D image. Note, however, that due to greater control over the electromagnetic fields, MR scanners can obtain data directly for a 3D volume in a single “sweep”, without having to go slice-by-slice.

Pulse Sequences

We can vary the combination of gradient fields, RF pulses, and aspects of the signal that is getting measured. Together, these are called a **pulse sequence**.

Two very common sequences are called “T1-weighted” and “T2-weighted” sequences (technically - these two are looking at different aspects of the same combination of electromagnetic fields). T1 produces greater contrast resolution for fat, and T2 produces greater detail in fluids. Quite often, a contrast medium is used along with a T1 sequence to make certain structures stand out. Thus, the gadolinium agent is often used in neuroradiology to improve the visibility of things like tumors and hemorrhages.

Many more sequences exist, including many which are proprietary to scanner manufacturers, and there is a field of medical physics that deals exclusively with pulse sequence design.

New Vocabulary

- **K-space data:** “raw” data generated by an MRI scanner. Images need to be reconstructed from it

In this section, we took a glimpse at how MRI scanners operate.

As you have seen, MRI scanners are probably some of the most complex inventions made by humankind. The design of one touches on hard problems in the fields of robotics, quantum physics, signal processing, mechanical, electrical, and software engineering.

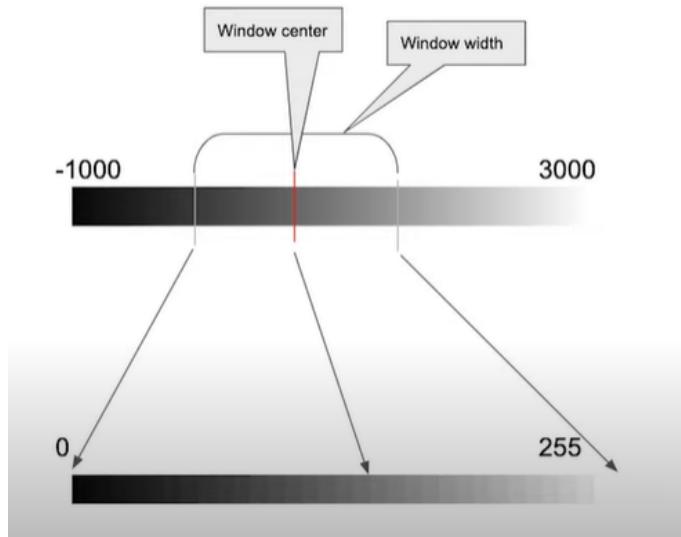
MRI scanners are very versatile machines that can provide great non-invasive insight into what is happening inside a human body, and they lend themselves to a lot of interesting AI problems.

Further Resources

- Facebook’s research on using AI to accelerate the MRI reconstruction process: [Overview](#) and a paper about [fastMRI: An Open Dataset and Benchmarks for Accelerated MRI](#).
- If you want to understand details of MR physics better, here is a paper on the subject, oriented at clinicians: [Ridgway, J. P. \(2010\). Cardiovascular magnetic resonance physics for clinicians: part I. Journal of Cardiovascular Magnetic Resonance, 12\(1\), doi: 10.1186/1532-429x-12-71.](#)
- If you would like to understand the process of MRI image reconstruction a bit better, here is an excellent in-depth overview: [Hansen, M. S., & Kellman, P. \(2014\). Image reconstruction: An overview for clinicians. Journal of Magnetic Resonance Imaging, 41\(3\), 573–585. doi: 10.1002/jmri.24687.](#)
- Finally, if you want to try and wrap your head around spatial frequency decomposition for image analysis, here is a good overview from the University of New Mexico: <https://www.cs.unm.edu/~brayer/vision/fourier.html>

Windowing

- Radiological images are mostly composed of values on a linear scale.
- The scale can be pretty large, range of 4000 for CT images, more for MRI
- Need to map to grayscale monitor space - the process is called windowing.



As you have seen, **windowing** is a fairly straightforward color mapping procedure. An interesting thing to keep in mind about windowing is that historically we have been mapping linear scales in which scanners acquire data to the linear grayscale which has the limitation of being only able to display 255 colors. People have been coming up with ideas on how to circumvent this limitation.

One such idea was building special medical monitors that use more than 8 bits per single color channel or are optimized specifically for grayscale representations (e.g., look up Barco monitors that have 10- and 12-bit grayscale technology). If you think that HDR TVs are new, think again – the medical imaging industry has been building those for decades!

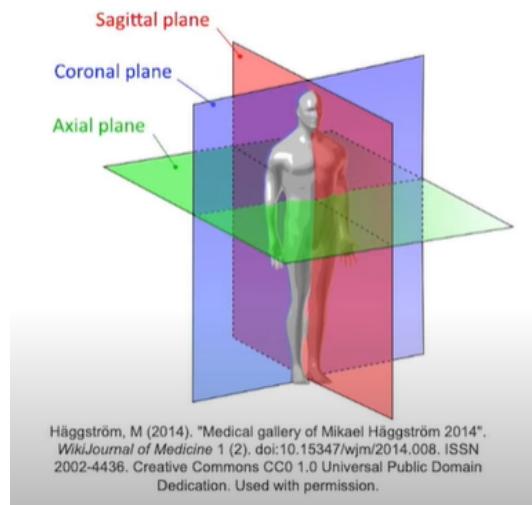
Another idea would be trying to use all colors of the display or somehow optimizing the representation to fit the grayscale range better. We will post a link to some interesting experiments in this area in the next lesson, once you've had the chance to learn how medical images are stored.

New Vocab

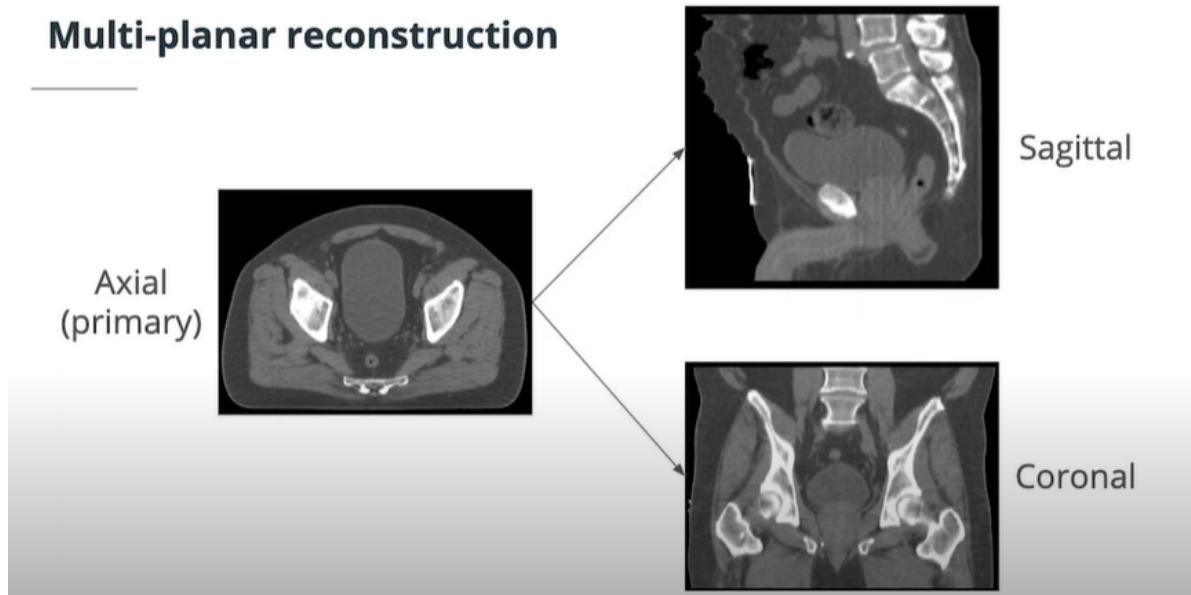
- **Windowing:** mapping high dynamic range of medical images onto the screen-space gray color scale

Multi-planar reconstruction

- Multi-planar reconstruction(MPR) refers to constructing additional cardinal plane views from the primary one.
- 3 Cardinal planes
 - Axial
 - Coronal
 - Sagittal
- One will be the primary acquisition plane
- Oblique reconstruction refers to reconstructing at an arbitrary angle



Multi-planar reconstruction



New Vocabulary

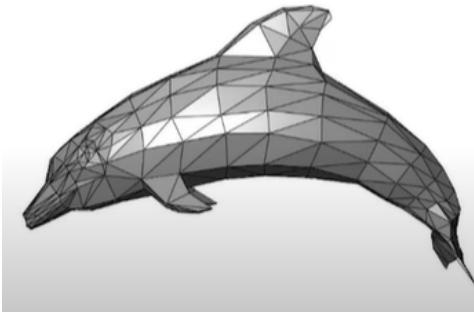
- **MPR:** multi-planar reconstruction - extraction of non-primary imaging planes from a 3D volume

