Computing Methods for Experimental Physics and Data Analysis

Data Analysis in Medical Physics

Lecture 1: Intro to Medical Image Processing and Analysis

Alessandra Retico
alessandra.retico@pi.infn.it
INFN - Pisa

Course objectives

- 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 and extract relevant information from medical images
- a variety of data sets (2D, 3D, 4D), acquired with the main medical imaging modalities (e.g. RX, CT, MRI) will be made available

Course Calendar

- 1. Friday, November 22 11.00-13.00 room S1

- 2. Monday, November 25 9->11 room X1
- 3. Monday, November 25 16->18 room X1
- 4. Thursday, November 28 9->11 room V1
- 5. Friday, November 29 11.00-13.00 room S1

- 6. Thursday, December 5 9->11 room V1

- 7. Monday, December 9 9->11 room X1
- 8. Monday, December 9 16->18 room X1
- 9. Thursday, December 12 9->11 room V1

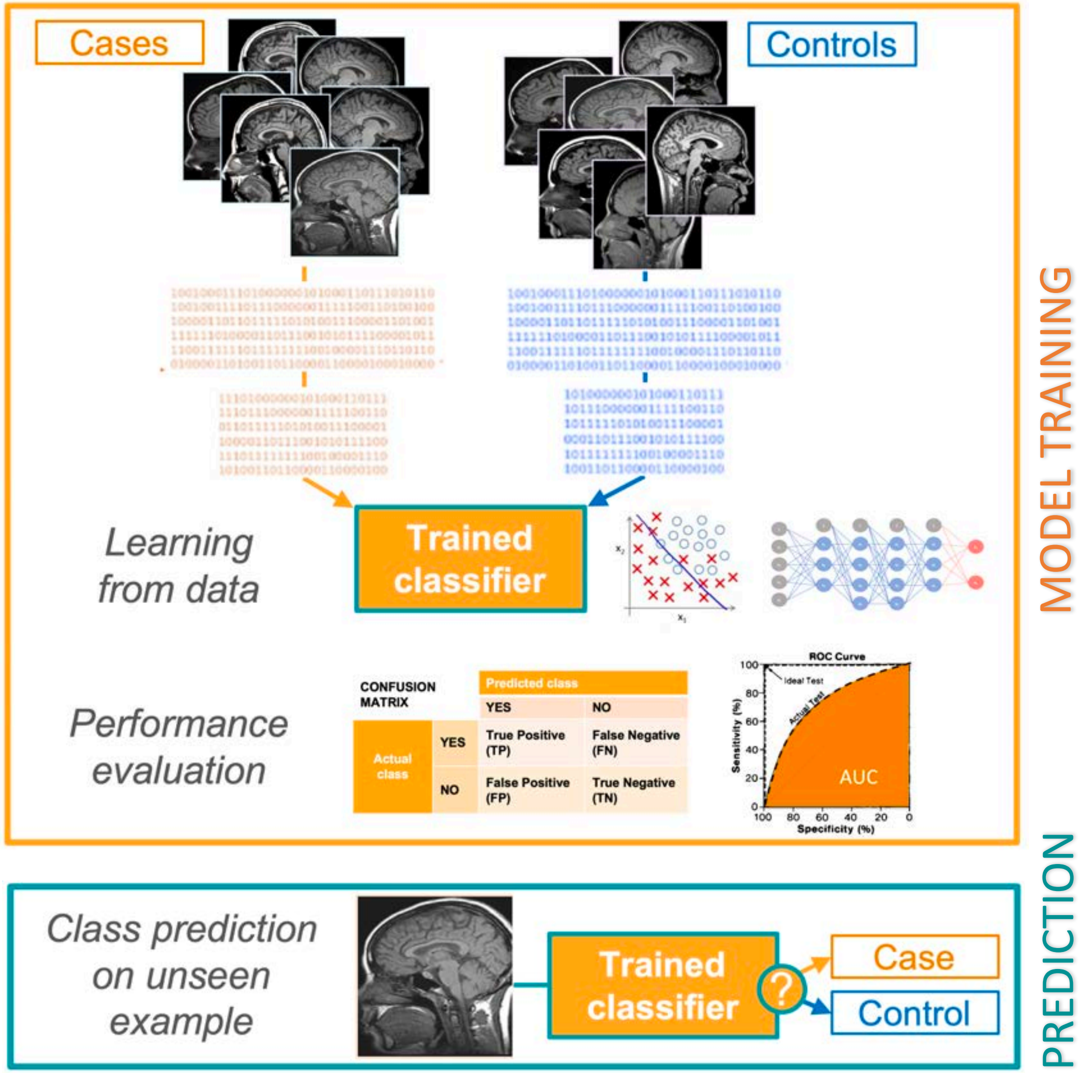
- 10. Monday, December 16 9->11 room X1
- 11. Monday, December 16 16->18 room X1
- 12. Thursday, December 19 9->11 room V1

Bring your laptop!

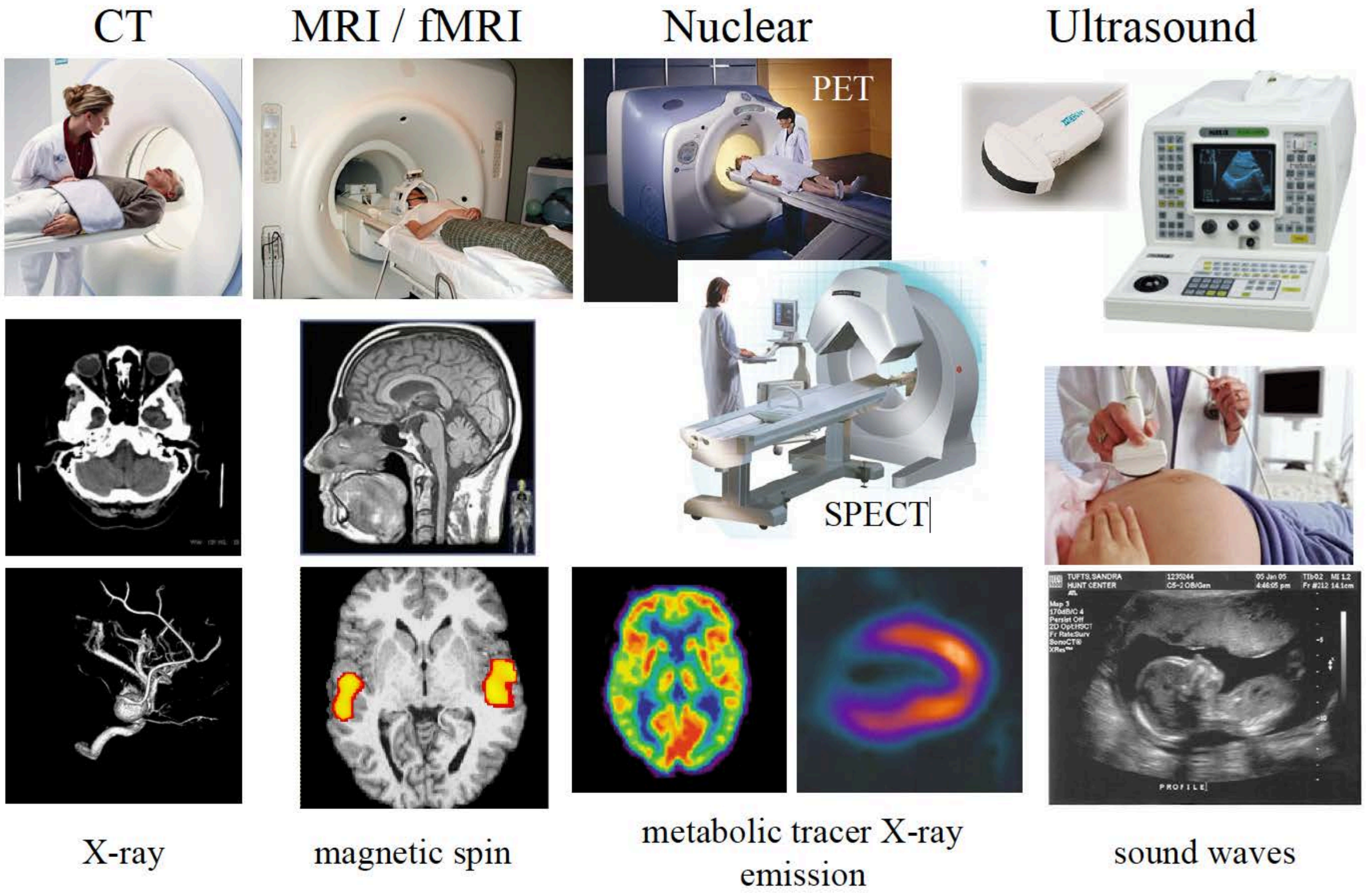
Course overview

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: figures of merit, 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

