Computing Methods for Experimental Physics and Data Analysis

Data Analysis in Medical Physics

Lecture 1: Intro to Medical Image Processing and Analysis

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Objectives of the Medical Physics module

- to provide students with an overview of the computational and mathematical methods used in **medical image processing**
- to complement the programming skills you acquired in the first two modules of this course with the knowledge of the **Matlab** programming language

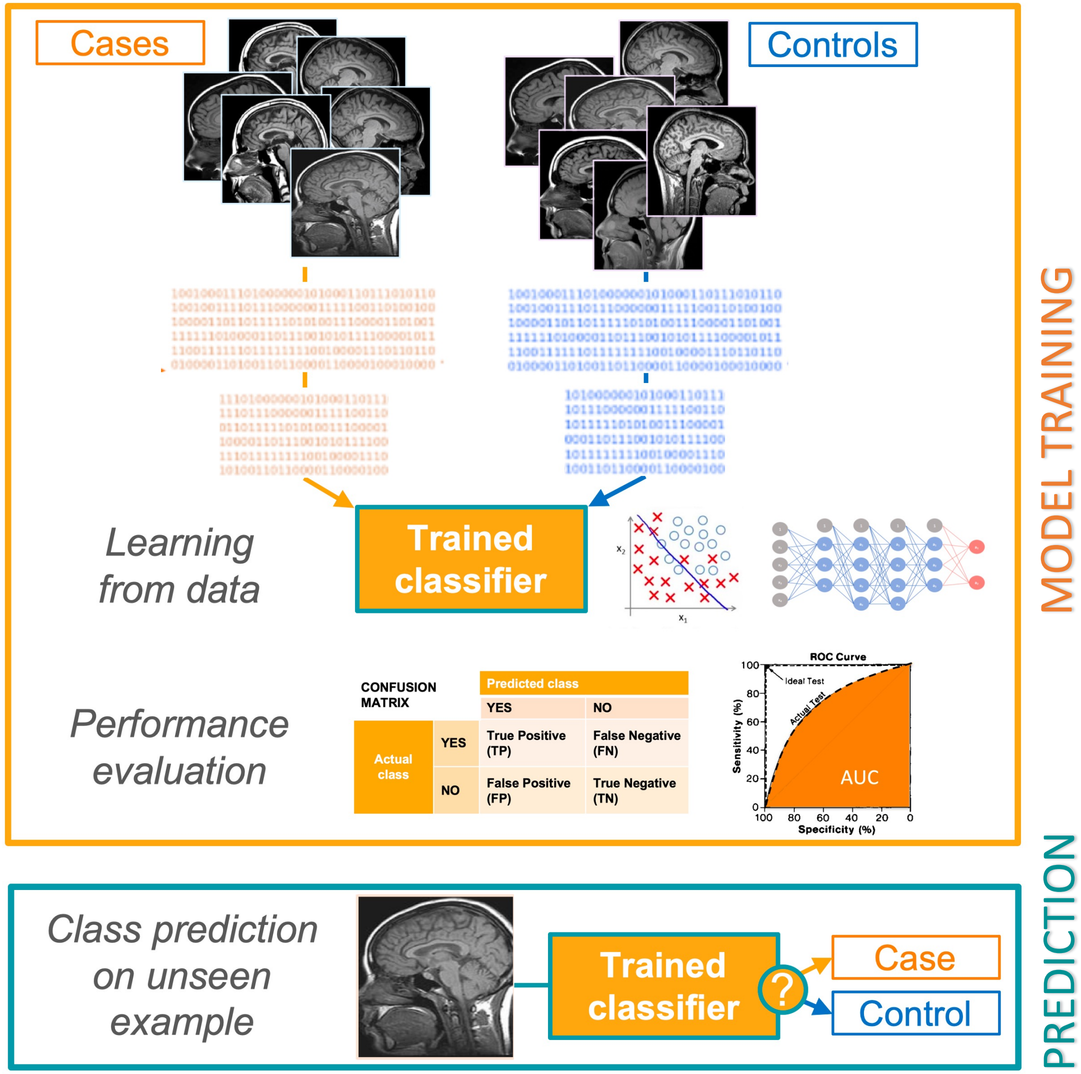
In demos and hands-on lectures:

- practical examples of several methods currently used to enhance, extract and exploit relevant information encoded in medical images
- a variety of data sets (2D, 3D, 4D), acquired with the main medical imaging modalities (e.g. RX, CT, MRI) are made available to practice

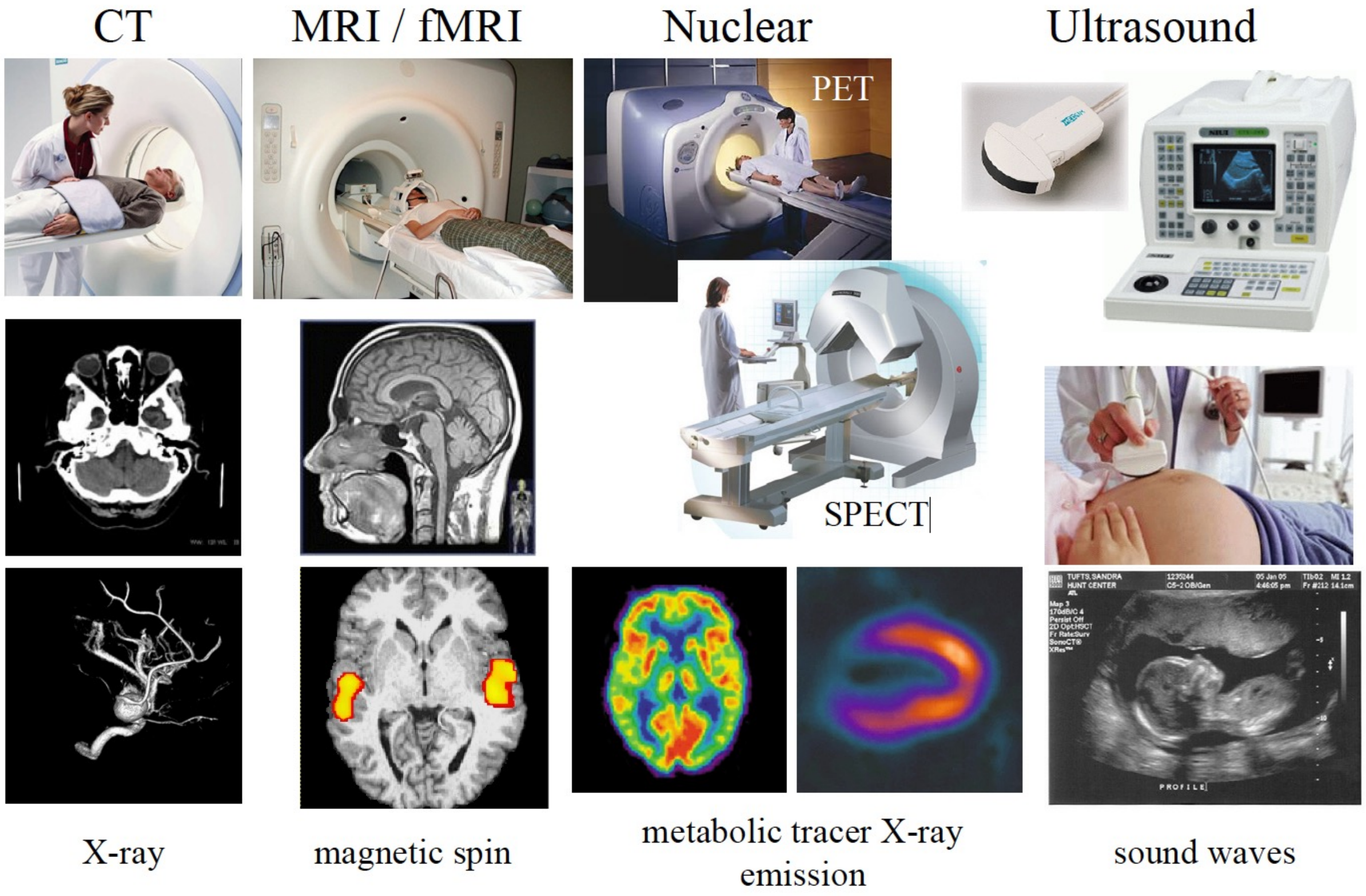
Course overview

Medical data processing, feature extraction, feature/image classification:

- Handling standard-format medical data (DICOM), data anonymization, visualization
- Deriving features form images, image segmentation
- Data quality control pipelines, outlier removal, dimensionality reduction
- Data analysis and classification
- Performance evaluation: evaluation metrics, cross-validation, permutation test
- Machine-learning and deep-learning tools for segmentation and classification
- Data augmentation, transfer learning, retrieving localization information



Medical Imaging: focus on diagnostic modalities



Medical images are more than pictures!!!

http://www.humanconnectomeproject.org/

Medical vs. non-medical images

- Medical images reflect various physical properties of the body
  - Images are formed by interaction of radiation/ultrasounds with tissues/organs

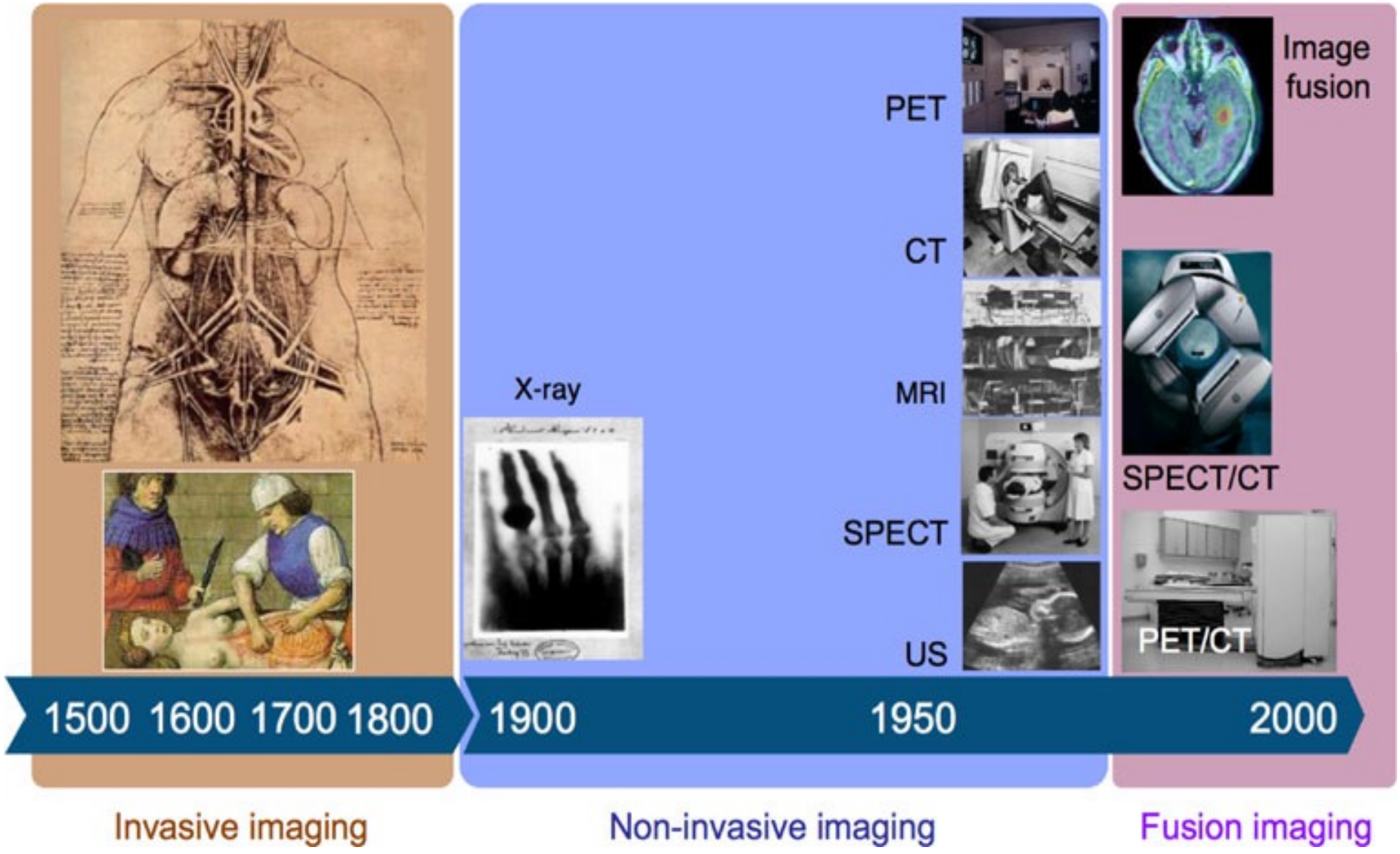
- Medical images are not limited to 2D, as natural pictures generally are