3D Reconstruction

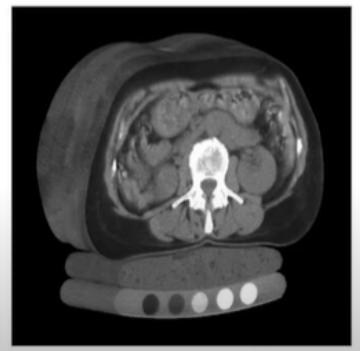
- Images are acquired in slices
- Volumetric pixels(Voxel) is a pixel with location in 3D space/volume
- 3D reconstruction = producing a 3D object from a set of 2D slices

3D Reconstruction

Surface (polygon) mesh



Volume mesh



TASK

Creating a 2D image from k-space data

MRI data reconstruction

Extracting a 2D image in coronal plane from an image which has been acquired in sagittal

Multi-planar reconstruction

Creating a 2D image from a sinogram

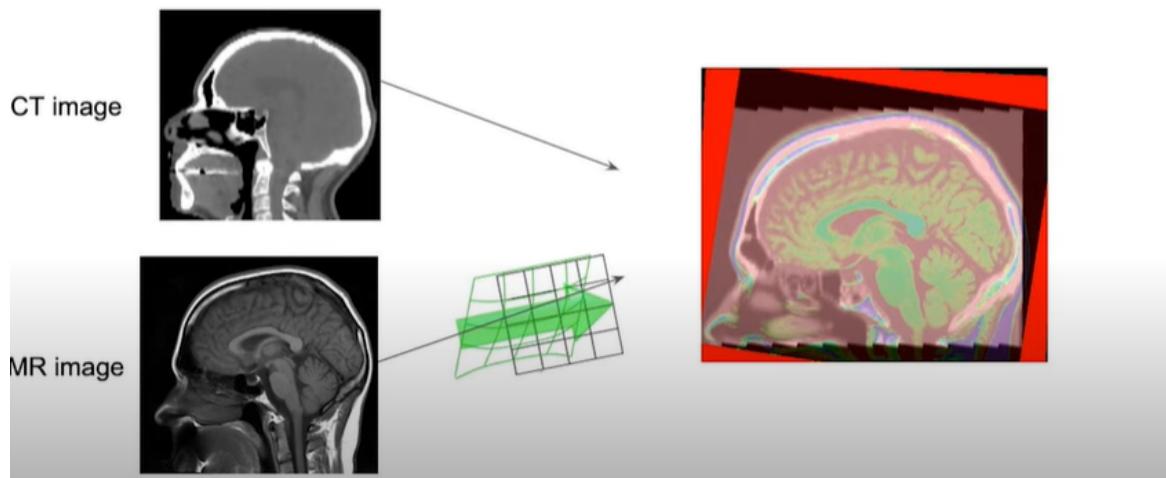
CT image reconstruction through filtered backprojection

Creating a 3D volume from CT data

3D reconstruction

Registration

- Sometimes we need to superimpose anatomy from the different modalities or time points
- Registration = shifting all voxels from one image (moving image) to another (fixed) so that some constraints are fulfilled:
 - Rigid registration: only rotation and translation
 - Affine registration: can do scaling
 - Deformable registration: arbitrary mapping of one point to another



3D Imaging Tasks: Summary

We have touched on some of the most typical tasks that you would likely need to deal with when working with 3D imaging data.

You will probably use **3D reconstruction** to visualize your volumes. Typically 3D reconstruction capabilities are incorporated into medical imaging viewers and range from basic to very elaborate. In later lessons, we will take a look at some of the tools that you can leverage for this.

Multi-planar reconstruction is something that you will do naturally as you will want to extract slices from volumes. MPR is something that any 3D medical image viewer can do, but a data scientist would likely be dealing with cuts through different planes a lot too. We will see examples of MPR further in this course, and you will be writing your own code to do this.

Windowing task would have you map 10 or more bits of grayscale to the 256 colors your screen could display (or maybe the RGB colorspace). Windowing is the very standard very basic operation of any medical image viewer (not only 3D one)

Registration will pop up if you are looking at tasks that involve combining data from multiple imaging modalities or change of structures in the same patient over time. Registration on its own is not a strictly defined task. There are options - you need to decide e.g. if distances should be preserved in the moving image, or if parallel lines need to be preserved, but the image can be shrunken or expanded. Because of such tradeoffs, registration is always defined within a context of a clinical task. Registration sometimes is available in more advanced image viewers, and there are also tools and libraries that you can lean upon to do it programmatically

An interesting thing about registration is that it can be formulated as an optimization problem. This problem is quite well studied and has some good analytical solutions, but can also be addressed by deep learning methods.

Further Resources

- A great overview of registration, methods, and various issues: [Alam, Fakhre & Ur Rahman, Sami & Din, Aziz & Qayum, Fawad. \(2018\). Medical image registration: Classification, applications and issues. Journal of Postgraduate Medical Institute. 32. 300-307.](#)
- A couple of papers looking at registration as an optimization problem and applying deep learning methods:
 - [Song G, Han J, Zhao Y, Wang Z, Du H. A Review on Medical Image Registration as an Optimization Problem. Curr Med Imaging Rev. 2017;13\(3\):274-283. doi:10.2174/1573405612666160920123955](#)
 - [Haskins G, Kruger U, Yan P. \(2020\). Deep Learning in Medical Image Registration: A Survey. Retrieved Mar 2020 from the arXiv database.](#)
- Siemens Healthineers is doing some great research around the photorealistic rendering of medical volumes. Check out their related webpage to see some of the very compelling ways to do 3D

reconstruction: <https://www.siemens-healthineers.com/medical-imaging-it/advanced-visualization-solutions/syngovia-cinematic>

3D Imaging Exploratory Data Analysis

The DICOM Standard

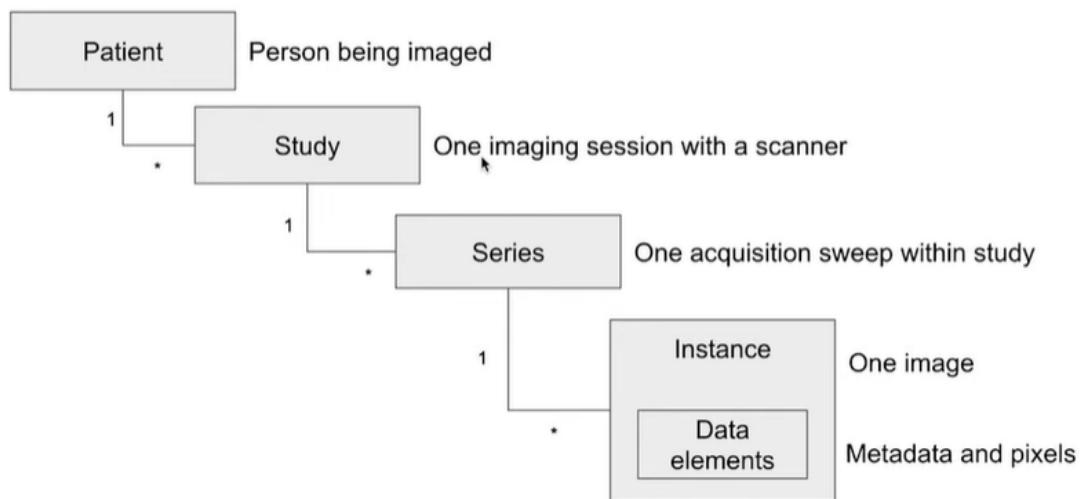
DICOM stands for “Digital Imaging and Communications in Medicine”. It is a standard that defines how medical imaging (primarily) data is stored and moved over the network. It’s been around since the '80s and eventual adoption of this standard by all manufacturers of medical imaging equipment has been a huge enabler for medical data interoperability and clinical research in general.

It is an open standard that is maintained by the National Electrical Manufacturers Association (NEMA) and is available at <http://dicom.nema.org/>. The standard is updated a few times per year, as we update our views on how medical imaging data needs to be stored, and all prior versions are also available. When referencing the DICOM standard in your documentation, it is important to be clear about whether you are referencing the current or past versions of the standard. In this course, I will be referencing version 2020a of the standard.

DICOM is a vast and quite complex standard, and you don’t need to know it all unless you are developing a medical imaging modality or storage software. However, since you are very likely to get data as DICOM, it is important to know what is there, and how to look up things.

In this lesson, we will focus on the storage portion of the standard - the part that defines how the data acquired by the scanners is stored as files on filesystems, and what metadata accompanies these files.

DICOM Data Hierarchy of a DICOM Object



DICOM Entity-Relationship Model

DICOM standard defines Information Entities that represent various real-world entities and relationships between them. The cornerstone of the DICOM standard are the following objects and relationships:

Patient is, naturally, the patient undergoing the imaging study. A patient object contains one or more *studies*.