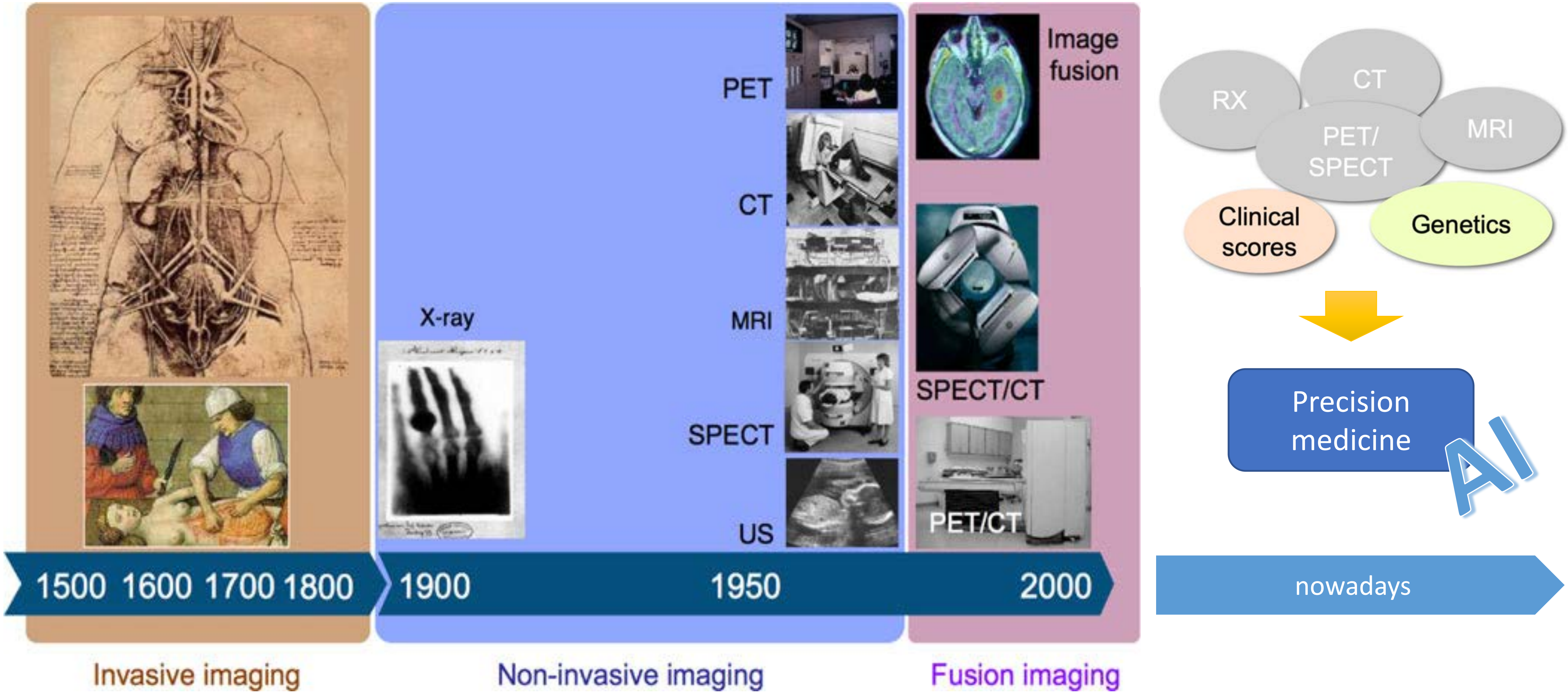
- Medical images are not limited to 2D, as natural pictures generally are

- 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

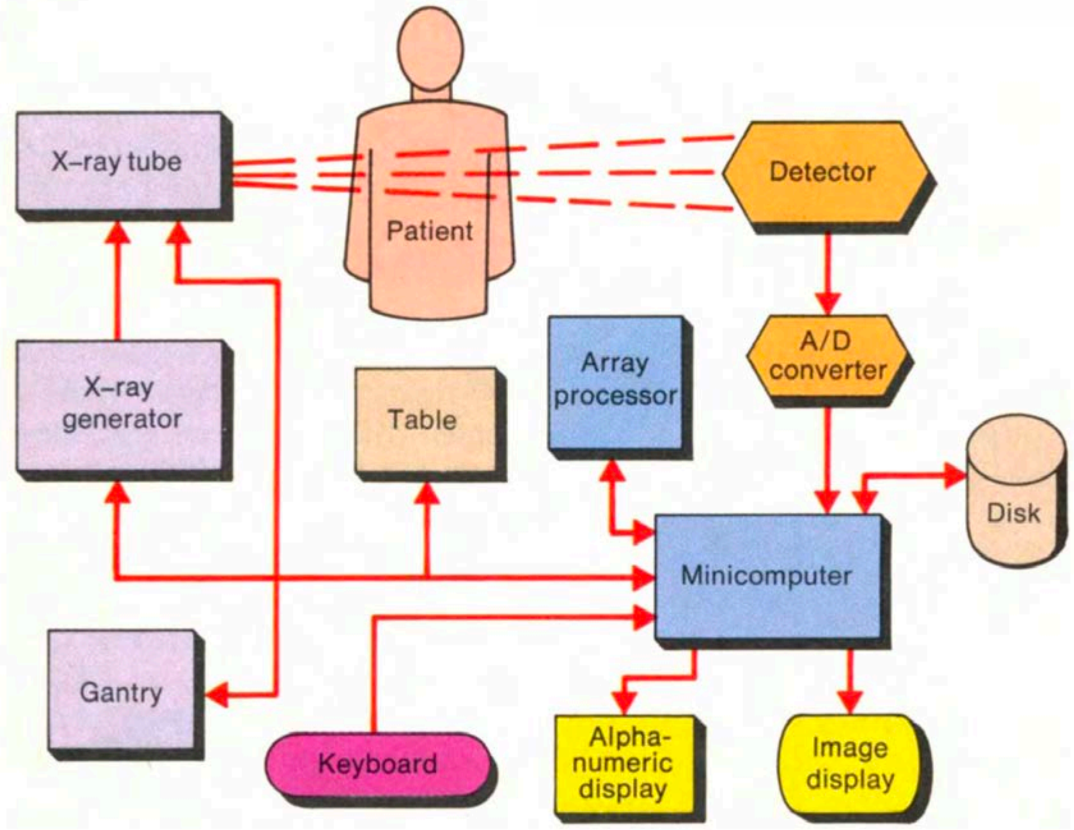
The computer revolution in medical imaging systems

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

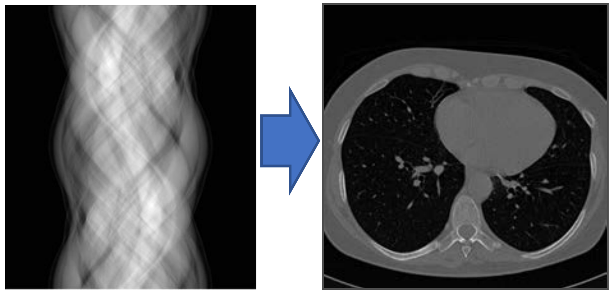
In a computerized tomography system, the X-ray data are acquired by a detector and converted to digital data. These data are then processed by the array processor and the minicomputer to generate the image, which is then displayed on a CRT.