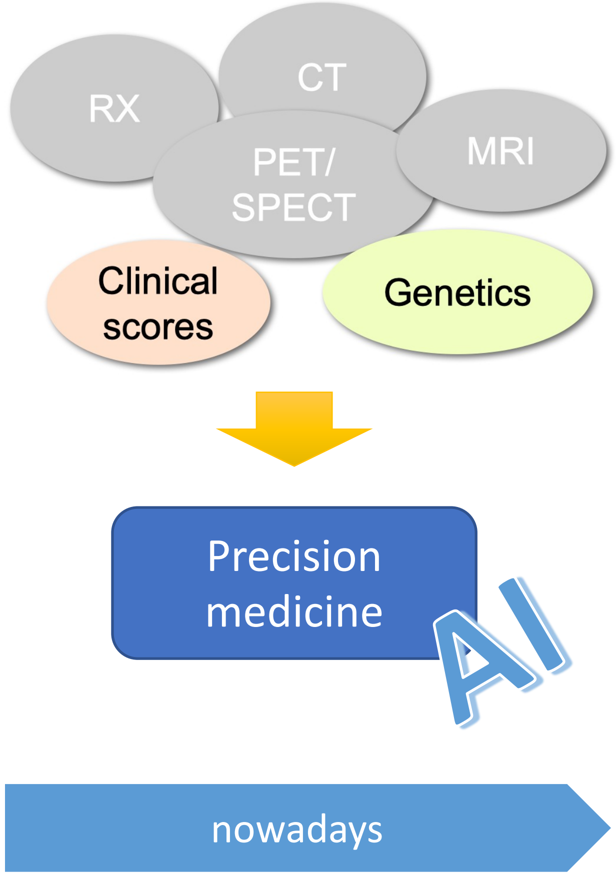
- Medical images may allow to study:
  - the structure of tissues/organs
  - the function tissues/organs

The main diagnostic imaging modalities

TECHNIQUE	MEASURED PHYSICAL QUANTITY	INDIRECT CLINICAL INFORMATION
X-Ray (Radiography, Computed tomography)	Intensity of transmitted X rays	Mapping tissue radiodensity. Mapping body cavity (e.g. vessels) through contrast agents
Nuclear Medicine (SPECT, PET)	Intensity of emitted γ rays	Distribution functional radiotracers
Ultrasound (US, Doppler)	Intensity / frequency of reflected ultrasound	Mapping tissue with different acoustic properties. Mapping blood velocity
Nuclear Magnetic Resonance (MRI, fMRI, …)	Intensity of stimulated emission of radiofrequency waves	Mapping tissues with different relaxation properties, different water content and different water aggregation status
…	…	…

Medical Imaging: historical perspective





from T. Beyer et al., Insights Imaging (2011)

The role of computers in Medical Imaging

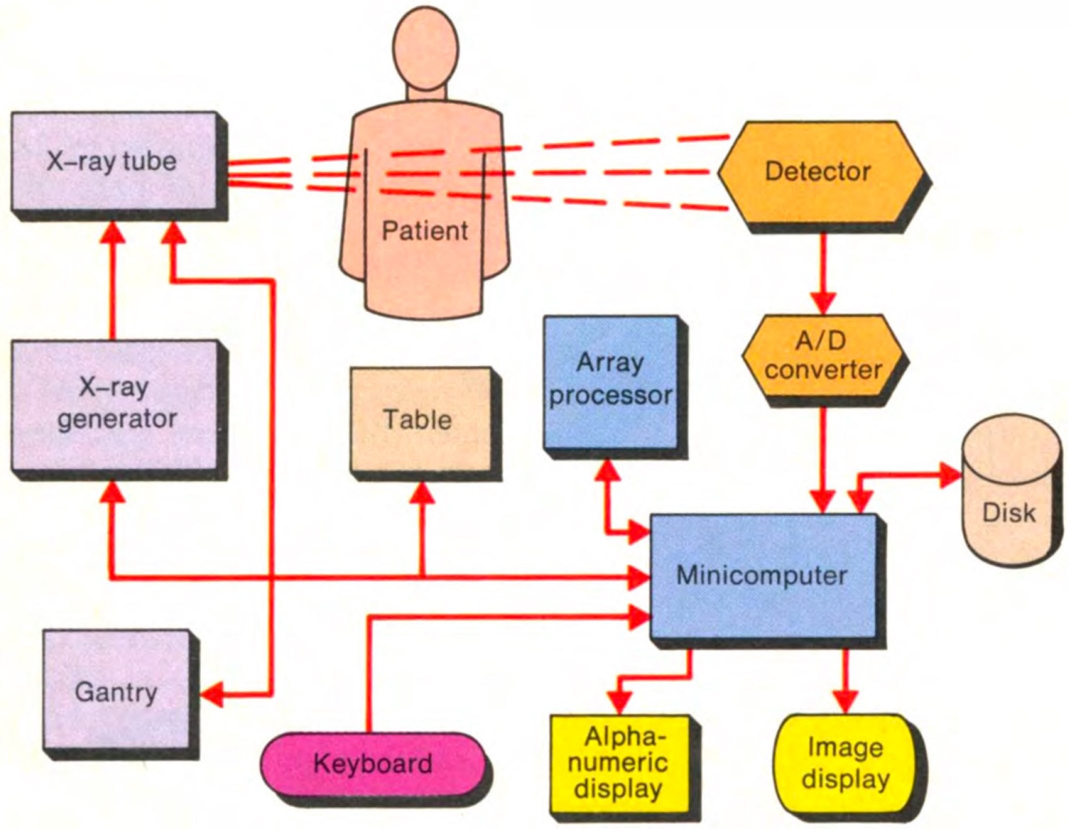
The computer revolution in medical imaging systems

Louis J. Heitlinger

Computers have become an essential part of medical imaging, where their many uses include control of hardware and image enhancement and generation

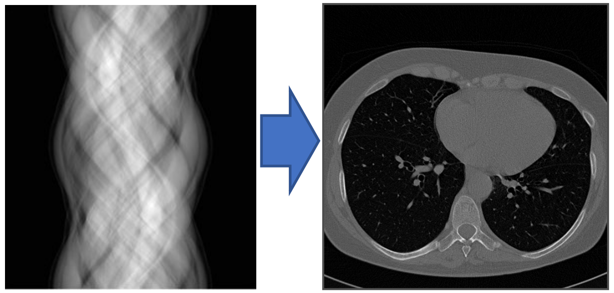
In a computerized tomography system, the X-ray data are acquired by a detector and converted to digital data. These data are then processed by the array processor and the minicomputer to generate the image, which is then displayed on a CRT.