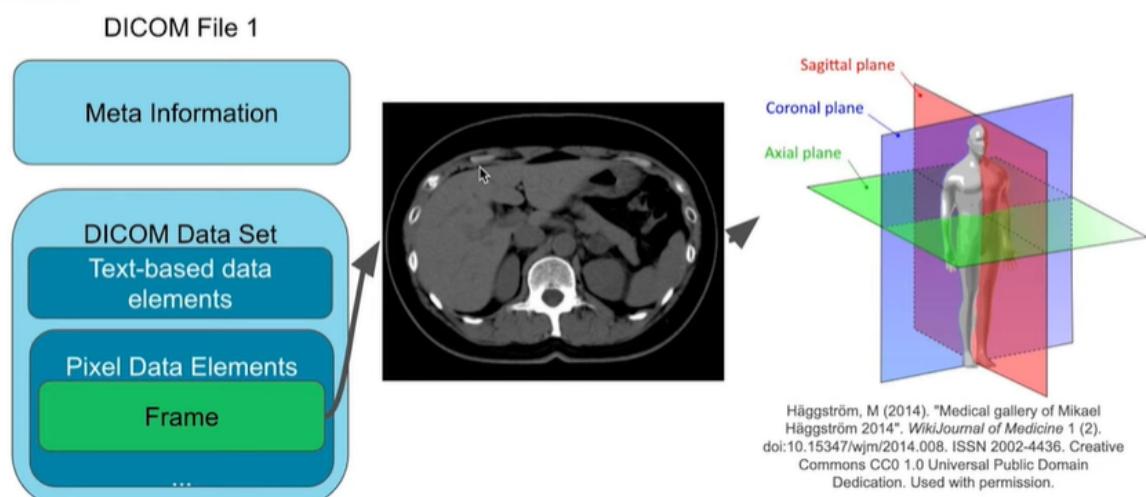
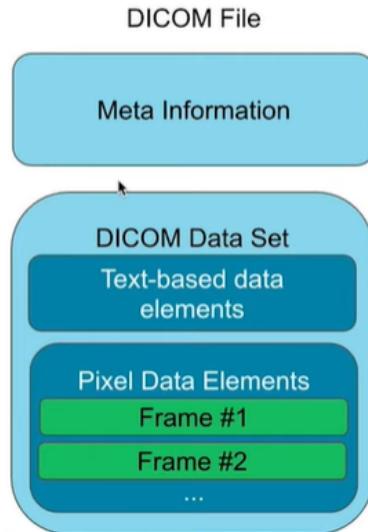
Study - a representation of a “medical study” performed on a patient. You can think of a study as a single visit to a hospital for the purpose of taking one or more images, usually within. A Study contains one or more *series*.

Series - a representation of a single “acquisition sweep”. I.e., a CT scanner took multiple slices to compose a 3D image would be one image series. A set of MRI T1 images at different axial levels would also be called one image series. Series, among other things, consists of one or more *instances*.

Instance - (or Image Information Entity instance) is an entity that represents a single scan, like a 2D image that is a result of filtered backprojection from CT or reconstruction at a given level for MR. Instances contain pixel data and metadata (Data Elements in DICOM lingo).

There are many more entities defined by the DICOM standard, but we will focus on these for the purposes of this course. You can look up the comprehensive list in [Section A.1.2 of Part 3](#) of the standard.

Anatomy of DICOM File



DICOM Standard - SOP Classes

Digital Intra-Oral X-Ray Image Storage - For Processing	1.2.840.10008.5.1.4.1.1.1.3.1	Digital Intra-Oral X-Ray Image IOD (see Section B.5.1.3)
CT Image Storage	1.2.840.10008.5.1.4.1.1.2	CT Image IOD
Enhanced CT Image Storage	1.2.840.10008.5.1.4.1.1.2.1	Enhanced CT Image IOD (see Section B.5.1.7)
Legacy Converted Enhanced CT Image Storage	1.2.840.10008.5.1.4.1.1.2.2	Legacy Converted Enhanced CT Image IOD (see Section B.5.1.7)
Ultrasound Multi-frame Image Storage	1.2.840.10008.5.1.4.1.1.3.1	Ultrasound Multi-frame Image IOD
MR Image Storage	1.2.840.10008.5.1.4.1.1.4	MR Image IOD
Enhanced MR Image Storage	1.2.840.10008.5.1.4.1.1.4.1	Enhanced MR Image IOD (see Section B.5.1.6)
MR Spectroscopy Storage	1.2.840.10008.5.1.4.1.1.4.2	MR Spectroscopy IOD
Enhanced MR Color Image Storage	1.2.840.10008.5.1.4.1.1.4.3	Enhanced MR Color Image IOD
Legacy Converted Enhanced MR Image Storage	1.2.840.10008.5.1.4.1.1.4.4	Legacy Converted Enhanced MR Image IOD (see Section B.5.1.6)
Ultrasound Image Storage	1.2.840.10008.5.1.4.1.1.6.1	Ultrasound Image IOD
Enhanced US Volume Storage	1.2.840.10008.5.1.4.1.1.6.2	Enhanced US Volume IOD
Secondary Capture Image Storage	1.2.840.10008.5.1.4.1.1.7	Secondary Capture Image IOD
Multi-frame Single Bit Secondary Capture Image Storage	1.2.840.10008.5.1.4.1.1.7.1	Multi-frame Single Bit Secondary Capture Image IOD

One of the important things to capture here is that per the DICOM standard, 3D medical images are stored as files on a file system where each file represents an instance of Image DICOM Information Entity. In the case of 3D medical images, each such instance shares context with other instances that belong to the same series and same study. Thus, each DICOM file stores metadata that describes attributes of study and series that the respective instance is a part of, and this metadata is replicated across other instances that belong to the same study. DICOM files are usually stored with *.dcm* extension and are usually grouped in directories (but they don't have to be) to represent data from series, studies and patients. Relationships between individual *.dcm* files are defined by the metadata stored within them.

New Vocabulary

SOP - Service-Object Pair. DICOM standard defines the concept of an Information Object, which is the representation of a real-world persistent object, such as an MRI image (DICOM Information Objects consist of Information Entities). The standard also defines the concept of Services that could be performed on Information Objects. One such service is the Storage service (we will touch on others later in the course), and a DICOM image stored as a file on a file system is an instance of Storage service performed on an Image Information Object. Such Service-Object Pairs have unique identifiers that help unambiguously define what type of data we are dealing with. A list of SOP Classes can be found in [Part 4 of the Standard](#). This list is a useful reference for all possible data types that could be stored per the DICOM standard.

Data Element - a DICOM metadata "field", which is uniquely identified by a tuple of integer numbers called *group id* and *element id*. The convention is to write the element identifier as group id followed by the element id in parentheses like so: (0008,0020) - this one is the DICOM Element for Study Date. DICOM data elements are usually called "tags". You can find the list of all possible DICOM tags in [Part 6, Chapter 6 of the standard](#).

VR - Value Representation. This is the data type of a DICOM data element. DICOM standard imposes some restrictions on what form the data can take. There are short strings, long strings, integers, floats, datetime types, and more. You can find the reference for DICOM data types in [Part 5, Section 6 of the standard](#).

Data Element Type - identifiers that are used by Information Object Definitions to specify if Data Elements are mandatory, conditional or optional. Data Element Type reference can be found in [Part 5, Section 7 of the standard](#)

IOD - Information Object Definition. Information Object Definition specifies what metadata fields have to be in place for a DICOM Information Object to be valid. Scanner manufacturers follow the relevant parts of the DICOM standard when saving the digital data acquired by the scanner. When parsing DICOM data, it is often useful to reference the relevant IODs to see what data elements could be expected in the particular class of information objects, and what they mean. For example, in Part 3 of the standard, you can find [MR Image IOD](#) and [CT Image IOD](#) which we will use in this course quite a bit. You might have noticed that the table with all DICOM data elements does not really provide any description of what these elements mean. The reason for that is that

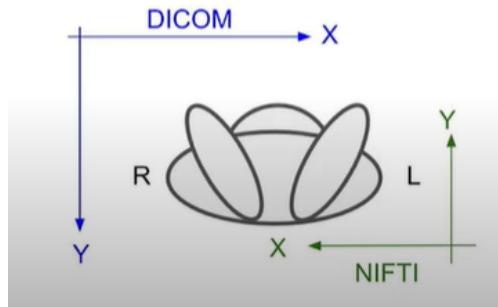
elements may mean slightly different things depending on what Information Object Definition uses them, therefore, to find the real meaning of the element you need to look them up in the respective IOD.

NIFTI File Format

- Standard developed to conveniently store MRI data
- Not generated by scanners
- Represents image series as single file
- Widely used in data science competitions and could be a convenient method to exchange series

NIFTI vs. DICOM File Format

- Stores pixel dimensions
- Units of measurement (DICOM uses mm)
- Orientation is different from DICOM



Like DICOM, NIFTI, which stands for Neuroimaging Informatics Technology Initiative, is an open standard that is available at <https://nifti.nimh.nih.gov/nifti-2>. The standard has started out as a format to store neurological imaging data and has slowly seen a larger adoption across other types of biomedical imaging fields.