IEEE POTENTIALS • DECEMBER 1984

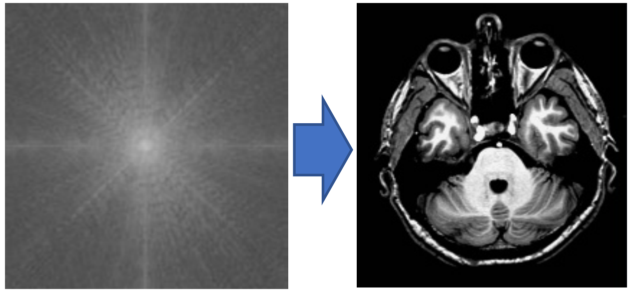


The role of computers in Medical Imaging

- To reconstruct acquired signals to form diagnostic images

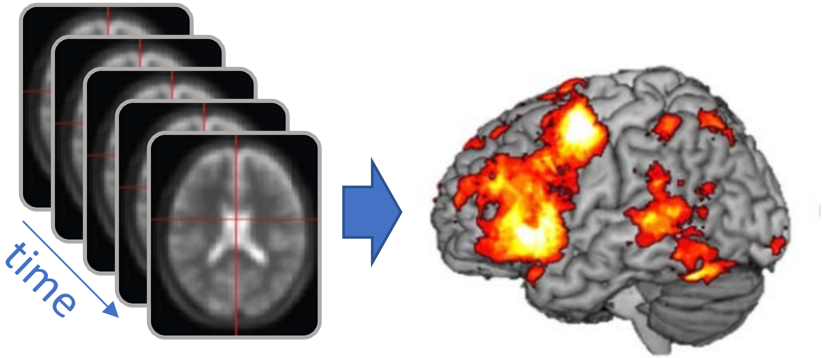


CT image reconstruction from sinogram

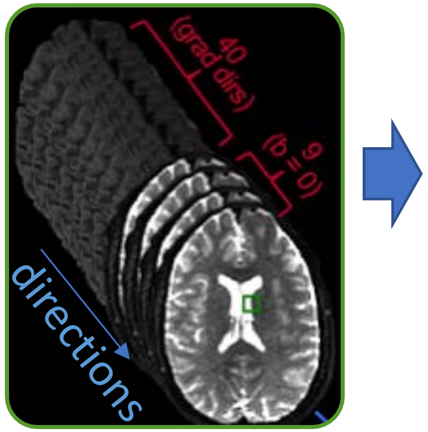


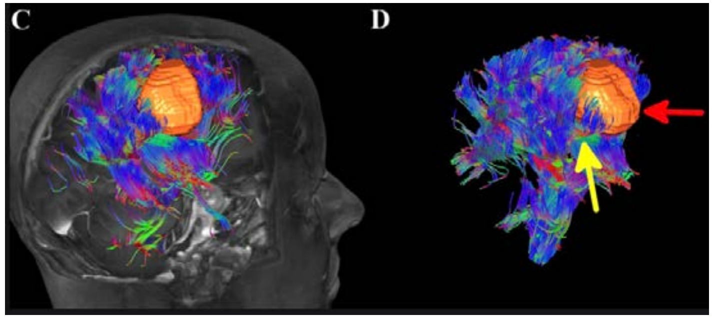
MRI image reconstruction from k-space data

- To allow the visualization of the acquired information



Activated brain areas while executing a task



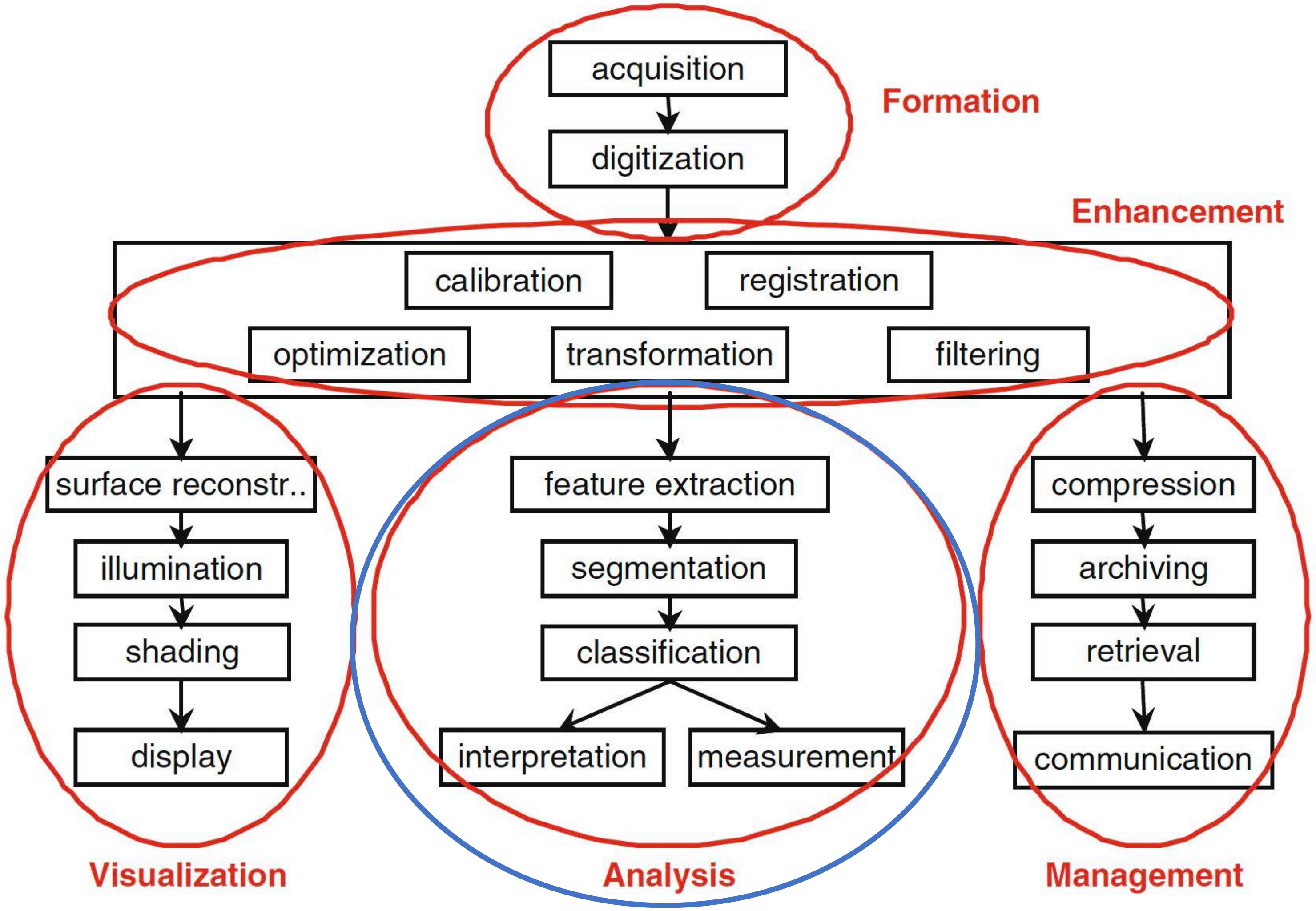


Axon fiber tracts from diffusion-weighted MRI data

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 grow rate of lesions)
- To assessment treatment efficacy

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

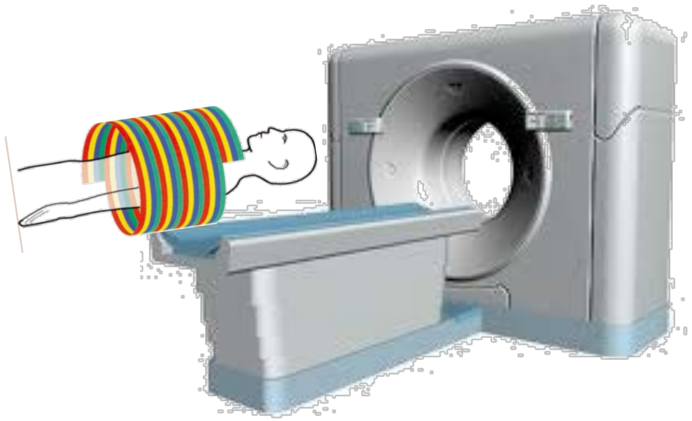
→ *Computer Aided Detection/ Diagnosis (CAD) systems*

Historical development of CAD systems:

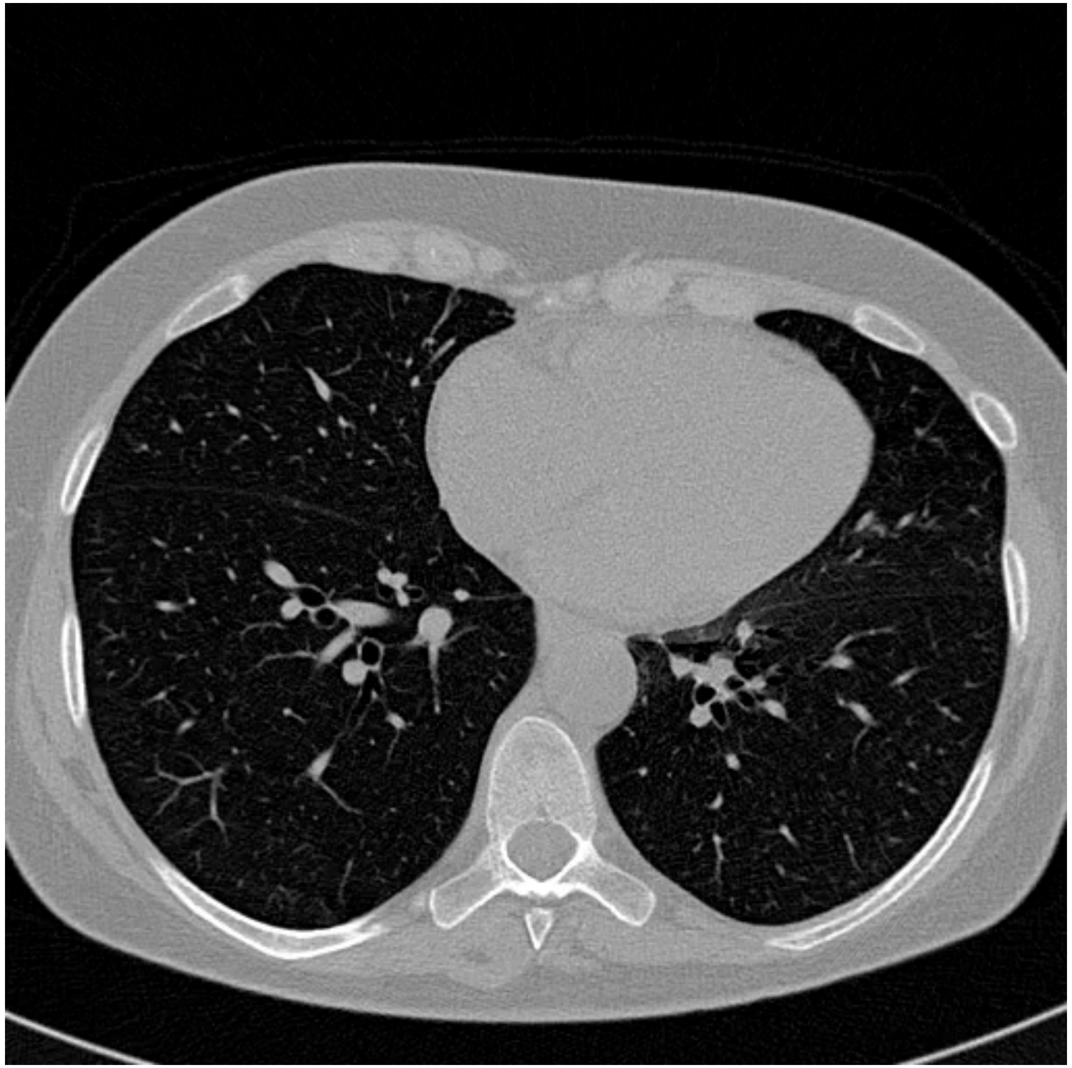
1) ’90 - Old-fashion systems (Rule-based decision systems)
2) 2000-today - Hand-crafted feature and Machine Learning classification
3) since 2016 - Deep Learning-based data/image classification

Data dimensionality: 3D images

- Computed Tomography

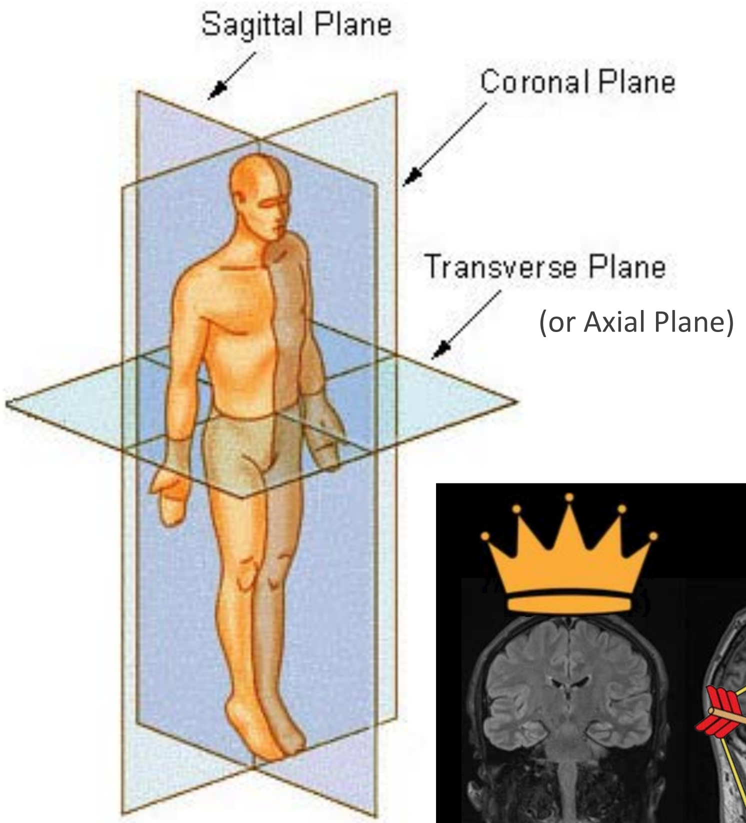


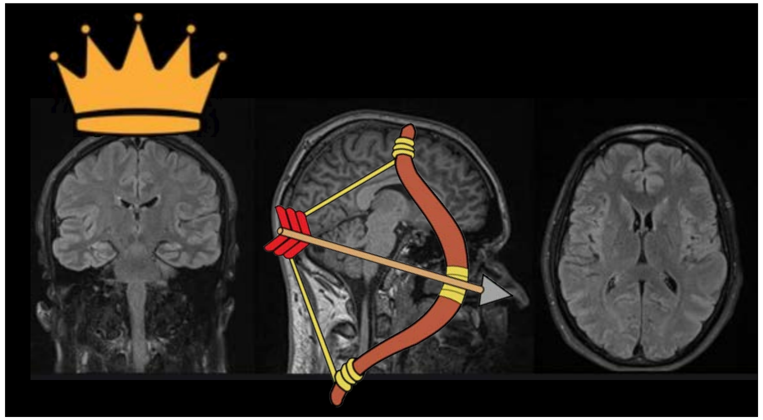
A thin-slice lung CT exam generates ~300 slices per subject