IEEE POTENTIALS • DECEMBER 1984

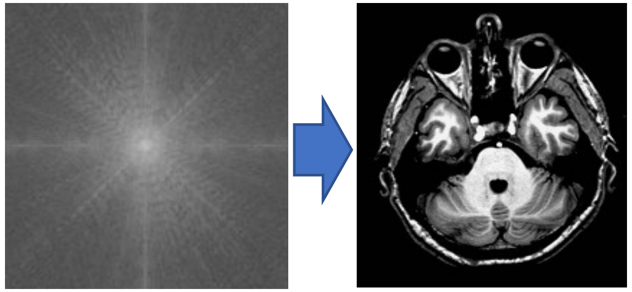


The role of computers in Medical Imaging

- To reconstruct acquired signals to form diagnostic images

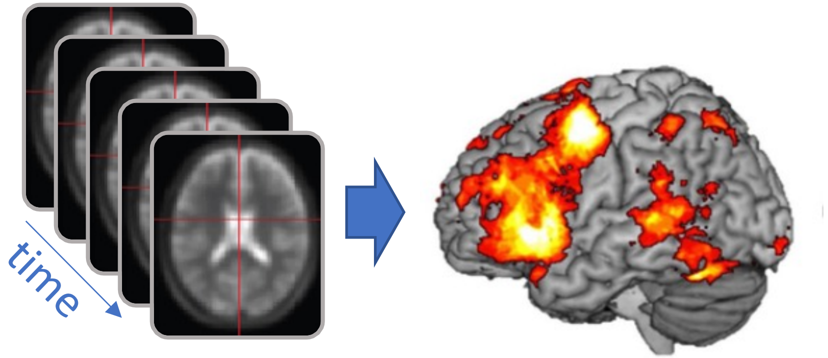


CT image reconstruction from sinogram

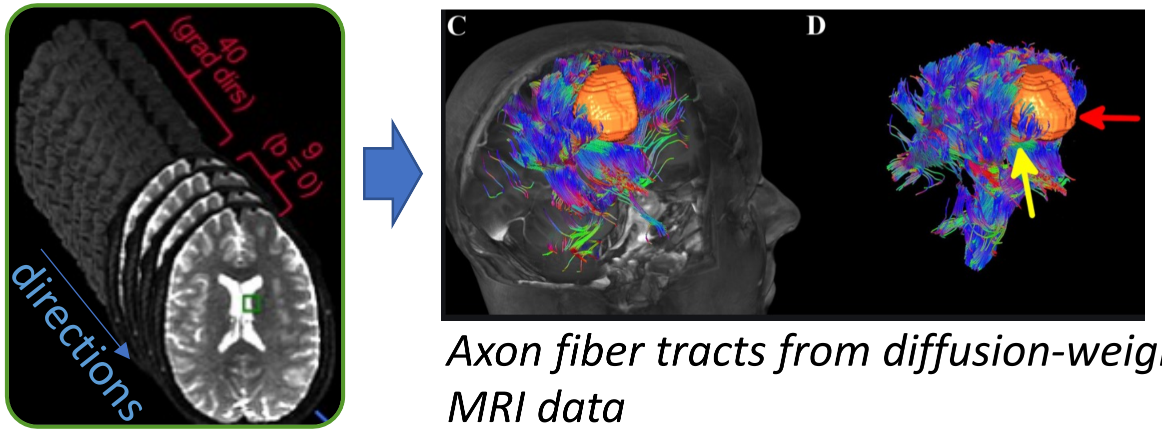


MRI image reconstruction from k-space data

- To allow the visualization of the acquired information



Activated brain areas while executing a task

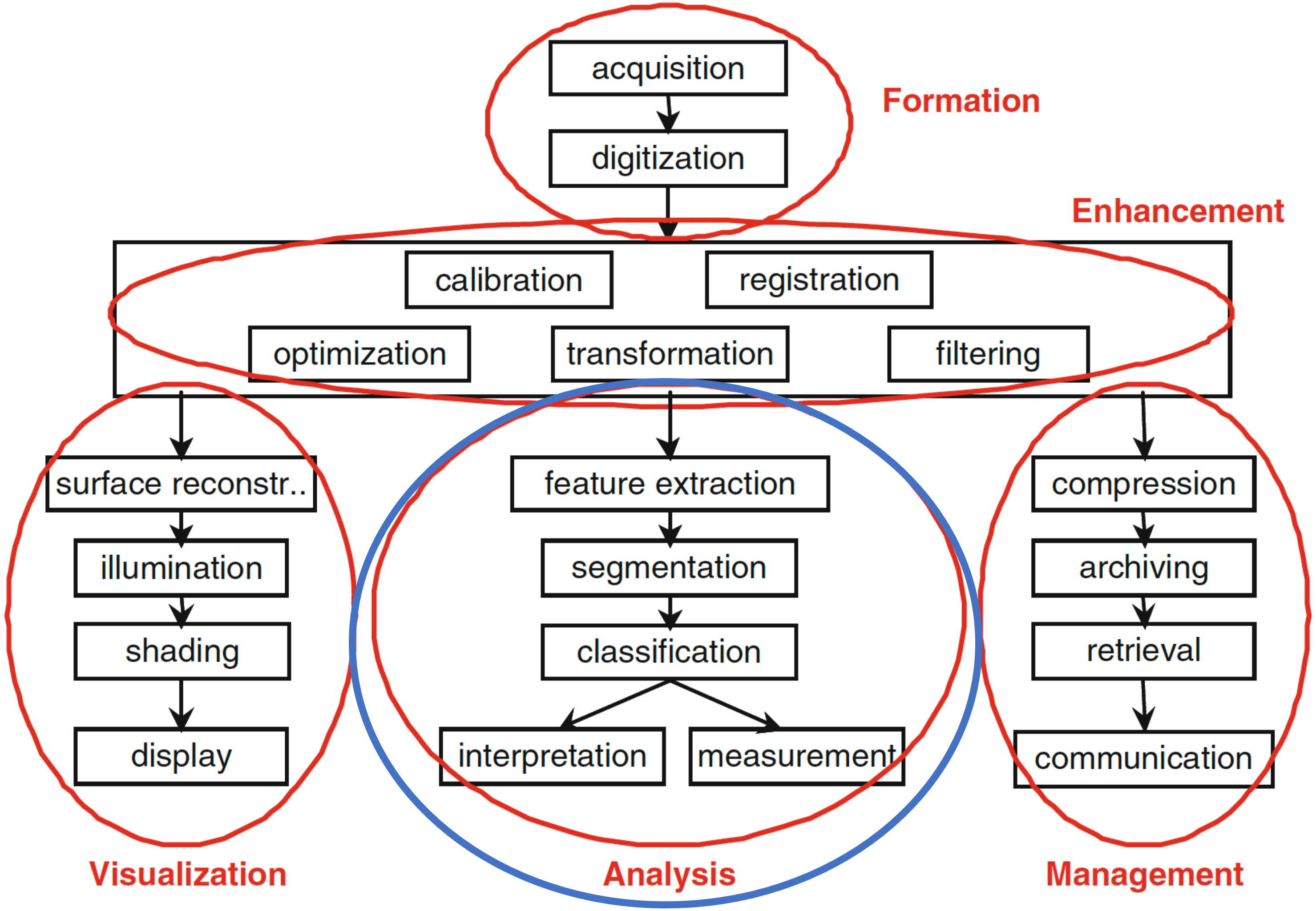


Axon fiber tracts from diffusion-weighted MRI data

The role of computers in Medical Imaging

- Algorithms for information processing enter at many levels in the image formation pipeline

- We will focus in this course on the high-level Analysis procedures, and we will not cover the countless other possibilities



Biomedical image processing and analysis

The main objectives are:

- To detect abnormalities in diagnostic images (lesions, etc.)
- To follow up pathological conditions (e.g. measuring the growth rate of lesions)
- To assess treatment efficacy

The aim is to assist clinicians in their tasks,
not to replace them:

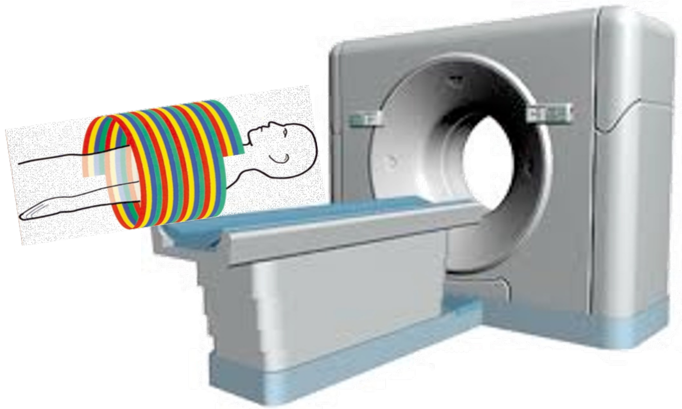
→ *Computer Aided Detection/ Diagnosis (CAD) systems/ Decision Support Systems (DSS)*

Historical development of CAD systems:

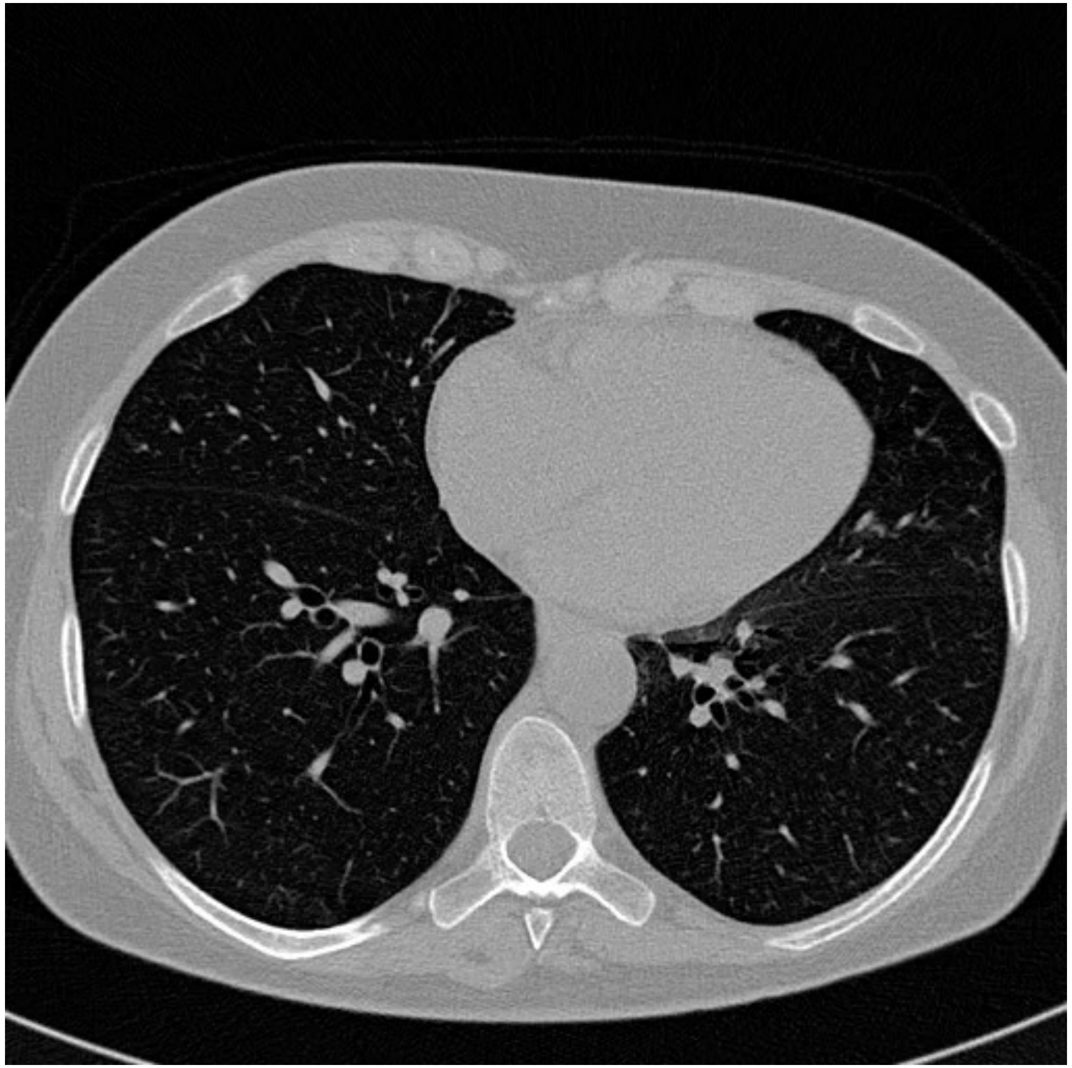
1) ’90 - Old-fashion systems (Rule-based decision systems)
2) 2000-today - Hand-crafted feature and Machine Learning classification
3) since 2016 - Deep Learning-based data/image classification