Some things that distinguish NIFTI from DICOM, though are:

- NIFTI is optimized to store serial data and thus can store entire image series (and even study) in a single file.
- NIFTI is not generated by scanners; therefore, it does not define nearly as many data elements as DICOM does. Compared to DICOM, there are barely any, and mostly they have to do with geometric aspects of the image. Therefore, NIFTI files by themselves can not constitute a valid patient record but could be used to optimize storage, alongside some sort of patient info database.
- NIFTI files have fields that define units of measurements and while DICOM files store all dimensions in mm, it's always a good idea to check what units of measurement are used by NIFTI.
- When addressing voxels, DICOM uses a *right-handed coordinate system* for X, Y and Z axes, while NIFTI uses a *left-handed coordinate system*. Something to keep in mind, especially when mixing NIFTI and DICOM data.

Further Resources

- Background and history of the NIFTI: <https://nifti.nimh.nih.gov/background/>
- The most “official” reference of NIFTI data fields could be found in this C header file, published on the standard page: <https://nifti.nimh.nih.gov/pub/dist/src/niftilib/nifti1.h> or on this, slightly better-organized page: <https://nifti.nimh.nih.gov/nifti-1/documentation/nifti1fields>
- A great blog post on NIFTI file format: <https://brainder.org/2012/09/23/the-nifti-file-format/>

Viewing 3D medical images

MicroDicom

One tool is called MicroDicom and is available for Windows OS. This tool is a lightweight DICOM image viewer and provides a very convenient way to explore the DICOM tags.



Microdicom (Windows only): <http://www.microdicom.com/>

3D Slicer

Another tool is called 3D slicer and is available for Windows, Linux, and Mac.

It is an open-source modular 3D medical image viewer with a focus on a research community that can view both DICOM and NIFTI. It is quite complex and has a bit of a learning curve to it, but it is very powerful for a variety of tasks.



3D Slicer: <https://www.slicer.org/>

Also, here are some other tools that were not covered in the lesson, but could also come in handy:

- Radiant - another medical image viewer: <https://www.radiantviewer.com/>
- Osirix (Mac only): <https://www.osirix-viewer.com/>
- ViewMyScans - a quick online viewer that doesn't require a local installation: <https://viewmyscans.com/viewer/>

Important Parameters of Medical Images

We have learned about some of the important parameters that you should be on the lookout for when analyzing medical imaging datasets.

These are parameters that have to do with geometric and photometric aspects of medical images.

Orientation parameters

For DICOM two parameters that define the relative position of a 2D in the 3D space would be:

(0020,0037) Image Orientation Patient - a parameter that stores two vectors (directional cosines to be precise) that define the orientation of the first row and first column of the image.

(0020,0032) Image Position Patient - a parameter that stores x, y, and z coordinates of the upper left-hand corner of the image.

Both of these are Type 1 (mandatory) parameters for MR and CT IODs, so it is generally safe to rely on them.

For NIFTI, the same purpose is served by srow_*, qoffset_* vectors.

Physical spacing parameters

(0028,0030) Pixel Spacing - two values that store the physical distance between centers of pixels across x and y axes.

(0018,0050) Slice Thickness - thickness of a single slice. Note that this one is a Type 2 (required, but can be zero) parameter for CT and MR data. If you find those unavailable, you can deduce slice thickness from IPP parameters. This can happen if your volume has non-uniform slice thickness.

Photometric parameters

There are quite a few of those, as DICOM can store both grayscale and color data, so lots of parameters deal with color palettes. CT and MR images usually have monochrome pixel representation (defined by tag **(0028,0004) Photometric Interpretation**).

Most notable ones of this group are:

(0028,0100) Bits Allocated - parameter that defines the number of bits allocated per pixel (since we have CPUs that operate in bytes, this parameter is always a multiple of 8).

(0028,0101) Bits Stored - parameter that defines the number of bits that are actually used - quite often, you could see Bits Allocated set to 16, but Bits Stored set to 12.

Image size parameters

Of worthy mention are parameters that define the size of the 3D volume. There are Type 1 parameters that define the width and height of each 2D slice:

(0020,0010) Rows - this is the height of the slice, in voxels

(0020,0011) Columns - width of the slice, in voxels

Both of these need to be consistent across all DICOM files that comprise a series.

Note that there isn't really anything in DICOM metadata that has to tell you how many slices you have in the series. There are tags that can hint at this (like *(0054,0081) Number of Slices*, or *(0020,0013) Instance Number*), but none of them are mandatory, Type 1 tags for CT or MR data. The most reliable way to determine the number of slices in the DICOM series is to look at the number of files that you have, and ideally validate that they make up a correct volume by checking for the consistency of IPP values.

Further Resources

If you want to dive deeper into the subjects of coordinate spaces for medical images, and parameters of DICOM files in general, some useful resources:

- Section on IPP and IOP parameters in the DICOM standard: http://dicom.nema.org/medical/dicom/2020a/output/chtml/part03/sect_C.7.6.2.html
- A solid explanation of how coordinate systems work in NIFTI: https://nipy.org/nibabel/coordinate_systems.html
- A company called Innolitics (a vendor of various DICOM software) maintains a great reference of the DICOM standard which sometimes could be quite a bit more convenient than the official standard: <https://dicom.innolitics.com/ciods>

Exploratory Data Analysis of DICOM datasets

Now let me walk you through a Python Notebook where I analyze a single 3D medical image volume. This notebook and the volume used by it are available among the course materials.

<https://youtu.be/WArVyluv3kM>

We have just seen a few basic techniques for working with medical imaging volumes. We have hit on a few quite important things to remember when exploring your data and thinking of preparing volumes for downstream machine learning pipelines. You are welcome to explore the Notebook on your own at the bottom of the page.

Voxel spacing

DICOM voxels do not have to be perfect cubes (as they are in many computer vision problems). There are DICOM Data Elements that will tell you what exactly are the dimensions of voxels. The most important ones are Pixel Spacing and Slice Thickness. However, there are others, and if your project involves measuring things, make sure you get the transformation right by closely inspecting the tags in your dataset and comparing them with the list of elements in the IOD table for the respective modality.

Data ranges

We have seen how with CT, you may have data in your dataset that will represent synthetic material or items artificially added by scanners. It is always a good idea to see if there is something outstanding in the image you are dealing with and if it represents something that you need to think about in your downstream processing.

Conversions between DICOM values and screen space are particularly important if you are planning to visualize slices for any kind of diagnostic use or overlay them on top of diagnostic information. We have not really touched the aspects of visualization other than being mindful of bit depth and doing our own windowing, but DICOM images contain quite a lot of information that defines how exactly you are expected to map the data to the screen colorspace. If you are interested in exploring this further or need to accurately represent the data, take a closer look at elements in DICOM's [**ImagePixel module**](#). Things like Pixel Representation, Photometric Interpretation, Rescale Slope, Rescale Intercept and many others define how values should be transformed for accurate representation.

DICOM Volume Dataset EDA

Methods for dataset analysis basically boil down to using the same tricks as you'd do for individual volume analysis and being on the lookout for inconsistencies in data.

Inconsistencies usually boil down to two classes:

- **Clinical anomalies** - the things related to either anatomical anomalies like missing organs, pathologies like tumors or implants such as limb prosthesis, ports/cannulas, surgical implants, presence of contrast media, etc. Sometimes these things can result in artifacts in the images, so it's good to be aware of them
- **Informatics anomalies** - things related to specifics of data acquisition or variations in DICOM encoding coming from different scanners. These would be things like slice spacing consistency, image dimensions, variations in photometric encoding, etc

Basic knowledge of DICOM and intuition for what things could go wrong are always useful when analyzing the datasets. I will post some examples of great dataset EDA at the end of this lesson as well.

Further Resources

Some great examples of EDA adventures could be found in the following competitions/challenges:

- [**The 2019 RSNA Intracranial Hemorrhage Detection Challenge**](#)
- [**2018 RSNA Pneumonia Detection Challenge**](#)
- [**2017 Data Science Bowl**](#)
- [**Multimodal Brain Tumor Segmentation Challenge 2019**](#)

And here are some notebooks presenting interesting tricks to try with DICOM data:

- As mentioned in the previous lesson, now that you know some DICOM, take a look at some creating windowing approaches: <https://www.kaggle.com/jhoward/don-t-see-like-a-radiologist-fastai>
- This one provides a good basis for windowing responsibly <https://www.kaggle.com/dcstang/see-like-a-radiologist-with-systematic-windowing>
- And this Notebook covers some useful tricks to keep handy as you are working through 3D imaging datasets: <https://www.kaggle.com/jhoward/some-dicom-gotchas-to-be-aware-of-fastai>

3D Medical Imaging - End to End Deep Learning Applications

<https://youtu.be/bqrpWKXTps8>

We have just discussed several types of convolutions that could be used for feature extraction of 3D medical images:

2D Convolution is an operation visualized in the image above, where a convolutional filter is applied to a single 2D image. Applying a 2D convolution approach to a 3D medical image would mean applying it to every single slice of the image. A neural network can be constructed to either process slices one at a time, or to stack such convolutions into a stack of 2D feature maps. Such an approach is fastest of all and uses least memory, but fails to use any information about the topology of the image in the 3rd dimension.