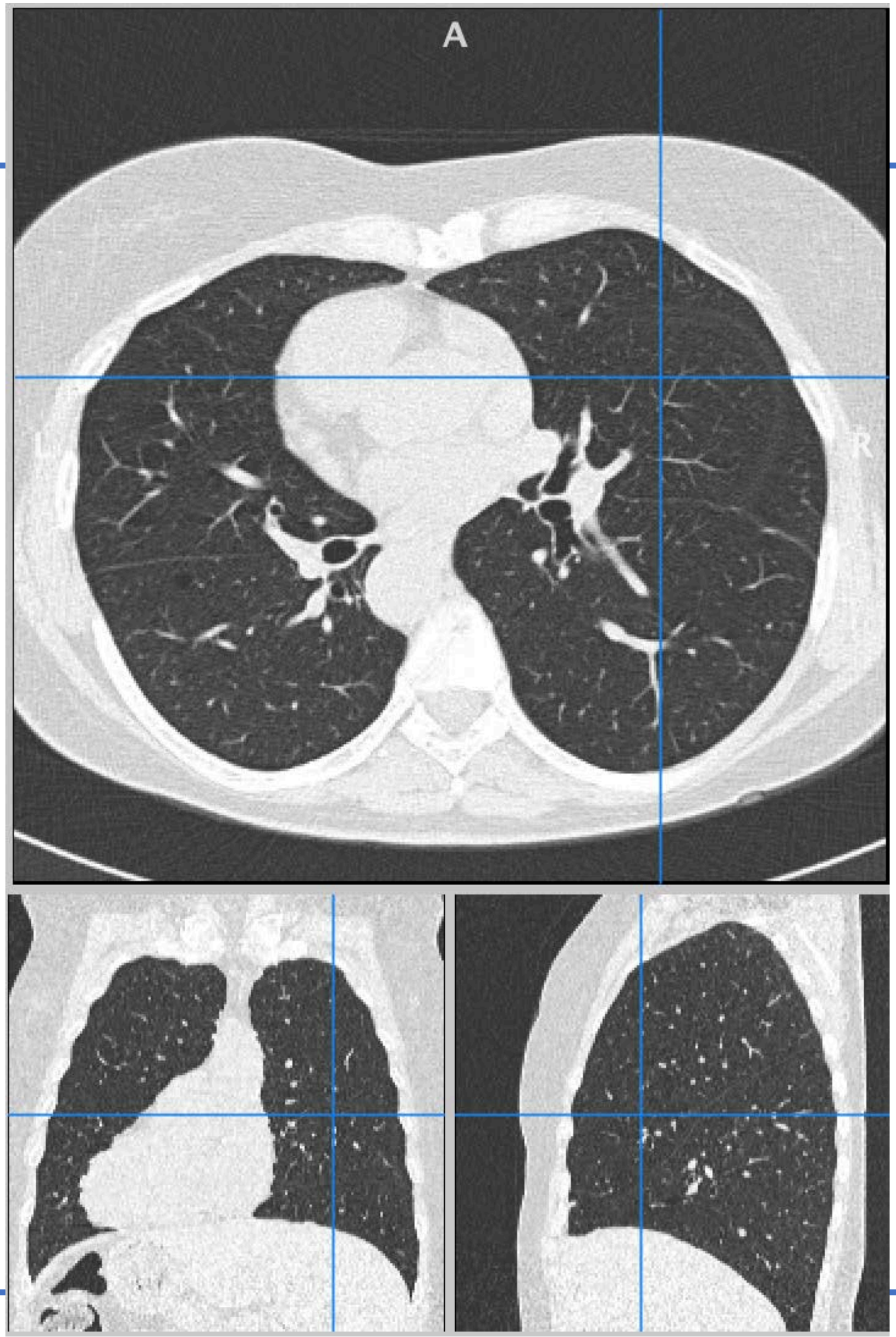


Volume display planes

- Medical images are usually displayed by anatomical planes





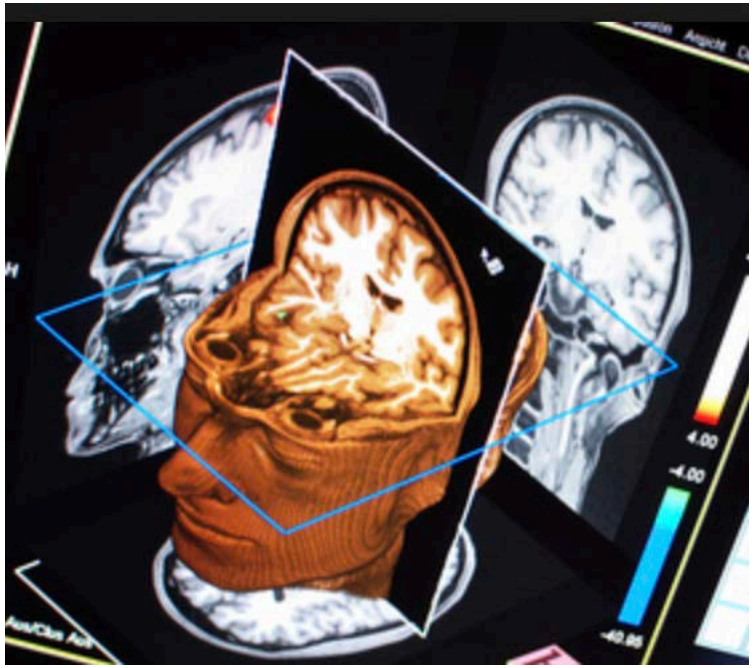


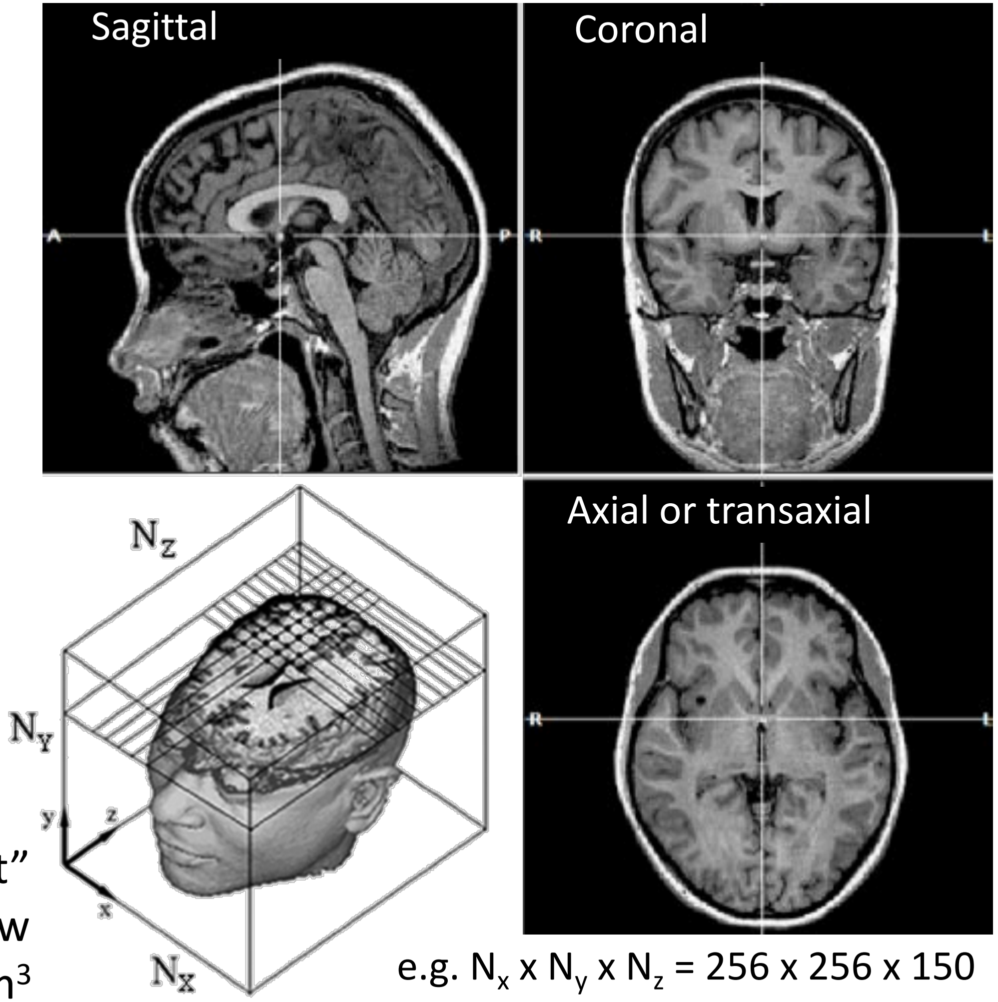
Data dimensionality: 3D and more…

- **Example: brain imaging**
  - **Structure**
    - Structural Magnetic Resonance imaging — MRI
    - Diffusion Tensor Imaging — DTI
    - Computed Tomography — CT
  - **Function**
    - Functional Magnetic Resonance Imaging — fMRI
    - Positron Emission Tomography — PET

3D | 3D | 4D | 3D | 4D | 4D

Structural MRI T_1-weighted images





3D array of data:

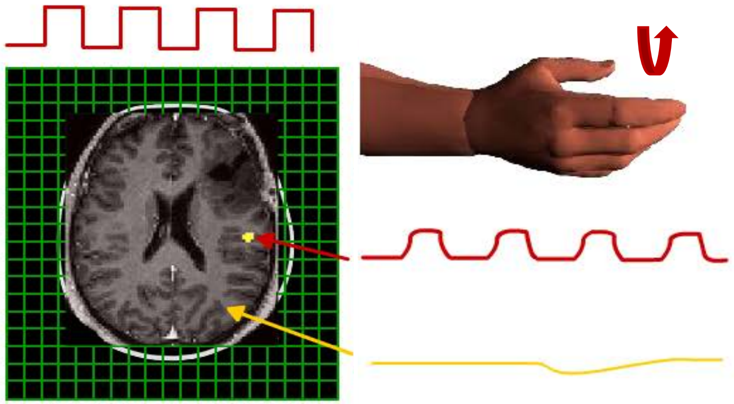
- The voxel is the "volume element"
- Typical "High resolution" MRI T_1-w images: $v_x \times v_y \times v_z \approx 1 \times 1 \times 1$ mm^3

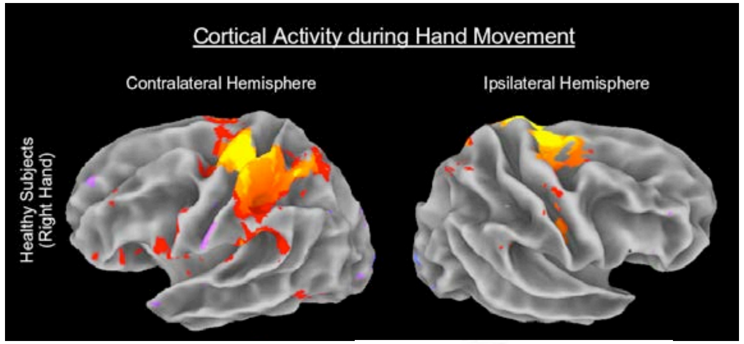
e.g. $N_x \times N_y \times N_z = 256 \times 256 \times 150$
16 bit ~**20 MB**

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

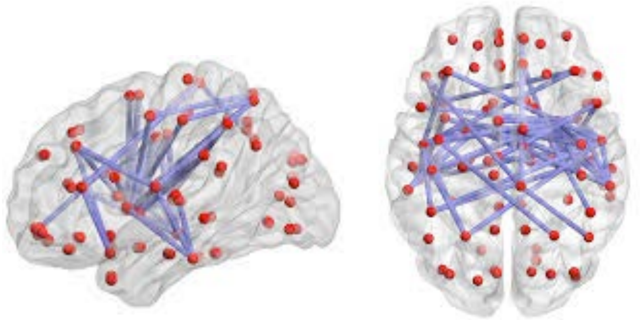
- Analysis of data time series to look for up-and-down signals that match the stimulus time series





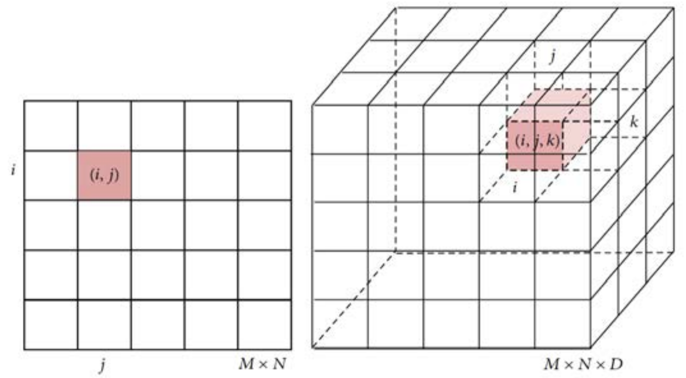
Functional connectivity

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



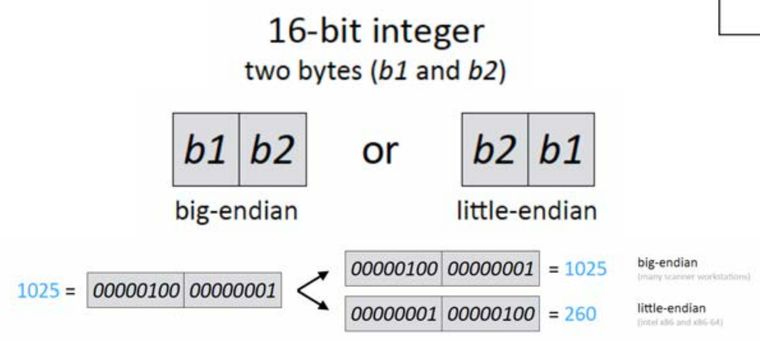
Data dimensionality: 2D/3D/4D/..nD images

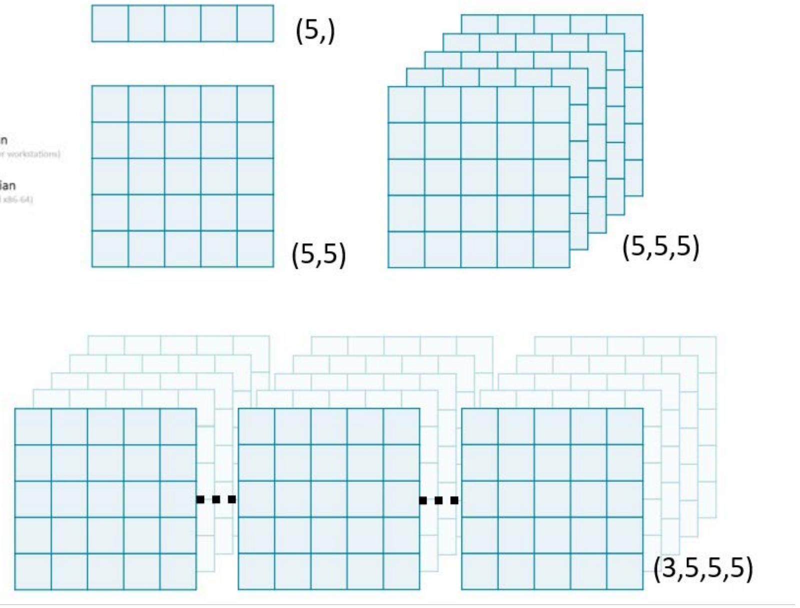
- Image element:
  - pixel: picture element
  - voxel: volume element



- 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)



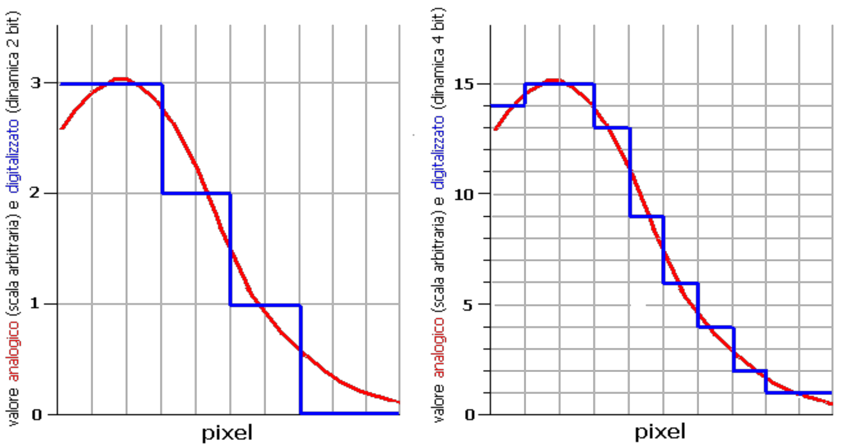


- Metadata is required for correct interpretation, e.g.:
  - pixel/voxel dimension (e.g. voxel size (mm): v_x , v_y , v_z)
  - machine settings
  - parameters used to produce the image
  - patient’s positioning
  - patient’s information (age, sex,…)
  - Intensity scaling information (only integers are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