Data dimensionality: 3D images

- Computed Tomography

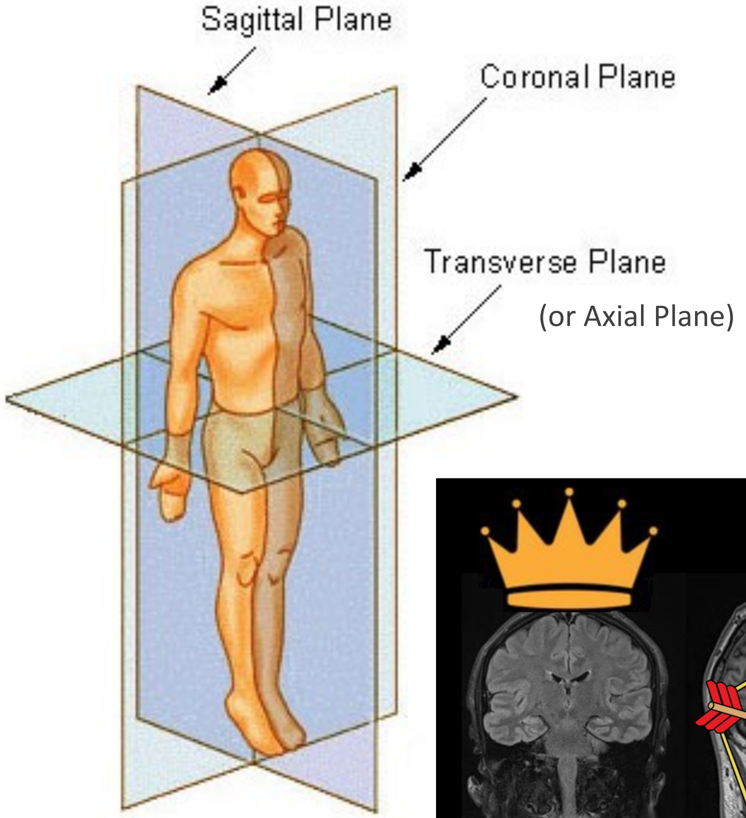


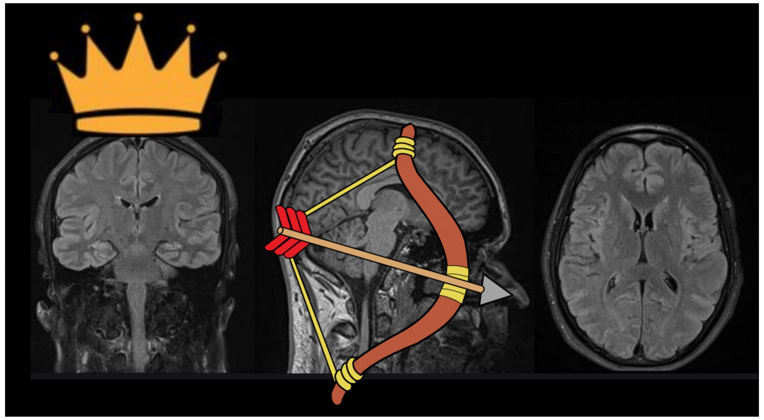
A thin-slice lung CT exam generates ~300 slices per subject

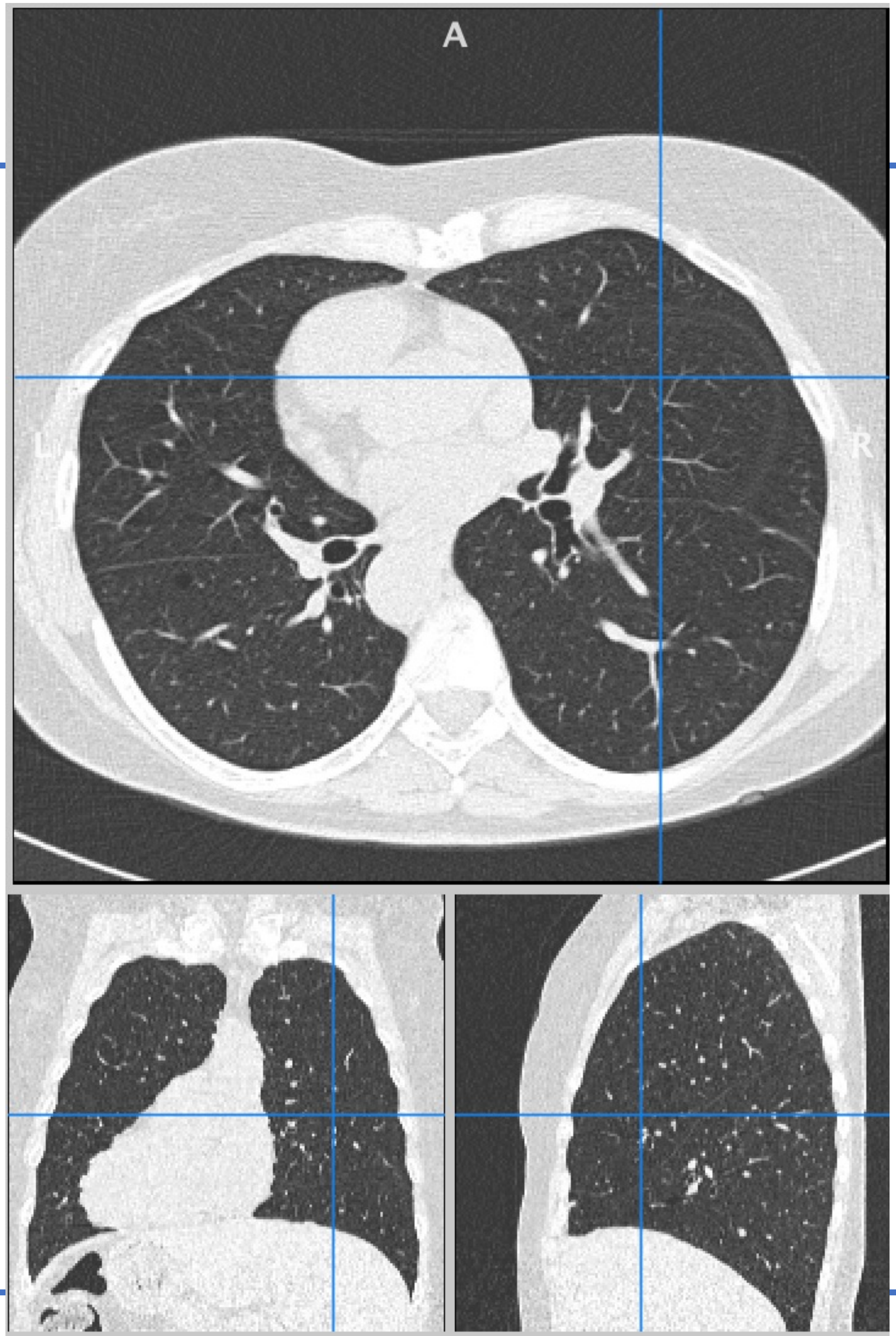


Volume display planes

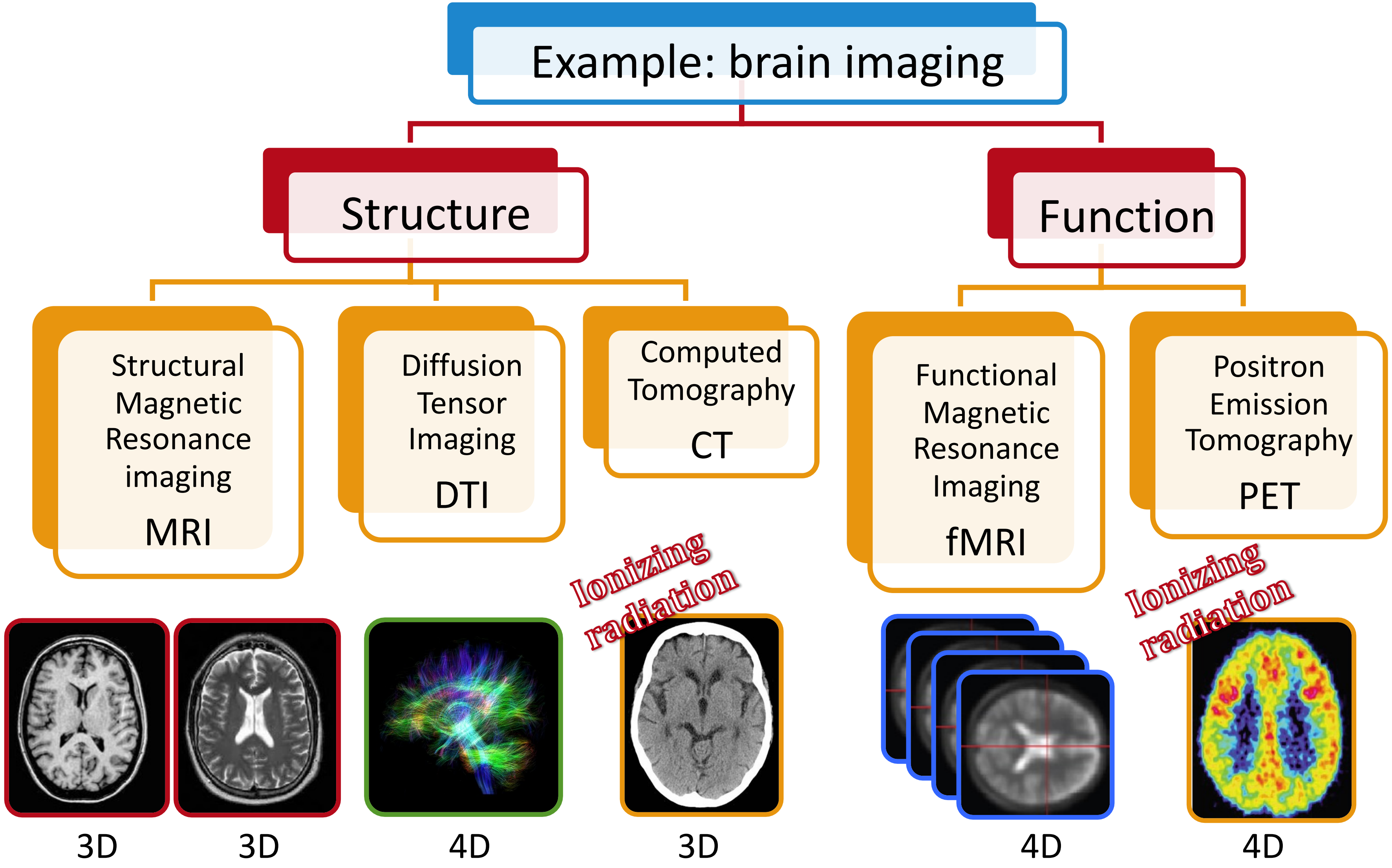
- Medical images are usually displayed by anatomical planes