2.5D Convolution is an approach where 2D convolutions are applied independently to areas around each voxel (either in neighboring planes or in orthogonal planes) and their results are summed up to form a 2D feature map. Such an approach leverages some dimensional information.

3D Convolution is an approach where the convolutional kernel is 3 dimensional and thus combines information from all 3 dimensions into the feature map. This approach leverages the 3-dimensional nature of the image, but uses the most memory and compute resources.

Understanding these is essential to being able to put together efficient deep neural networks where convolutions together with downsampling are used to extract higher-order semantic features from the image.

Next up, we will take a closer look at how convolutions operate by running through a notebook and performing an exercise.

Classification: Summary

This is the end of our section on classification and object detection.

Note that we did not spend too much time on the actual methods for building networks for classification and object detection, and as you will see further in the lesson, there is more focus on segmentation, especially on performance metrics and coding exercises.

The reason for that is that classification problems in 3D medical imaging can leverage a lot of techniques used for 2D image classification, and the course on AI for 2D medical image analysis, which is a part of this nanodegree, already provides an excellent deep dive into some of the approaches for classification and object detection problems. We talked about some of the differences between 2D and 3D classification problems such as 3D and 2.5D convolutions and hopefully, through our convolutions exercise, got you a feel of how these work and how you would code one yourself. But if you want to ground yourself better in applying CNNs for classification and object detection problems, I suggest going through the course on AI for 2D medical image analysis.

Further Resources

- If you think you're lost in convolutions - check out this [2D Visualization of a Convolutional Neural Network](#) by Adam W. Harley.
- [A guide to convolution arithmetic for deep learning](#) is a great overview of the arithmetic of the various convolution operations.
- The paper I had mentioned in the slides where the authors use 2.5D convolutions for a variety of pathology classifiers: [H. R. Roth et al., "Improving Computer-Aided Detection Using Convolutional Neural Networks and Random View Aggregation," in IEEE Transactions on Medical Imaging, vol. 35, no. 5, pp. 1170-1181, May 2016.](#)
- Another paper by the same authors presenting a 2.5D convolutions approach for lymph node detection: [Roth, Holger R., et al. "A New 2.5D Representation for Lymph Node Detection Using Random Sets of Deep Convolutional Neural Network Observations." Medical Image Computing and Computer-Assisted Intervention – MICCAI 2014 Lecture Notes in Computer Science, 2014, pp. 520–527, doi:10.1007/978-3-319-10404-1_65.](#)
- This paper is comparing 3D and 2D network architectures for lung nodule classification problem: [Kang G, Liu K, Hou B, Zhang N \(2017\) 3D multi-view convolutional neural networks for lung nodule classification. PLoS ONE 12\(11\): e0188290. https://doi.org/10.1371/journal.pone.0188290](#)

Segmentation: Introduction and Use Cases

We have discussed the problem statement for semantic segmentation and a few use cases for segmentation in 3D medical imaging:

- **Longitudinal follow up:** Measuring volumes of things and monitoring how they change over time. These methods are very valuable in, e.g., oncology for tracking slow-growing tumors.
- **Quantifying disease severity:** Quite often, it is possible to identify structures in the organism whose size correlates well with the progression of the disease. For example, the size of the hippocampus can tell clinicians about the progression of Alzheimer's disease.
- **Radiation Therapy Planning:** One of the methods of treating cancer is exposing the tumor to ionizing radiation. In order to target the radiation, an accurate plan has to be created first, and this plan requires careful delineation of all affected organs on a CT scan
- **Novel Scenarios:** Segmentation is a tedious process that is not quite often done in clinical practice. However, knowing the sizes and extents of the objects holds a lot of promise, especially when combined with other data types. Thus, the field of **radiogenomics** refers to the study of how the quantitative information obtained from radiological images can be combined with the genetic-molecular features of the organism to discover information not possible before.

Now, let's take a look at some of the methods that are commonly used for building segmentation CNNs.

Segmentation Methods

A U-Net architecture has been very successful in analyzing 3D medical images and has spawned multiple offshoots. You will get a chance to get more familiar with it in the exercise that follows, but if you would like to understand the principles better, I recommend that you check out the webpage on U-net created by one of the authors of the original paper, Olaf Ronneberger: <https://lmb.informatik.uni-freiburg.de/people/ronneber/u-net/index.html>. You will find the link to the original paper and a few materials explaining how and why this architecture works.

Ground Truth for Segmentation

Some of the challenges in creating the ground truth for segmentation have to do with the fact that it is rarely routinely created in clinical practice. Radiation oncology is one of the few fields where segmentation is generated as part of the treatment path, but normally segmentation projects require custom labeling efforts.

One of the things to keep in mind when dealing with a labeled (segmented) dataset is that interpretation of radiological images is ambiguous and quite often, two independent clinicians (observers) would not label things in the same way. This phenomenon is called Interobserver Variability and has been studied in the literature.

- This is the paper that I have mentioned where the authors present results of measuring the variability between radiation oncologists segmenting structures in the head and neck region: [Mukesh, M et al. "Interobserver variation in clinical target volume and organs at risk segmentation in post-parotidectomy radiotherapy: can segmentation protocols help?" The British journal of radiology vol. 85,1016 \(2012\): e530-6. doi:10.1259/bjir/66693547](#)
- While I worked on Microsoft's Project InnerEye we also did our own IOV study for how conformant people are in contouring pelvic anatomy in prostate cancer patients, and included it into our paper which you can read here: [Macomber, M. W., Phillips, M., Tarapov, I., Jena, R., Nori, A., Carter, D., ... Nyflot, M. J. \(2018\). Autosegmentation of prostate anatomy for radiation treatment planning using deep decision forests of radiomic features. Physics in Medicine & Biology, 63\(23\), 235002. doi: 10.1088/1361-6560/aaeaa4](#)

When it comes to tooling for creating ground truth, **3D Slicer** is a popular free tool used in the research community, and I will walk you through using it for creation and review of segmentation labels in the next lessons. **MITK** is another one. However, many medical imaging startups and larger companies use tools of their own.

Evaluating Performance as a Data Scientist

<https://youtu.be/5laZNKLiGKY>

We have discussed four metrics that you can use to evaluate the performance of your segmentation models. As usual, a great explanation of these can also be found on Wikipedia which I'm linking here if you are looking for additional details:

- [Sensitivity and Specificity](#)
- [Dice Similarity Coefficient](#)
- [Jaccard Index](#)
- [Hausdorff Distance](#)

Note these metrics as they are very handy as you are publishing your model's validation reports, but also they could be used to construct more elaborate cost functions. We will take a closer look at how these metrics work, but for now, let's see how clinicians think of performance.

Evaluating Performance as a Clinician

<https://youtu.be/18c8fjD-EBQ>

Note how I am talking about performance in a different sense. As a clinician, I need to make decisions about the presence of conditions or selecting the course of treatment. For that, clinicians operate in terms of Likelihood Ratios.

The likelihood ratio for a diagnostic test result can be calculated if the predictive characteristics (sensitivity and specificity) of that test are known. Likelihood ratios are known for common diagnostic tests performed by humans (e.g., correctly identifying viral pneumonia from chest CT scans). This means that for example, your ML segmentation algorithm may be measuring the volume of a specific anomaly in the lung very accurately, but this measurement, while important to quantify the degree of lung involvement by some disease state, may be not specific at all for predicting whether that state is due to a viral pneumonia (e.g., presence of such anomalies could mean viral pneumonia, bacterial pneumonia or non-infectious causes like hemorrhage or edema). Thus, your algorithm with high Dice scores may end up being not very useful to solve a clinical task if the goal is a specific diagnosis.

Machine Learning Methods Recap and Looking Beyond

Use cases for deep learning

- Registration
- Automatic discovery of reconstruction pipelines
- Image Retrieval
- Generative methods - super-resolution, GT augmentation

In this lesson, we have covered the following:

- A quick refresher on how convolutional neural networks operate and took a closer look at the different types of convolutions that underlie the operation of these networks.
- Ways to approach segmentation and classification problems for 3D medical imaging
- We did an exercise where we trained our own segmentation network on a medical imaging dataset

- Technical methods for evaluating performance of CNNs for 3D medical image analysis, and talked about the clinical aspect of evaluating performance.

Before we are ready to implement the full-scale AI solution in the final project, there is one final set of concepts that I want you to get familiar with - how to integrate such algorithms into real-world systems, and what these real-world systems look like. This would be the topic of our next lesson.