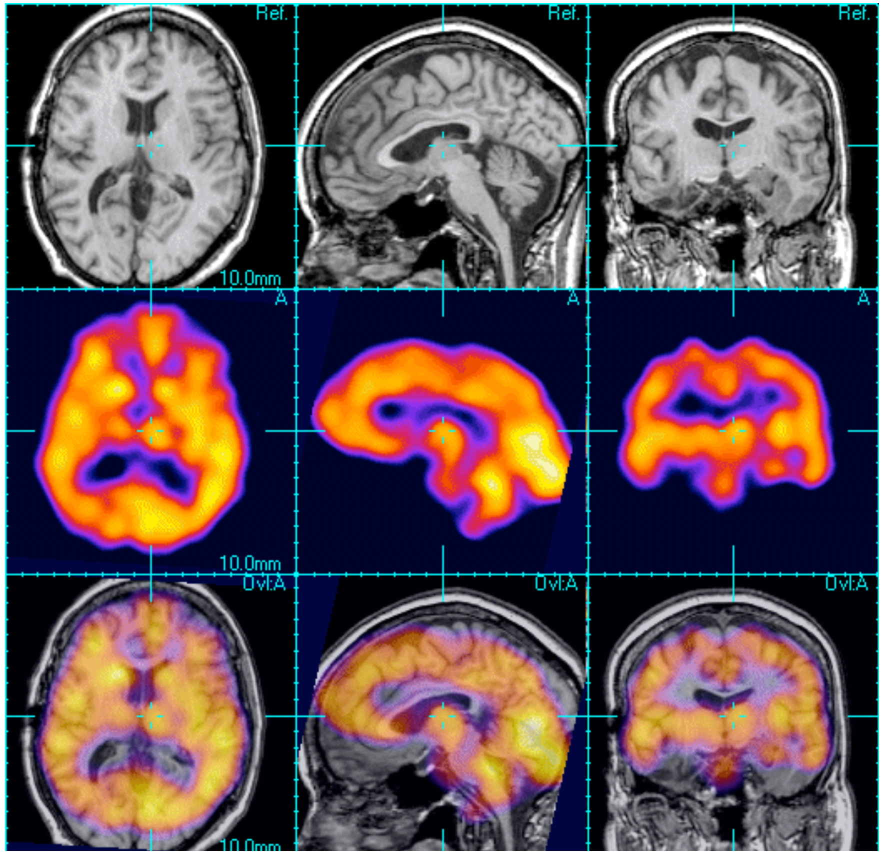
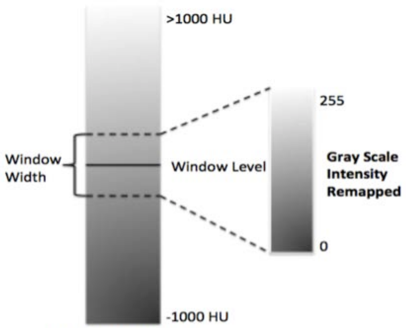


Image windowing

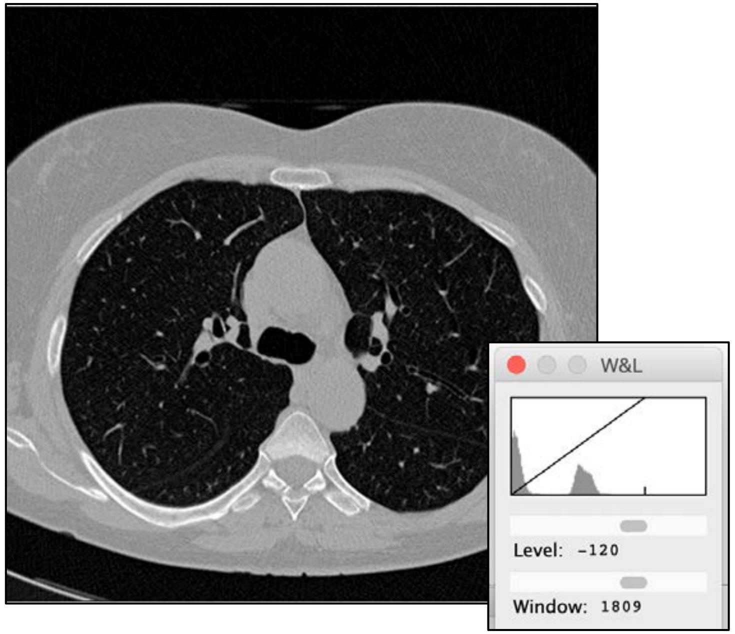
- In Computed Tomography (CT) voxel intensities are expressed in Hounsfield Units (HU)
- The HU scale is a linear transformation of the original linear attenuation coefficient measurement into one in which the radiodensity of distilled water at standard pressure and temperature is defined as zero HU
- HU values of human tissues range in [-1000, 1000] HU
- 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

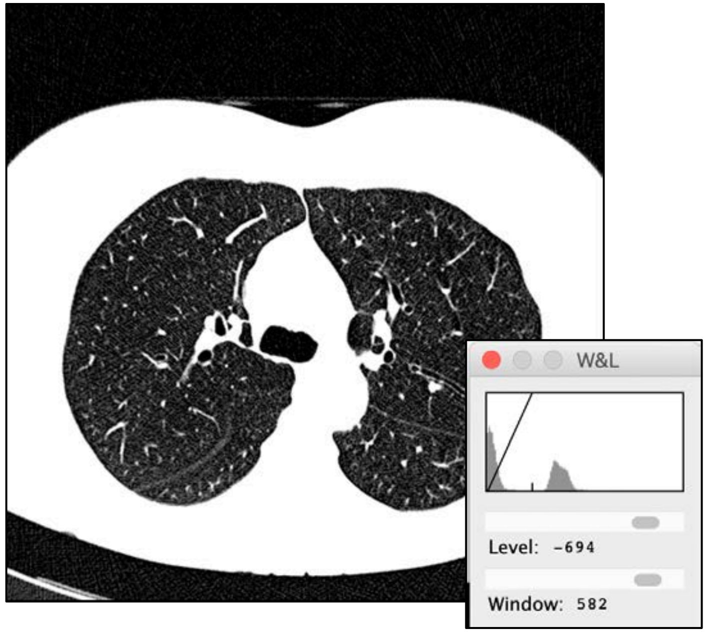
$$HU = 1000 \times \frac{\mu - \mu_{\text{water}}}{\mu_{\text{water}} - \mu_{\text{air}}}$$



Hounsfield Units for human body

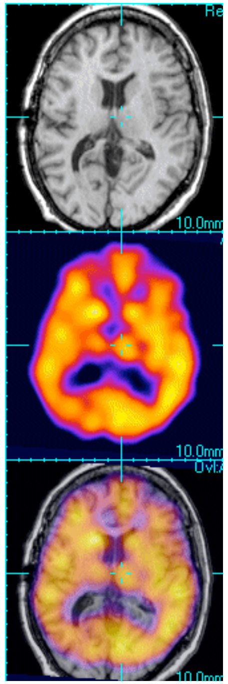
Bone	*1000*
Liver	*40 to 60*
White Matter	*46*
Grey Matter	*43*
Blood	*40*
Muscle	*10 to 40*
Kidney	*30*
Cerebrospinal Fluid	*15*
Water	*0*
Fat	*-50 to -100*
Air	*-1000*

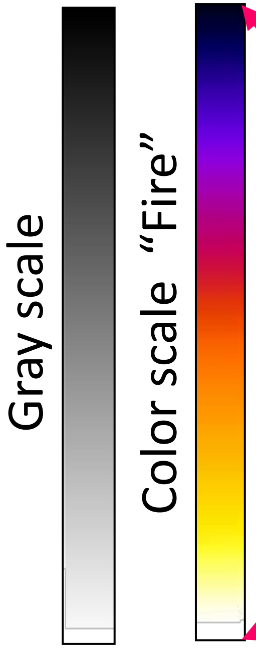




Look-up tables (LUTs)

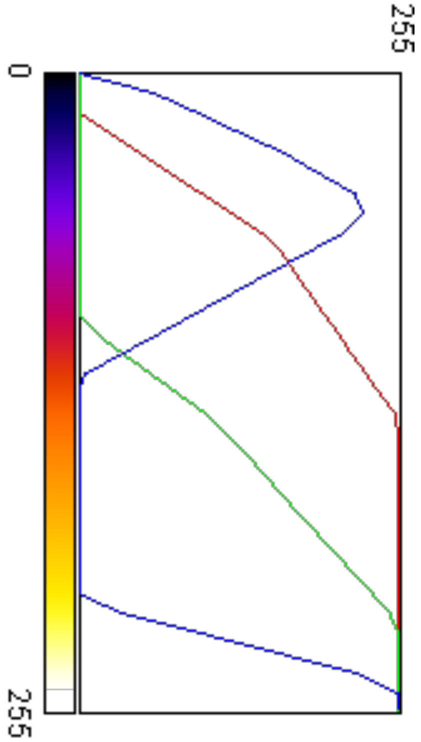
- Look-up tables (LUTs) are used for pseudo coloring.
  - Computer graphic boards typically limit the number of gray scales to 256 (8 bit), but offer 256^3 (~ 16 10^6) colors.
  - Pseudo coloring allows presentation of data without reducing the information as it would result from windowing