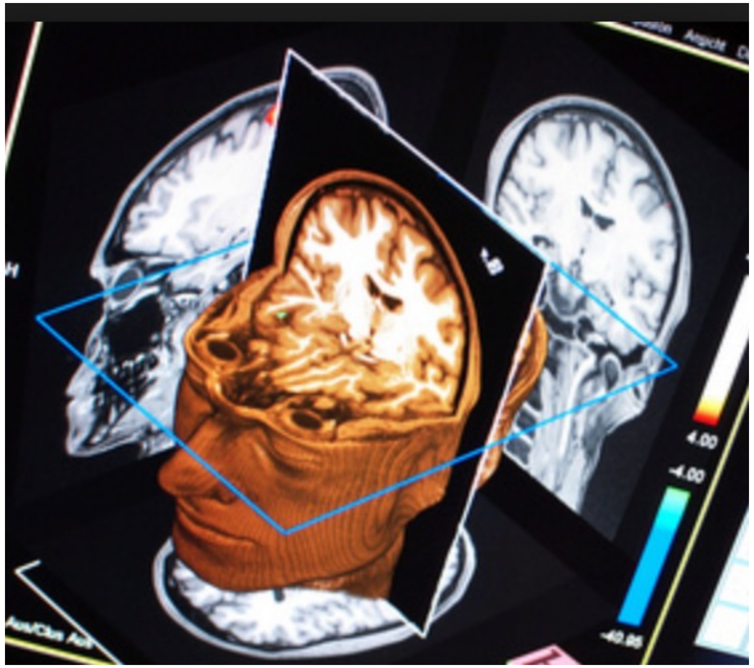


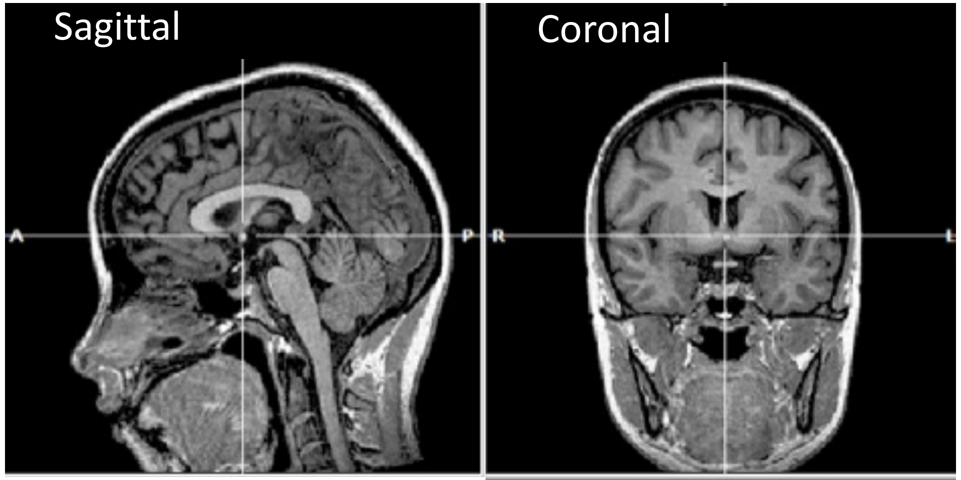


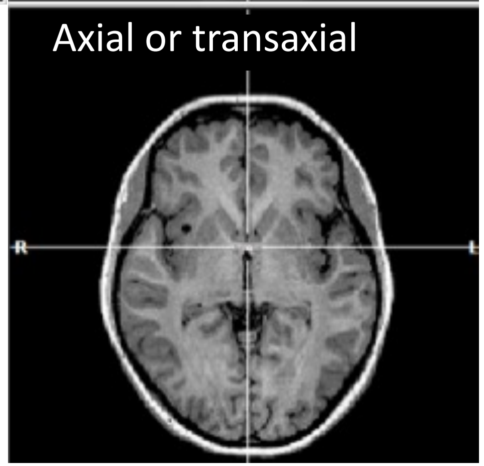
Data dimensionality: 3D and more…

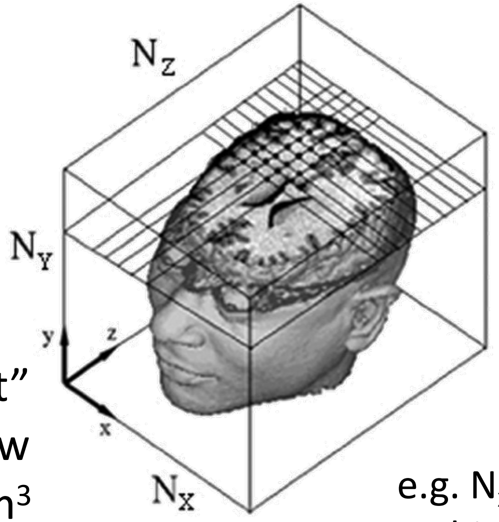


Structural MRI T_1-weighted images









3D array of data: 

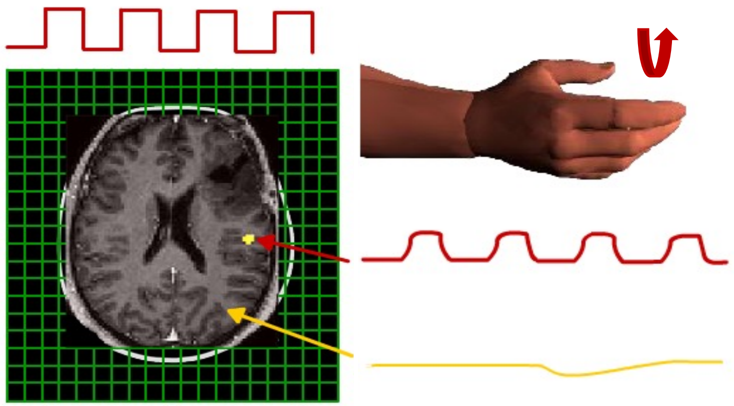
- The voxel is the "volume element"
- Typical "High resolution" MRI T_1-w images: $v_x \times v_y \times v_z \approx 1 \times 1 \times 1$ mm^3

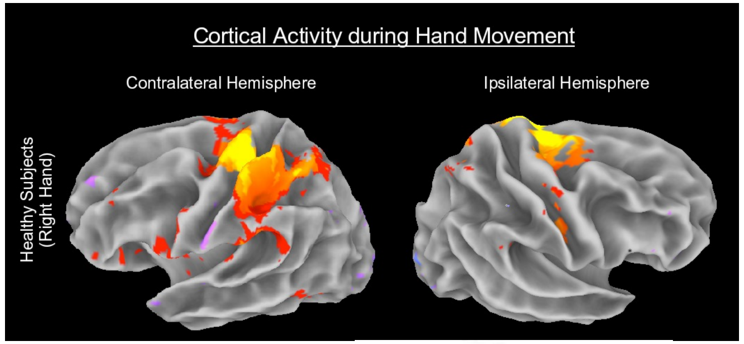
e.g. N_x x N_y x N_z = 256 x 256 x 150
16 bit ~**20 MB**

Functional MRI (fMRI)

- BOLD Response: blood-oxygen-level-dependent (BOLD) contrast
- Typically, 1 volume per second (3x3x3mm^3) is acquired for 4-5 min
- Stimuli (visual, auditory, tactile, …) are administered to the subject during the scan

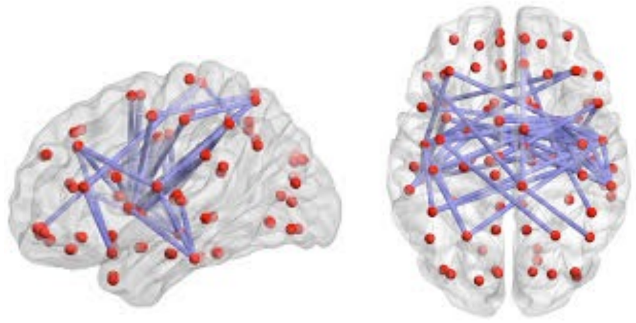
- Analysis of data time series to look for up-and-down signals that match the stimulus time series





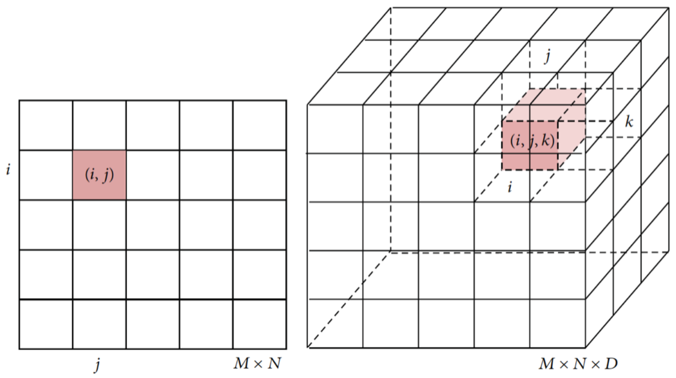
Functional connectivity

- Resting state rs-fMRI: study of temporal correlations between spatially remote neurophysiological events



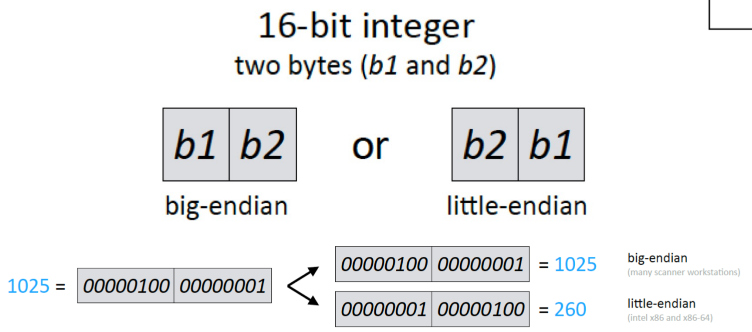
Data dimensionality: 2D/3D/4D/..nD images

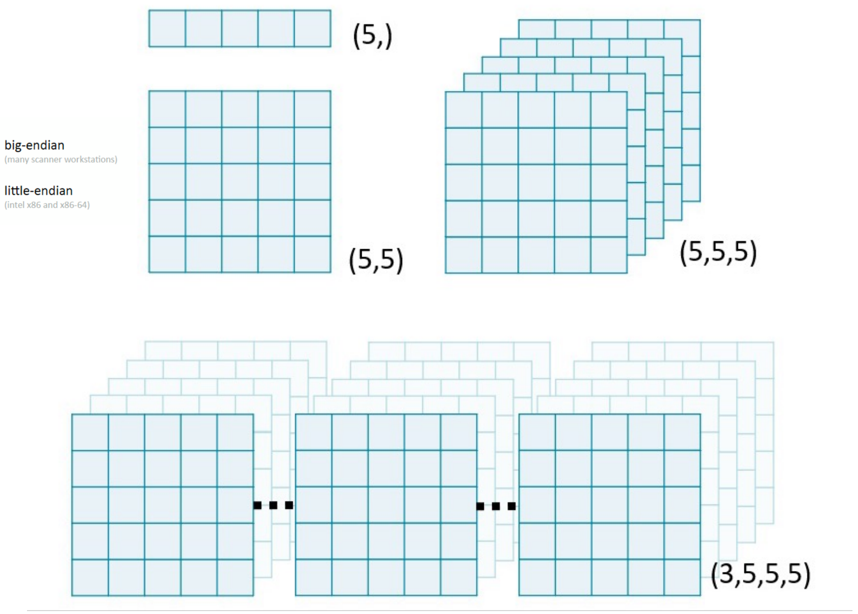
- Image element:
  - pixel: picture element
  - voxel: volume element



- Images are n-D matrices of numbers (integer, real, complex)

- Typical data types:
  - signed/unsigned byte (8-bit)
  - signed/unsigned short (16-bit)
  - signed/unsigned int (32-bit)
  - float (32-bit) and double (64-bit)



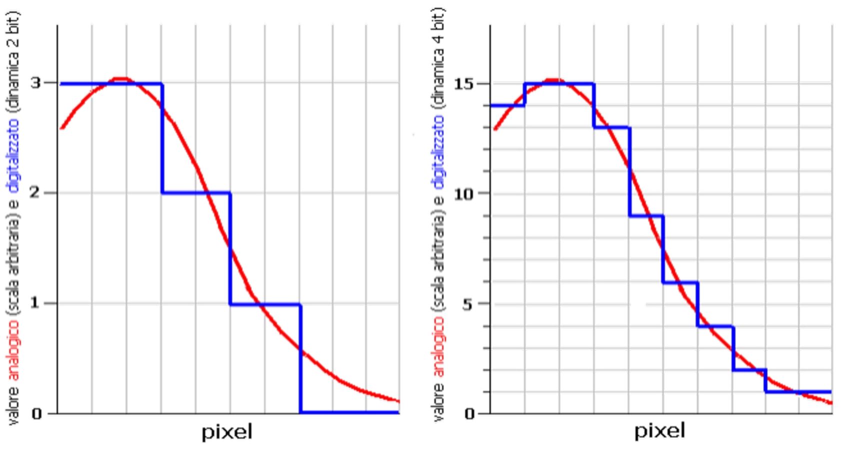


- Metadata is required for correct interpretation, e.g.:
  - pixel/voxel dimension (e.g. voxel size (mm): v_x , v_y , v_z)
  - machine settings
  - parameters used to produce the image
  - patient's positioning
  - patient's information (age, sex,…)
  - Intensity scaling information (only integers are often stored)