Further Resources

More problems

As mentioned in my closing remarks, machine learning problems in 3D medical imaging do not boil down to only classification and segmentation. The two problems we've looked at here help you understand the principles, but there is so much more you can do. Here are some pointers for some amazing things people do with deep neural networks in 3D medical imaging:

- Using deep learning to increase the resolution of low-res scans: [Chaudhari AS, Fang Z, Kogan F, et al. Super-resolution musculoskeletal MRI using deep learning. Magn Reson Med. 2018;80\(5\):2139–2154.](#)
[doi:10.1002/mrm.27178](#)
- GANs for synthetic MRI: [Frid-Adar, M., Diamant, I., Klang, E., Amitai, M., Goldberger, J., & Greenspan, H. \(2018\). GAN-based synthetic medical image augmentation for increased CNN performance in liver lesion classification. Neurocomputing, 321, 321–331.](#) doi: [10.1016/j.neucom.2018.09.013](#)
- A survey of deep learning methods for medical image registration: [Haskins, G., Kruger, U. & Yan, P. Deep learning in medical image registration: a survey. Machine Vision and Applications 31, 8 \(2020\).](#)
[https://doi.org/10.1007/s00138-020-01060-x](#)
- Overview of opportunities for deep learning on MRIs: [Lundervold, A. S., & Lundervold, A. \(2019\). An overview of deep learning in medical imaging focusing on MRI. Zeitschrift Für Medizinische Physik, 29\(2\), 102–127.](#) doi: [10.1016/j.zemedi.2018.11.002](#)

Tools and libraries

We tried to minimize the dependency on external libraries and focus on understanding some key concepts. At the same time, there are many tools that the community has developed, which will help you get moving faster with the tasks typical for medical imaging ML workflows.

A few tools/repos worthy of attention are:

- Fast.ai - python library for medical image analysis, with focus on ML: [https://dev.fast.ai/medical.imaging](#)
- MedPy - a library for medical image processing with lots of various higher-order processing methods: [https://pypi.org/project/MedPy/](#)
- Deepmedic, a library for 3D CNNs for medical image segmentation: [https://github.com/deepmedic/deepmedic](#)
- Work by the German Cancer Research Institute:
 - [https://github.com/MIC-DKFZ/trixi](#) - a boilerplate for machine learning experiment
 - [https://github.com/MIC-DKFZ/batchgenerators](#) - tooling for data augmentation
- A publication about a project dedicated to large-scale medical imaging ML model evaluation which includes a comprehensive overview of annotation tools and related problems (including inter-observer variability): [https://link.springer.com/chapter/10.1007%2F978-3-319-49644-3_4](#)

Books

Some resources readily available online for free will help you grasp the basic concepts of computer vision and overall machine learning.

- [https://d2l.ai/](#) - deep learning with a special section on computer vision by Alexander Smola et al. Alexander has a strong history of publications on machine learning algorithms and statistical analysis and is presently

serving as a director for machine learning at Amazon Web Services in Palo Alto, CA

- <http://www.mbmbook.com/> - a book on general concepts of machine learning by Christopher Bishop et al. Christopher has a distinguished career as a machine learning scientist and presently is in charge of Microsoft Research lab in Cambridge, UK, where I had the honor to work on **project InnerEye** for several years.

More notable papers

- If you're curious about segmentation space specifically, you may appreciate a foray into non-ML-based methods for segmentation. A couple of papers that can provide an introduction into that space are:
 - **Boykov, Y., & Jolly, M.-P. (2000). Interactive Organ Segmentation Using Graph Cuts. Medical Image Computing and Computer-Assisted Intervention – MICCAI 2000 Lecture Notes in Computer Science., 276–286. doi: 10.1007/978-3-540-40899-4_28**
 - **Probabilistic Graphical Models for Medical Image Segmentation**
- This GitHub repo provides an excellent overview of CNN-based seg methods for general image domain: <https://github.com/mrgloom/awesome-semantic-segmentation>

Deploying AI Algorithms in Real World Scenario

Clinical Network Architecture

When it comes to moving medical images around the hospital, the DICOM standard comes to the rescue. Alongside the definition of the format for storing images and metadata (which we have looked at in detail in previous lessons), it defines the networking protocol for moving the images around.

In the following few concepts, we will be talking about DICOM networking services, which are defined in [Part 7 and Part 8 of the standard](#).

DICOM Networking: DIMSE Services

1. There are two types of DICOM networking: DIMSE (DICOM Message Service Element) and DICOM Web. The former is designed to support data exchange in protected clinical networks that are largely isolated from the Internet. The latter is a set of RESTful APIs ([link to the Standard](#)) that are designed to communicate over the Internet. DIMSE networking does not have a notion of authentication and is prevalent inside hospitals.
2. DICOM DIMSE networking defines how DICOM *Application Entities* talk to each other on protected networks
3. DICOM Application Entities that talk to each other take on roles of **Service Class Users** and **Service Class Providers**.
4. SCPs typically respond to requests and SCUs issue them
5. Full list of DIMSE services could be found in the [Part 7 of the DICOM Standard](#), ones that you are most likely run into are:
 - C-Echo - “DICOM ping” - checks if the other party can speak DICOM
 - C-Store - request to store an instance
6. An Application Entity is defined by three parameters:
 - Port
 - IP Address
 - Application Entity Title (AET) - an alphanumeric string

Clinical Networks

Clinical networking is an industry on its own and an AI engineer will probably be exposed to a very small subset of that. So, it's important to understand the basics - what are the systems that are important to a clinical network and how do they all fit together.

New Vocabulary

PACS - Picture Archiving and Communication System. An archive for medical images. A PACS product typically also includes "diagnostic workstations" - software for radiologists that is used for viewing and reporting on medical images.

VNA - Vendor Neutral Archive. A PACS that is not tied to a particular equipment manufacturer. A newer generation of PACS. Often deployed in a cloud environment.

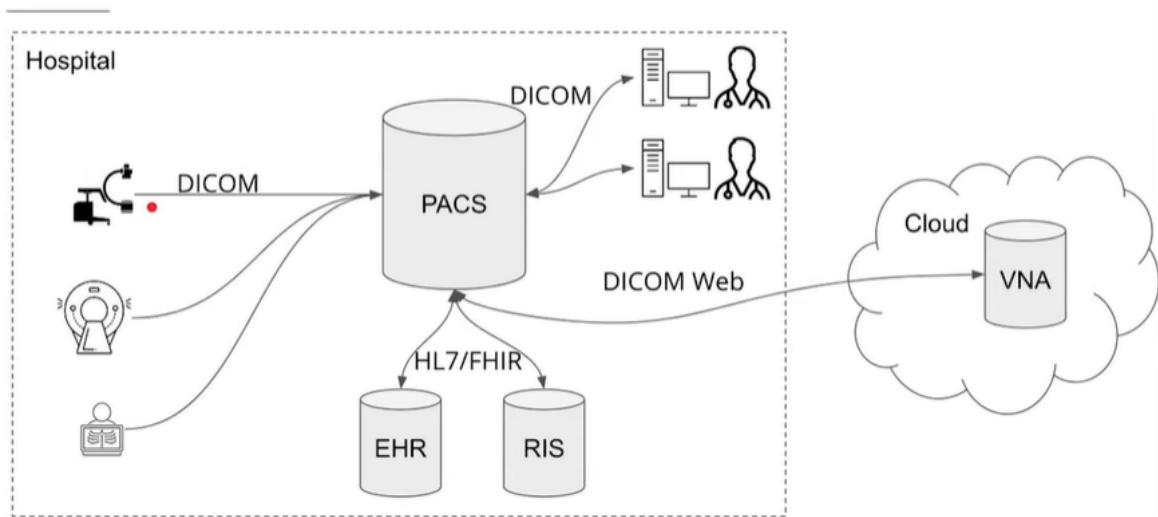
EHR - Electronic Health Record. A system that stores clinical and administrative information about the patients. If you've been to a doctor's office where they would pull your information on a computer screen and type up the information - it is an EHR system that they are interacting with. EHR system typically interfaces with all other data systems in the hospital and serves as a hub for all patient information. You may also see the acronym "EMR", which typically refers to the electronic medical records stored by the EHR systems.

RIS - Radiology Information System. Think of those as "mini-EHRs" for radiology departments. These systems hold patient data, but they are primarily used to schedule patient visits and manage certain administrative tasks like ordering and billing. RIS typically interacts with both PACS and EHR.

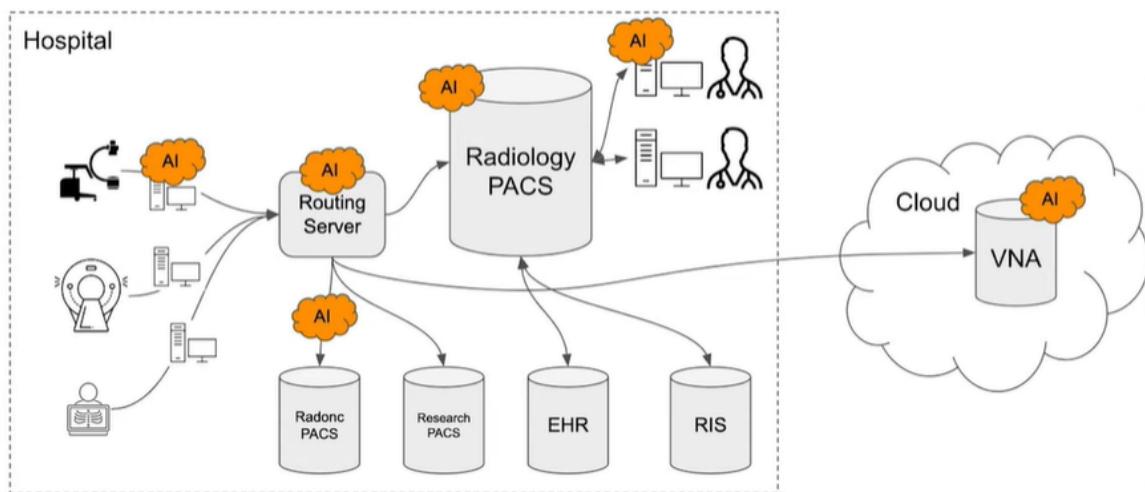
In addition to DICOM protocol there are two more (among many) that you might run into:

HL7 - Health Level 7. A protocol used to exchange patient data between systems as well as data about physician orders (lab tests, imaging exams)

FHIR - Fast Healthcare Interoperability Resources. Another protocol for healthcare data exchange. HL7 dates back to the '80s and many design decisions of this protocol start showing their age. You can think of FHIR as the new generation of HL7 built for the open web.



Let's see what a more realistic network scenario could look like, and what could be the possible integration points for AI technology:



Requirements for Integration of AI Algorithms

When you start thinking of deploying your AI algorithms, you will want to set some requirements as to data that is sent to these algorithms, and the environment they operate in. When defining those, you may want to think of the following:

- Series selection. As we've seen, modalities typically use C-STORE requests to send entire studies. How are you going to identify images/series that your algorithms will process?
- Imaging protocols. There are lots of ways images can be acquired - we've talked about MR pulse sequences, and there are just physiological parameters, like contrast media or FoV. How do you make sure that your algorithm processes images that are consistent with what it has been trained on?
- Workflow disruptions. If the algorithm introduces something new into the radiologists' workflow - how is this interaction going to happen?
- Interfaces with existing systems. If your algorithm produces an output - where does it go? What should the systems processing your algorithm's output be capable of doing?

Clinical Network Architecture Summary

In this section, we have discussed some of the basics of the DICOM networking, including services such as C-ECHO and C-STORE. We looked at how clinical networks are built and what actors are there. We considered possible integration points for AI algorithms and some of the requirements to keep in mind when integrating the AI tools.

Further Resources

- As usual, DICOM standard is a great reference for DICOM networking: http://dicom.nema.org/medical/dicom/2020a/output/chtml/part07/sect_7.5.html#sect_7.5.1
- This paper from NIH offers (a bit dated, but still very valid) overview of the networking portion of DICOM: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC61235/>
- This book has a comprehensive overview of the standard and is a must-have for any deep DICOM development: Digital Imaging and Communications in Medicine (DICOM). A Practical Introduction and Survival Guide. Authors: Pianykh, Oleg S. <http://www.springer.com/us/book/9783642108495>

Tools of the Trade - Scripting DICOM Networks

Here, we used some of the tools from the [DCMTK toolkit](#) to emulate the operation of a DICOM network. We have done the following:

- Used `dcmdump` tool to view the DICOM metadata of a DICOM file

- Used `storecsp` command to bring up an SCP listening to incoming C-STORE requests. The following is the command line that we used: `storescp 109 -v -aet TESTSCP -od . --sort-on-study-uid st`. This starts listening on port 109, with verbose logging, with AE Title "TESTSCP", putting all incoming files into the current directory and organizing studies into directories named as study instance UIDs, with prefix `st`
- Used `echoscu` command to verify that our SCP instance is alive and listening by running the following on the command line: `echoscu localhost 109 -v`
- Used `storescu` command to issue a set of C-STORE requests to our SCP and send several DICOM studies. We used the following command to accomplish this: `storescu localhost 109 -v -aec TESTSCU +r +sd .`. Here, `-aec` parameter specifies the AE title that our SCU will use to identify itself (some SCPs might only receive data from known AE titles); `+r` parameter tells our tool to process directories recursively and `+sd` parameter specifies a directory to send.

Tools of the Trade - Radiologists' Tools

We have observed the use of a clinical-grade medical image viewer system used by a clinician to analyze a radiological study. Note the following things that happened in this walkthrough:

- Inspection of several MR pulse sequences side-by-side, drawing upon the fact that tissues present differently in different types of series
- Measurement of a lesion was taken. Note how exactly the measurement was done - through taking two linear measurements of the largest diameters. This is a fairly standard way of taking measurements of lesions
- Image inspection tools were used - zoom, pan and window center/width adjustments
- The analysis ended with a "report" - a formal description of important findings on the image. Such a report would be converted into text, stored in EHR over HL7 and presented to the ordering physician when they review the results of the test

Note some challenges that were immediately seen as well:

- It is not that easy or practical to measure volumes of tumors. Such measurement was substituted by several linear measurements
- I was looking for a change of the tumor over time, but it was not really easy to see what exactly changed as images belonged to different studies and were not exactly matching up, spatially

Tools of the Trade - OHIF, the Zero-footprint Web-based Viewer

OHIF, Open Health Imaging Foundation is an organization supported by both academic and commercial collaborators, which aims to deliver an open-source framework for building modern (as of 2020) web-based medical imaging applications.

As you have probably noticed throughout this lesson, a lot of imaging IT technologies have been created back in the '70s and '80s in the pre-Internet, pre-UI era. This legacy lives on and it is not uncommon these days to find widely used clinical medical imaging applications that have the UX language of the '90s. OHIF set out to take an open-source project for Javascript-based medical image interactions, called Cornerstone and build a state-of-the-art responsive web application on it, using the latest and greatest in web development. A lot of viewers that have been commercialized by many recent AI startups are based on Cornerstone or OHIF.

If you are looking to prototype a UX solution for your AI technology, this would be a solid choice.

OHIF website: <http://ohif.org>/Cornerstone GitHub repository: <https://github.com/cornerstonejs/cornerstone>

Tools of the Trade - Viewers - 3D Slicer

Here, we took a closer look at how to work with segmentation masks in Slicer, walking you through loading a NIFTI volume and corresponding mask, displaying one on top of the other, and creating your own segmentation mask.

Segmentation formats

Let me take a bit of a sidetrack here and say a few words on formats for storing segmentations since this is how your segmentation ground truth data may come in and this is what you would be using a Slicer-like tool with. There are a few that are commonly used:

- **NIFTI**, which you are already familiar with, allows you to define what essentially is a scalar field - every point in some rectangular subset of a 3D space has a value (intensity) associated with it. Thus, a segmentation mask could be stored in NIFTI by using “one-hot” encoding, as we’ve seen in the machine learning lesson. Such a mask would assign one class label to all voxels inside the structure and another one outside. Due to convenience, NIFTI masks are very widespread in the ML community.
- **DICOM RT** is a DICOM IOD for “**Radiation Therapy Structure Set**”. We had mentioned radiation therapy in this course before - it is the treatment of cancers with radiation, and it relies on accurate mapping of the human anatomy which serves as an input into the radiation machine (typically called linac). The DICOM standard has several separate IODs that are specific just to radiation therapy space and one such IOD is the RT Structure Set, which is designed to store contours of the human anatomy, which will be used to target radiation. DICOM RT, unlike NIFTI, stores information about contours, i.e., curves within given slices, to define where structure boundaries are.
- **DICOM Segmentation** is **another DICOM IOD** for segmentations. It is specifically used for storing structure delineations for general purpose use, and this one is more similar to NIFTI in that segmentation masks are stored allocating a class to every voxel.

A couple of other notable formats which are not specific to medical imaging, but are still sometimes used are:

- **NRRD** - generic format for storing multidimensional raster data, and
- **HDF5** - format for storing hierarchical multimodal data (including multidimensional raster data, like segmentations)

Tools of the Trade - Summary

Hopefully, this section gave you a better understanding of some of the tools that you might be integrating with or using in your endeavors. In the next and final section, we will touch on the regulatory landscape that you will likely be dealing with, and for now, allow me to link to some resources.