Errors introduced by the analog to digital conversion

- Most medical imaging devices need to convert analog signals into digital ones
- The bit dynamic range should be appropriate to catch the signal variability with minimum errors

2-bit vs. 4-bit dynamics

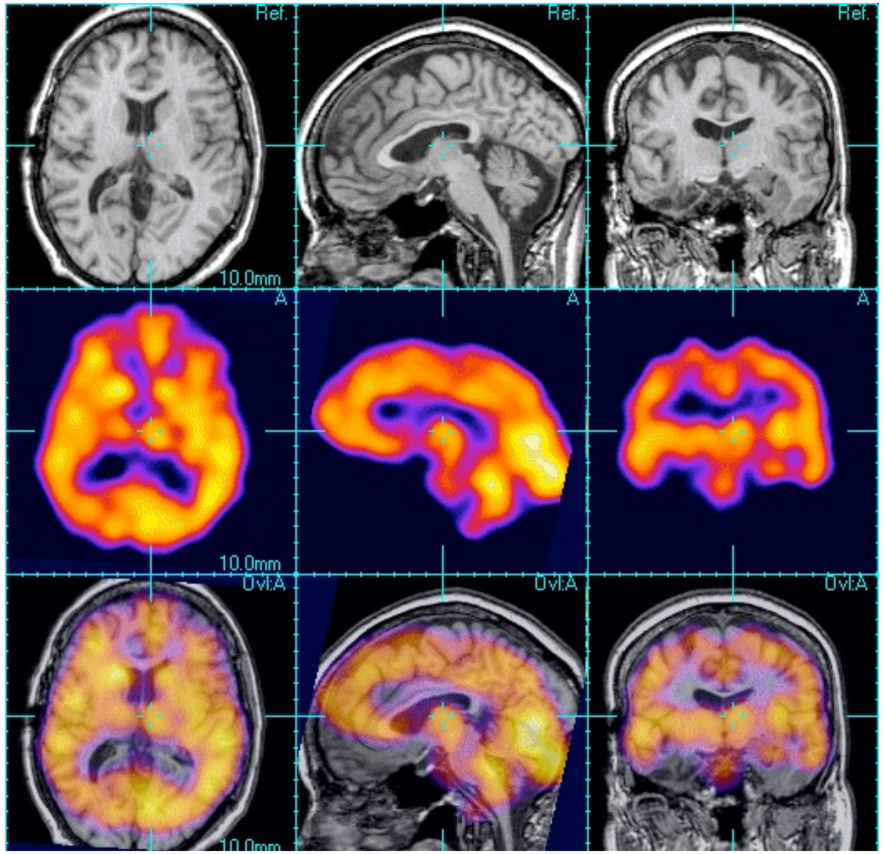


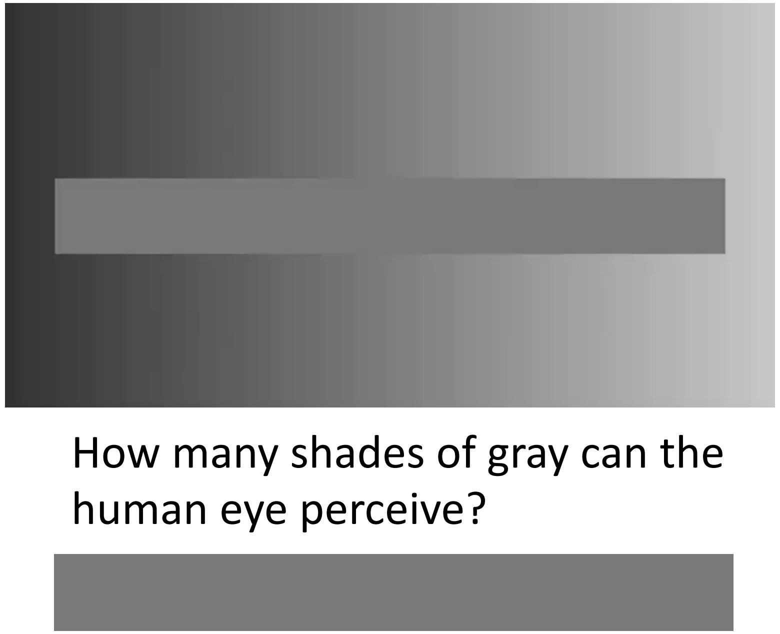
N. bit	Conversion dynamics	Decimal (binary) range of values	Maximum conversion error
2	$2^2 = 4$	from 0 (00) to 3 (11)	1/4*1/2=12.5%
4	$2^4 = 16$	from 0 (0000) to 15 (1111)	1/16*1/2= 3.1%
8	$2^8 = 256$	from 0 (00000000) to 255 (11111111)	1/256*1/2= 0.2%
12	$2^{12} = 4096$	from 0 (000000000000) to 4095 (111111111111)	1/4096*1/2= 0.012%
16	$2^{16} = 65536$	from 0 (0000000000000000) to 65535 (1111111111111111)	1/65536*1/2= $7\ 10^{-4}$ %

Image representation with gray and color scales

- Usually, anatomical images are represented in gray scales, functional images and parametric maps in color scales

  - Structural image
  - Functional image
  - Image overlay





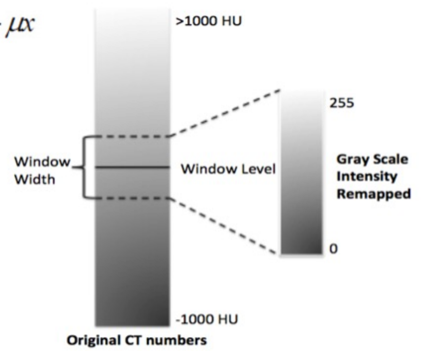
How many shades of gray can the human eye perceive?

Image windowing

- In Computed Tomography (CT) voxel intensities are expressed in Hounsfield Units (HU)
- The HU scale is a linear transformation of the original linear attenuation coefficient measurement into one in which the radiodensity of distilled water at standard pressure and temperature is defined as zero HU
- HU values of human tissues range in [-1000, 1000]
- **Windowing**:
  - To visualize CT images a window level (WL) and a window width (WW) should be chosen
  - A linear transform is applied that maps the lower bound to zero and the upper bound to the maximum gray level (i.e., 255 for 8 bit images) for visualization

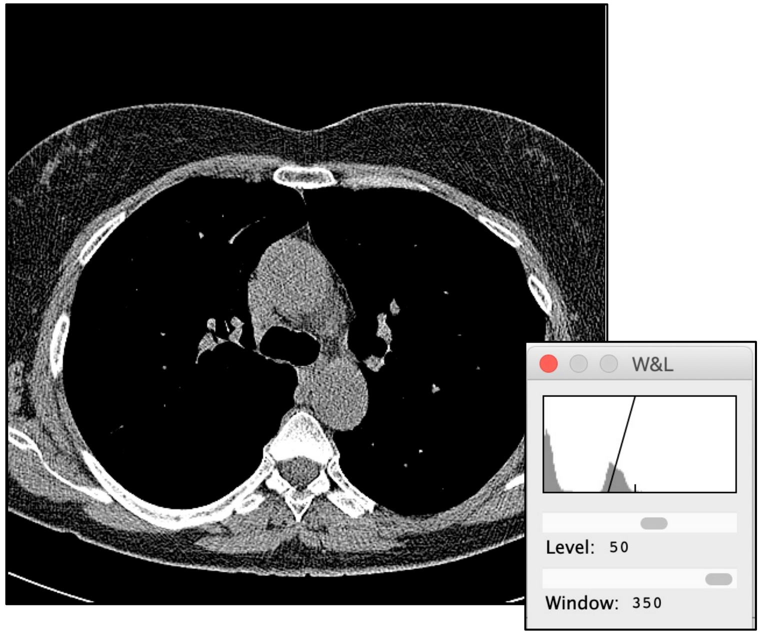
$$HU = 1000 \times \frac{\mu - \mu_{\text{water}}}{\mu_{\text{water}} - \mu_{\text{air}}}$$

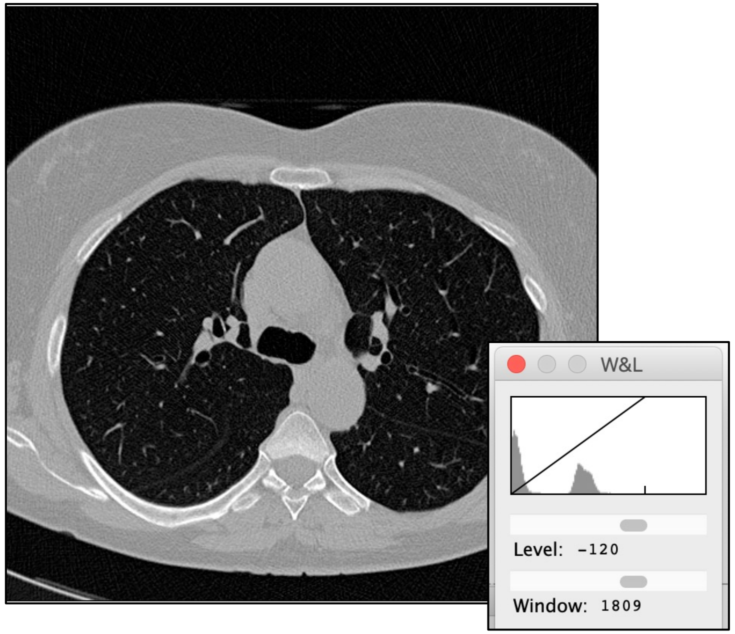
$$I = I_0 e^{-\mu x}$$

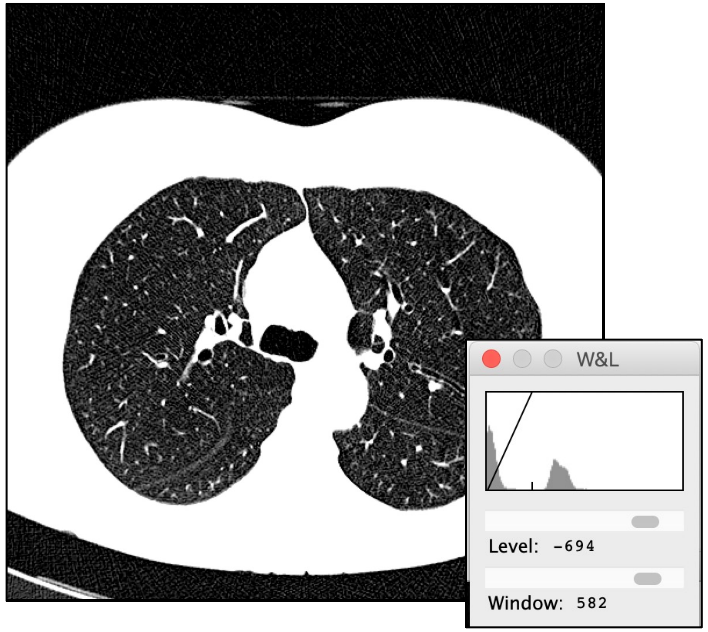


Hounsfield Units for human body

Bone	*1000*
Liver	*40 to 60*
White Matter	*46*
Grey Matter	*43*
Blood	*40*
Muscle	*10 to 40*
Kidney	*30*
Cerebrospinal Fluid	*15*
Water	*0*
Fat	*-50 to -100*
Air	*-1000*