Further Resources

- DCMTK - the swiss-army-knife for DICOM debugging: <https://dcmtk.org/dcmtk.php.en>
- Cornerstone - the open-source Javascript framework for viewing medical images: <https://github.com/cornerstonejs/cornerstone>
- OHIF - the open-source radiological image viewer: <http://ohif.org/>
- Orthanc (<https://www.orthanc-server.com/>) is a tool that we have not really discussed in the lesson, but will use in the final project. Orthanc is a free open-source implementation of a medical imaging archive that provides many features similar to a clinical PACS when it comes to storage
- Radiant (<https://www.radiantviewer.com/>) is another freeware viewer that has been used by Mazen in the clinical viewers video

Regulatory Landscape

In this final section, I will cover the basics of some of the regulatory standards that control the use of software in medicine. This video introduced the concepts of a “*medical device*”, which is central to many regulatory systems across the world. This is the concept that regulatory agencies use to draw the line between software that has to comply with regulations and the one that does not.

Here is how the US Foods and Drugs Administration (the main government regulatory body in all things healthcare) **defines a medical device**:

... An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory

which is:recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them,intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, orintended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals ...For comparison, this is how European Medical Device Regulation (MDR) defines the term:

'medical device' means any instrument, apparatus, software, implant, reagent, material or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes:diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease, diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability,investigation, replacement or modification of the anatomy or of a physiological or pathological process or state,providing information by means of in vitro examination of specimens derived from the human body, including organ, blood and tissue donations,

You can see the pattern here - something that is built with the purpose of diagnosing, preventing, or treating the disease is potentially a medical device that should conform with certain standards of safety and engineering rigor. The degree of this rigor that the regulatory bodies require depends on the risk class of the said device. Thus, for a device with lesser risk class (like a sterile bandage) often it is sufficient to just notify the respective regulatory body that device is being launched into the market while with high-risk devices (like an implantable defibrillator) there are requirements to clinical testing and engineering practices.

While "medical device" may sound like something that does not have much to do with software, the regulatory bodies actually include software in this notion as well, often operating with concepts of "software-as-a-medical-device". Sometimes a distinction is made between "medical device with embedded software" (like a CT scanner) or "software-only medical device" (like a PACS).

Key thing that determines whether something is a medical device or not, and what class it is, is its "intended use". The same device may have different risk classes (or not qualify as a medical device at all) depending on what use you have in mind for it. A key takeaway here is that the presence of an "AI algorithm" in a system that is used by clinicians does not automatically make it a medical device. You need to articulate the intended use of the system before you try to find out what the regulatory situation is for your product.

A couple of additional notes:

- Further in this section, I will be using USA regulations as an example, just to keep my examples simple. For fundamental things, regulations across all countries are quite similar.
- This section is not legal advice - it is meant to provide a general understanding of the process and the place of an AI engineer in it. If you are seeking to classify your medical device or prepare a 510(k) package, you could use this section for reference, but you should consult a trained professional to evaluate legal risks and determine the correct regulatory strategy

Regulatory Landscape: FDA Process

Regulatory process typically involves two big steps:

1. Submitting a document package - called "510(k)" for Class II medical devices or "PMA" for Class III devices. This document package needs to include engineering artifacts providing evidence that you have followed the process and your process resulted in certain deliverables. For example, a PMA package has to include things like "Design Review notes" or "Software Verification plans".
2. Establishing a Quality Management System. This system is a set of processes that are designed to ensure that you maintain a level of quality in your engineering and operations that is commensurate with the risk

that your device presents to patients and operators. For example, the QMS might define the need for a “post-launch surveillance” process that would ensure that you keep track of usage of the device in the field and have a feedback mechanism that has you reviewing potential risks that have been realized in the field and responding to them.

The former communicates your intent to launch a product to the regulatory body, and the FDA would review your documentation package to ensure that you have followed the prescribed procedures while developing it. The latter establishes certain engineering processes.

Note that the FDA or other agencies do not actually tell you *what* exactly do you have to produce. The rules are designed to ensure that you have the right process. It is up to you to decide how to apply this process to what you are doing.

An aspect of a QMS that is probably the most relevant to an AI engineer is the *validation process*. A QMS might define the need to perform product validation before you release a new version of a product, which means that you need to provide evidence that your software indeed performs. If the product has an AI component at its heart, you may need to provide input along the following lines:

- What is the intended use of the product?
- How was the training data collected?
- How did you label your training data?
- How was the performance of the algorithm measured and how was the real-world performance estimated?
- What data will the algorithm perform well in the real world and what data it might not perform well on?

As the owner of an AI algorithm, you would be best positioned to answer these questions and your input would be instrumental.

Further Resources

- FDA actually **publishes all clearances** that it issues, so you can take a look at how people described their medical devices and what the intended use was. For example, here is Arterys' submission for their Medical Imaging Cloud AI Platform: https://www.accessdata.fda.gov/cdrh_docs/pdf19/K192437.pdf
- FDA's Quality Management System requirements are available online as **21 CFR Part 820**. European and Canadian regulators require compliance with **ISO 13485 standard** (which is not publicly available)

Regulatory Landscape: HIPAA, Anonymization

Privacy laws vary from one country to another, but most of them are similar to HIPAA (USA) and GDPR (Europe).

If you want to learn more about it, there is more detail in the "EHR Data" course in this nanodegree. Consider this a bit of a recap with a focus on applying de-identification methods to DICOM data.

There are a lot of privacy laws, but something that has the greatest impact on an AI engineer are the requirements towards de-identifying the data that is coming in. De-identification is important because HIPAA Privacy rule (and GDPR) institute quite strict controls over “Protected Health Information” while at the same time **HIPAA has this to say about De-identified Health Information**:

De-Identified Health Information. There are no restrictions on the use or disclosure of de-identified health information. De-identified health information neither identifies nor provides a reasonable basis to identify an individual. There are two ways to de-identify information; either: (1) a formal determination by a qualified statistician; or (2) the removal of specified identifiers of the individual and of the individual's relatives, household members, and employers is required, and is adequate only if the covered entity has no actual knowledge that the remaining information could be used to identify the individual.

Essentially, a lot of restrictions and controls are removed for data that is considered de-identified. If you read this definition carefully, you will see that HIPAA suggests two methods for de-identification. Method #2 is actually somewhat straightforward as HIPAA lists things that are considered private in [45 CFR 165.514](#), and we will practice with some of these in our final exercise.

Method #1 is worth a note here, though. You may wonder what statisticians have to do with privacy, but it might make sense if you remember that statisticians are what machine learning engineers used to be called before ML became widespread :) On a serious note, there is more to de-identifying data than removing unique identifiers and other things that can identify a person. Thus, age alone is hardly good enough to identify a person. But what if the age of an individual is high, you know the country where they live, and you have access to additional information such as a newspaper article that interviews the longest-living person from that country who happens to have the same age as that in your "de-identified" dataset? Surely, that would be sufficient to identify that individual. This is where statistics becomes important and a prudent approach would be to prove, with statistical guarantees, the chances of re-identifying an individual based on patterns in the dataset. This is getting very close to the concept of [differential privacy](#) and is outside the scope of this course. However, I will post some links in the final section.

When it comes to DICOM medical images, anonymization typically boils down to cleaning out the DICOM metadata tags. However, depending on the dataset, you might also want to take a closer look at the pixels. Thus, you may see text that has been burnt directly into the images (not common in CT and MR, but quite common in XRays) or facial features (as we've seen in some of the Slicer visualizations throughout the course). As always, a good AI engineer will inspect the data and provide input if the data has potentially identifying characteristics.

Lesson Summary

And this brings our lesson to a close. I hope you learned something valuable and I hope that your newly acquired skills will help you make a greater impact on AI technology for 3D medical imaging!

In this lesson we have covered the following:

- Basics of DICOM networking
- How hospital networks operate and where would AI algorithms fit in
- Requirements for integration of AI algorithms
- Tools for simulating and debugging clinical environments:
 - scripting via DCMTK
 - OHIF - the zero-footprint medical image viewer
 - A deeper-dive into Slicer for annotation
- Medical imaging viewer as radiologist's tool
- Medical Device Regulations with the US FDA as an example
- Data privacy, HIPAA, and anonymization.

Let me leave you with some useful resources here before we move on to the final project.

Further Resources

- FDA's guidance for software validation: <https://www.fda.gov/media/73141/download>
- A very profound analysis done by the University of Cambridge of various regulatory frameworks, as it pertains to algorithms as medical devices: <https://www.phgfoundation.org/documents/algorithms-as-medical-devices.pdf>
- American College of Radiology has been hosting very good [webinars on all things medical imaging and AI](#).
- An [article by American College of Radiology](#) with some greatly structured thoughts on the roadmap for AI development in radiology

- A question that presents somewhat of a challenge to medical device regulators is what to do about machine learning systems that are continuously learning. As you have seen, the traditional regulatory frameworks assume a strict step-by-step process whereby evidence of device performance is collected and submitted once, and if updates are needed, it is submitted again, with 90 days or so review cycles. That doesn't quite work well for continuously learning systems. FDA has recently published some thoughts on what a framework for such systems could look like.