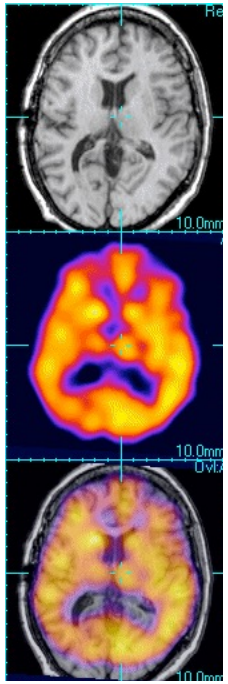


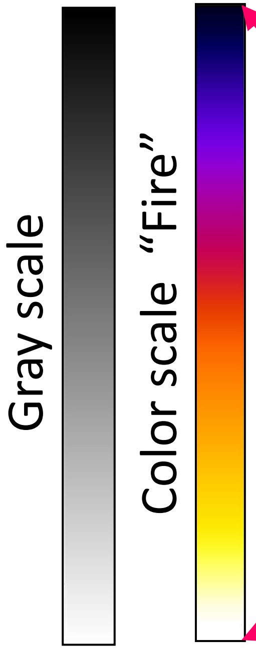




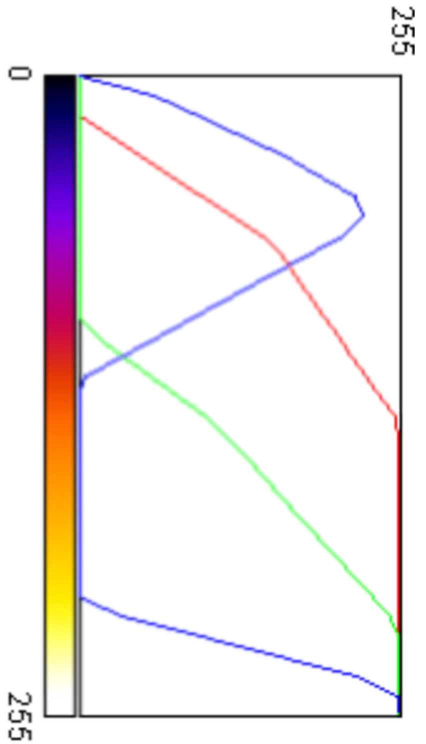
Look-up tables (LUTs)

- Look-up tables (LUTs) are used for pseudo coloring.
  - **24-bit color:** computer graphic boards typically offer 256^3 (~ $16\ 10^6$) colors.
  - **32-bit color:** supports $16\ 10^6$ colors plus an alpha channel to create gradients, shadows, and transparencies → supports $4\ 10^9$ color combinations.
  - Pseudo coloring allows presentation of data without reducing the information as it would result from windowing





LUT RGB			
value	red	green	blue
0	0	0	0
1	0	0	7
2	0	0	15
…			
128	240	79	0
…			
255	255	255	255



Medical image file formats

- The file format describes how the image data are organized in the file and how pixel data should be interpreted by a software for correct reading and visualization

- Numerical values of the pixels depend on image modality, acquisition protocol, reconstruction and applied post processing algorithms:
    - ➢ A medical image which is separated from the context information is meaningless

- Medical image file formats belong to two categories:
    - Those intended to standardize images generated by different diagnostic modalities, e.g. the DICOM standard
    - Those aiming to facilitate the post-processing analysis (e.g. NIfTI for neuroimaging)

DICOM file format

- In response to the increased use of digital images in radiology the American College of Radiology (ACR) and the National Electrical Manufacturers Association (NEMA) formed a joint committee in **1983** to create a **standard format for storing and transmitting medical images.**
- The committee published the original ACR-NEMA standard in **1985**.
- This standard has subsequently been revised and in **1993** it was renamed **DICOM**.

- **Digital Imaging and COmmunication in Medicine (DICOM):**
  - It is both a file format and communication protocol
  - It is the standard format used in digital imaging medical devices
  - The header and the image are contained in the same file
  - The header contains many information on the imaging device, the acquisition parameters, the patient and the physician
- DICOM supports most imaging modalities

DICOM file format

- DICOM is most commonly used for storing and transmitting medical images enabling the integration of medical imaging devices such as scanners, servers, workstations, printers, network hardware, and picture archiving and communication systems (PACS) from multiple manufacturers.

- Pixel data cannot be separated from the description of the image formation procedure:
  - Images should be self-descriptive

- The DICOM format (“anachronistically”) stores volume as a sequence of 2D slices.
  - (A 3D DICOM format exists, but it is not widespread).
  - It is not that bad to have images stored slice by slice, as some acquisition parameters may change slice-wise during the acquisition.

- The DICOM format only stores integer numbers as pixel values, thus a *slope* and an *intercept* to linearly transform data in the allowed range are specified

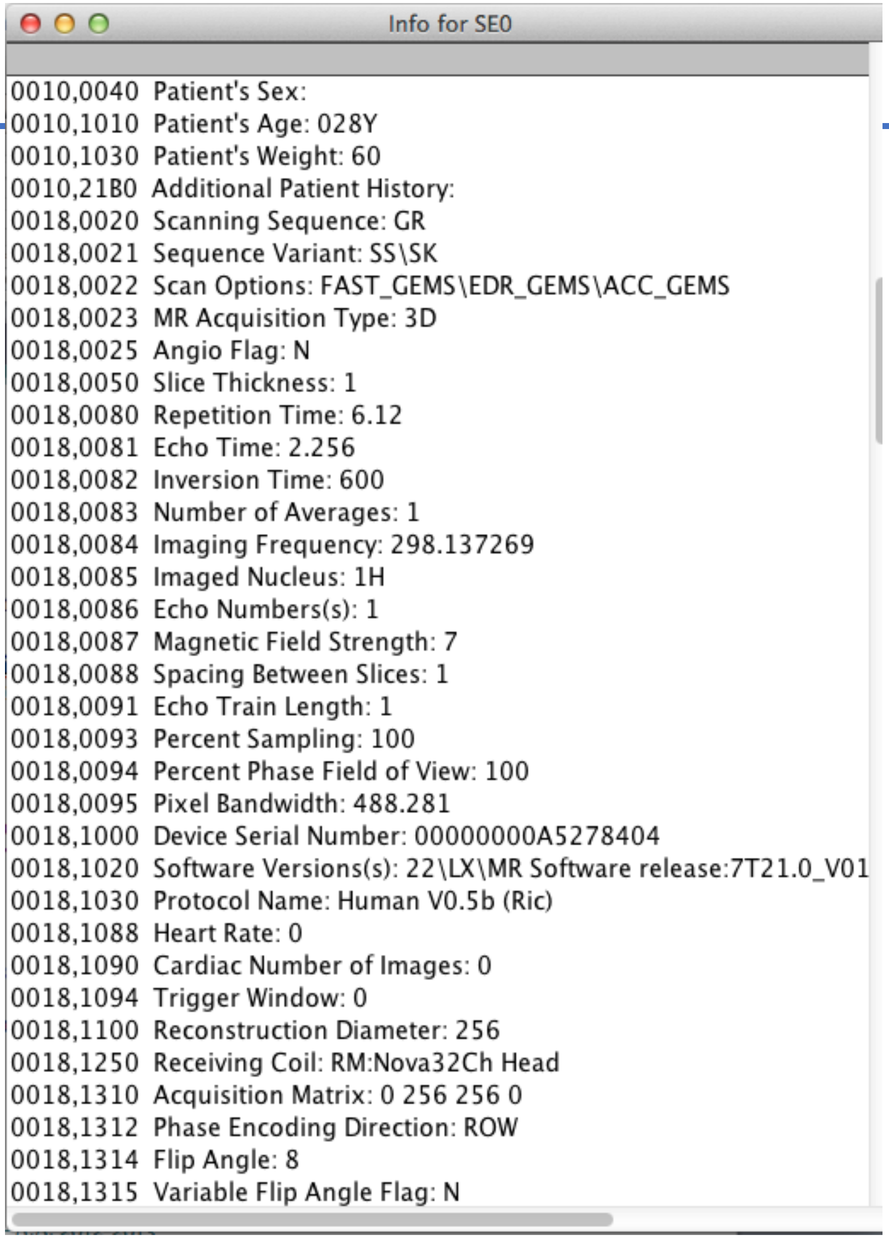
DICOM metadata

A **DICOM data element, or attribute,** is composed of the following most important parts:

- a **tag** that identifies the attribute, usually in the format (XXXX,XXXX) with hexadecimal numbers, and may be divided further into DICOM Group Number and DICOM Element Number;
- a **DICOM Value Representation (VR)** that describes the data type and format of the attribute value (e.g. PN: Person Name; DT: Date Time; SS: Signed Short).

Check **https://www.dicomlibrary.com/dicom/dicom-tags/**

- most fields are optional
- there are also vendors' private keys
- some examples:
  - Session Name and Study Number
    - (0008, 0090) ID Referring Physician
    - (0010,0010) Patient's Name
  - Image "Shape"
    - (0028, 0010) IMG Rows
    - (0028, 0011) IMG Columns
    - (0028, 0030) IMG Pixel Spacing
    - (0018, 0050) ACQ Slice Thickness
  - How and where the image data is stored
    - (0028, 0100) IMG Bits Allocated
    - (0028, 0101) IMG Bits Stored
    - (0028, 0102) IMG High Bit



The Neuroimaging Informatics Technology Initiative (NIfTI) file format

Another file format commonly used to store brain imaging data obtained using Magnetic Resonance Imaging methods is the Neuroimaging Informatics Technology Initiative (**NIfTI**)

- The NIfTI stored volumes can be:
  - in dual file format: file.hdr, file.img
  - in a single file: file.nii

- NIfTI is the default file format of most software packages for neuroimaging post-processing:
  - FSL, SPM, itk-SNAP, 3D Slicer, ITK & VTK, nipy, etc.

- The NIfTI format allows a double way to store the orientation of the image volume in the space:
  1. rotation + translation to be used to map voxel coordinates to the scanner reference frame
  2. 12-parameter or more general transformation adopted to realign the volume to a standard template coordinate system.

Images viewers

- MANGO: https://mangoviewer.com/mango.html

Mango for the Desktop

Mango supports Mac, Windows, and Linux operating systems.

Download for **Mac** (v4.1)

Download for **Windows** (v4.1)

Download for **Linux** (v4.1)

Download Previous Versions

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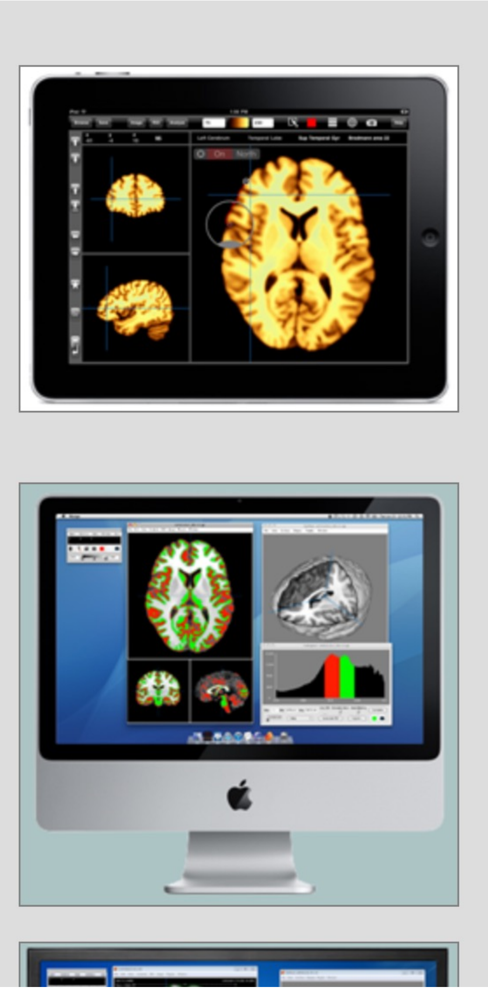
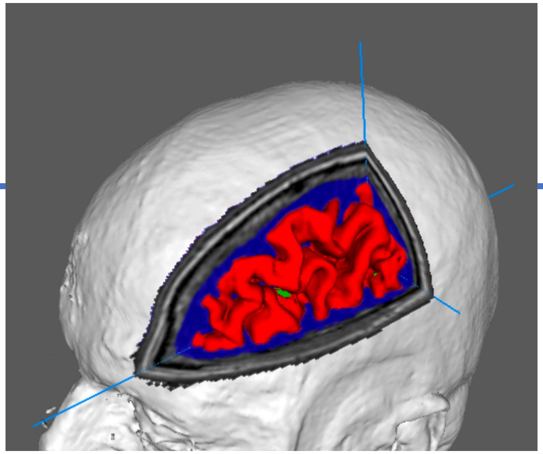
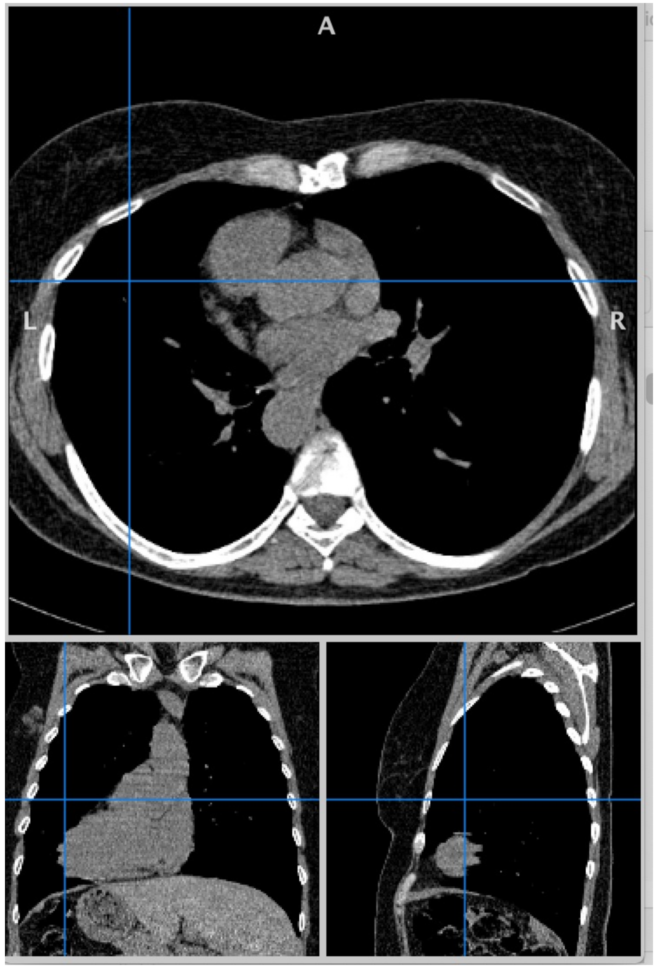


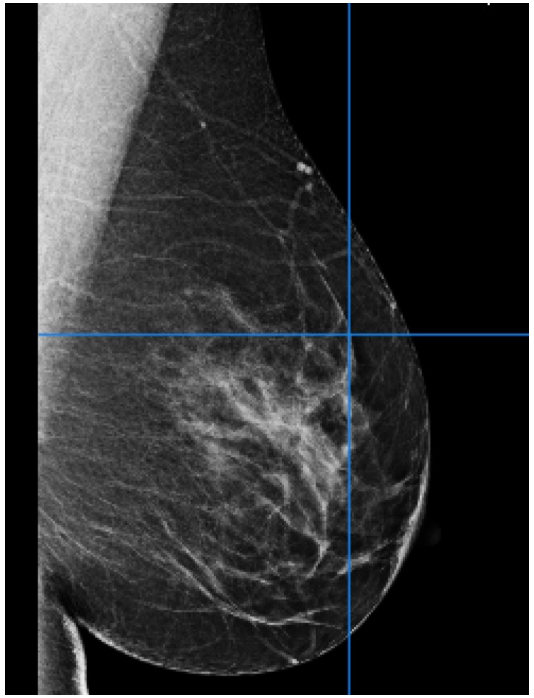
Mango

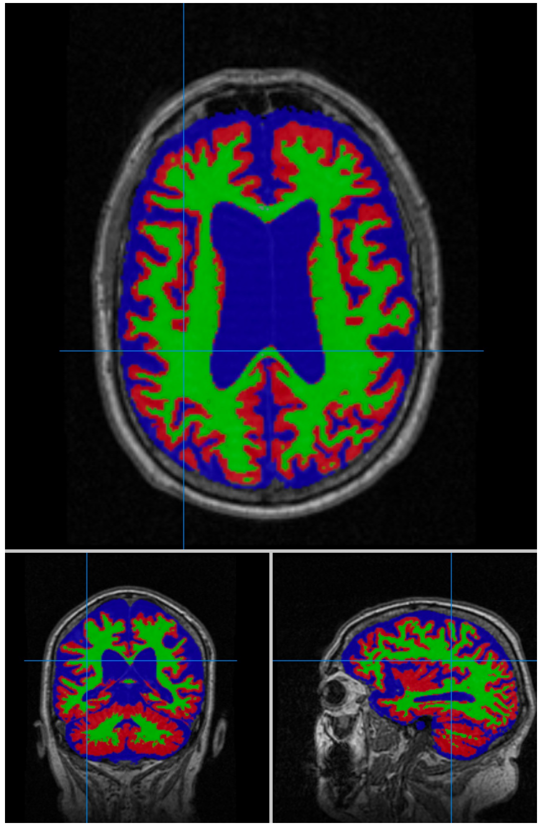
Let’s read real images with Mango …



- Explore 2D, 3D and 4D data sample
- Make image overlays







Other medical image viewers

- ImageJ
  - https://imagej.nih.gov/ij/
- OsiriX (only for Mac, iPhone, iPad)
  - https://www.osirix-viewer.com
- 3DSlicer
  - https://www.slicer.org
- itk-SNAP
  - http://www.itksnap.org/pmwiki/pmwiki.php
- …

The pydicom library

- Pydicom is a pure Python package for working with DICOM files such as medical images, reports, and radiotherapy objects.
- Pydicom makes it easy to read these complex files into natural pythonic structures for easy manipulation.

- Requirements:
  - numpy library is recommended, (it is only required if manipulating pixel data)
  - matplotlib is necessary to visualize data

See demo code (Jupyter notebooks):
- Lecture1_demo1 _read_DICOM_file.ipynb (read and visualize dicom files, e.g. a 2D slice)
- Lecture1_demo2 _read_DICOM_dir.ipynb (read and visualize dicom dirs, e.g. a 3D volume)

The General Data Protection Regulation (GDPR)

- The EU General Data Protection Regulation (GDPR) was approved by the EU Parliament on 14 April 2016
- It is designed to:
  - Harmonize data privacy laws across Europe
  - Protect and empower all EU citizens data privacy
  - Reshape the way organizations across the region approach data privacy

- GDPR and Data Science
  - De-identifying medical imaging is a fundamental prerequisite for data storing, processing and sharing within research projects in order to be compliant with GDPR:
    - Anonymization: using the Hash function (non-reversible)
    - Pseudonymization: the processing of personal data in such a manner that the personal data can no longer be attributed to a specific data subject without the use of additional information. Data is tokenized, a separate lookup file (with the original entry and the token) is generated and stored in a restricted database.

See demo code (Jupyter notebooks):
- Lecture1_demo3 _anonymize.ipynb (how to anonymize dicom files)

References and sources

- Books
  - The Essential Physics of Medical Imaging, Jerrold T. Bushberg
  - Digital Image Processing for Medical Applications, Geoff Dougherty
  - Handbook of Medical Image Processing and Analysis, Isaac N. Bankman
  - Image Processing and Acquisition using Python, Ravishankar Chityala & Sridevi Pudipeddi

- Sources
  - https://www.dicomstandard.org
  - https://gdpr.eu/
  - https://pydicom.github.io/pydicom/

You will find the repository of course materials on **https://github.com/retico/cmepda_medphys**
and the image data samples to use on **https://pandora.infn.it/public/cmepda**
and on **https://drive.google.com/open?id=1YqK7ZkM-P2IrqfD7Pj-SCmjz-GWd_1-Y**

To do ….

University of Pisa has a Campus license for MATLAB

- Download and install MATLAB on your laptop https://start.unipi.it/personale-t-a/strumenti-di-lavoro/strumenti-informatici/software-e-servizi-cloud/software-matlab/

https://matlab.mathworks.com/

MathWorks releases two stable versions of MATLAB per year, i.e.:
R202X**a** in March
R202X**b** in September

Download and install a Dicom viewer, e.g. Mango:

- https://mangoviewer.com/mango.html

System requirements and useful MATLAB toolboxes

- Check the system requirements for installation (Windows/Mac/Linux):
  - https://it.mathworks.com/support/requirements/matlab-system-requirements.html

- Download and install the (current) MATLAB release

- During the installation:
  - you are asked to "Log in with a MathWorks Account" (the one you have created with your **unipi.it** account)
  - you have to specify the products to be installed, i.e. the MATLAB toolboxes.
    - You may add some toolboxes you like to the suggested ones (e.g. the Image Processing, Curve Fitting, Mapping, Wavelet and Deep Learning toolboxes will be used in the exercises)
    - You can add more toolboxes even later on, whenever you need, from the Add-Ons drop down menu from the MATLAB desktop HOME tab.