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

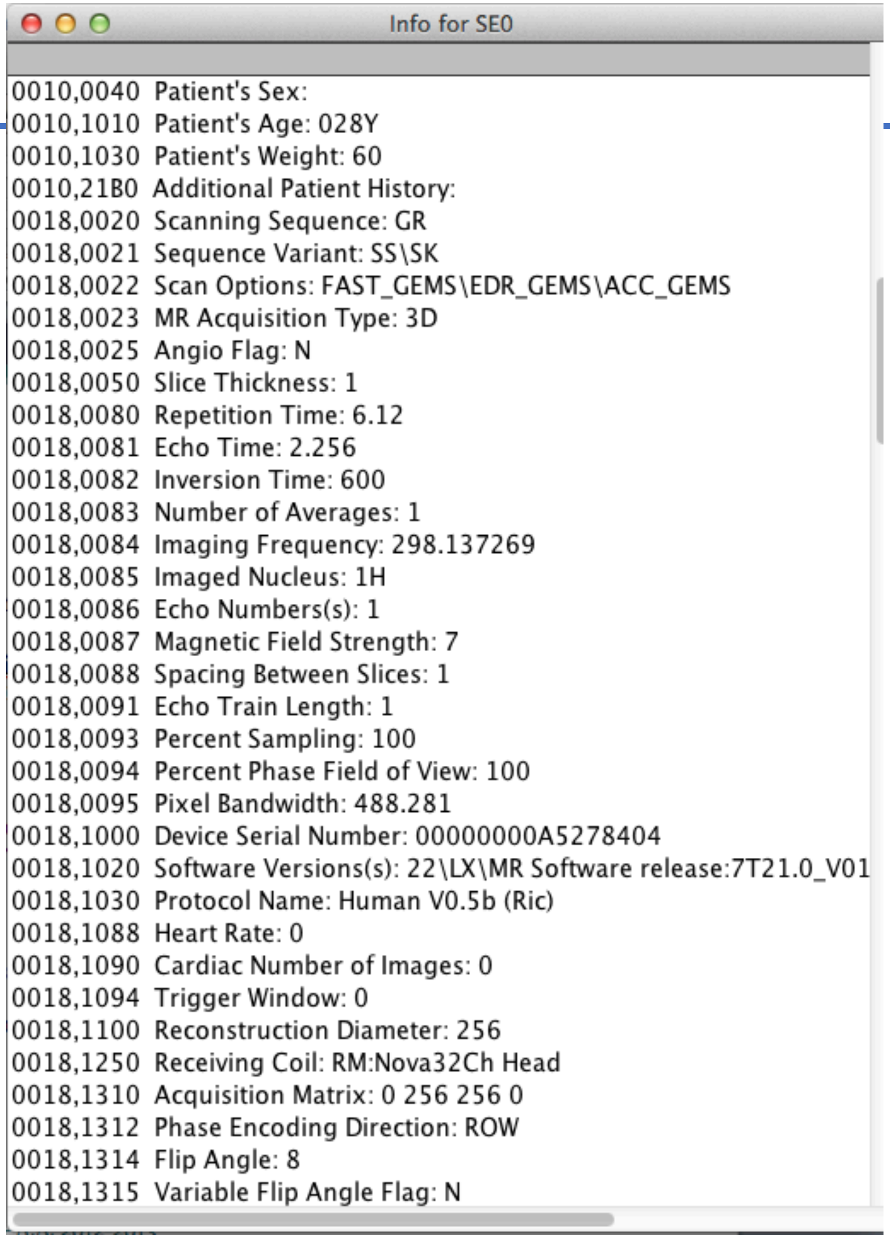
DICOM metadata

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.

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


Info for SE0

0010,0040 Patient's Sex:
0010,1010 Patient's Age: 028Y
0010,1030 Patient's Weight: 60
0010,21B0 Additional Patient History:
0018,0020 Scanning Sequence: GR
0018,0021 Sequence Variant: SS\SK
0018,0022 Scan Options: FAST_GEMS\EDR_GEMS\ACC_GEMS
0018,0023 MR Acquisition Type: 3D
0018,0025 Angio Flag: N
0018,0050 Slice Thickness: 1
0018,0080 Repetition Time: 6.12
0018,0081 Echo Time: 2.256
0018,0082 Inversion Time: 600
0018,0083 Number of Averages: 1
0018,0084 Imaging Frequency: 298.137269
0018,0085 Imaged Nucleus: 1H
0018,0086 Echo Numbers(s): 1
0018,0087 Magnetic Field Strength: 7
0018,0088 Spacing Between Slices: 1
0018,0091 Echo Train Length: 1
0018,0093 Percent Sampling: 100
0018,0094 Percent Phase Field of View: 100
0018,0095 Pixel Bandwidth: 488.281
0018,1000 Device Serial Number: 00000000A5278404
0018,1020 Software Versions(s): 22\LX\MR Software release:7T21.0_V01
0018,1030 Protocol Name: Human V0.5b (Ric)
0018,1088 Heart Rate: 0
0018,1090 Cardiac Number of Images: 0
0018,1094 Trigger Window: 0
0018,1100 Reconstruction Diameter: 256
0018,1250 Receiving Coil: RM:Nova32Ch Head
0018,1310 Acquisition Matrix: 0 256 256 0
0018,1312 Phase Encoding Direction: ROW
0018,1314 Flip Angle: 8
0018,1315 Variable Flip Angle Flag: N

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: http://ric.uthscsa.edu/mango/index.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)

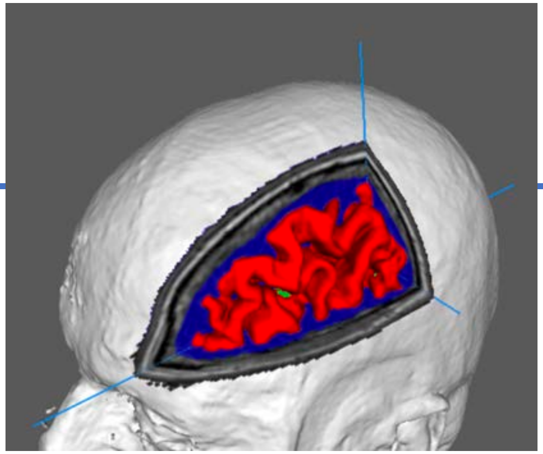
Download Previous Versions

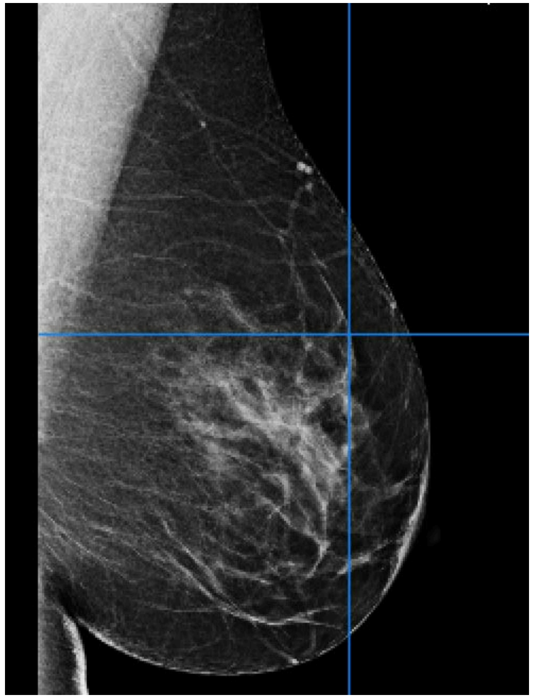
License

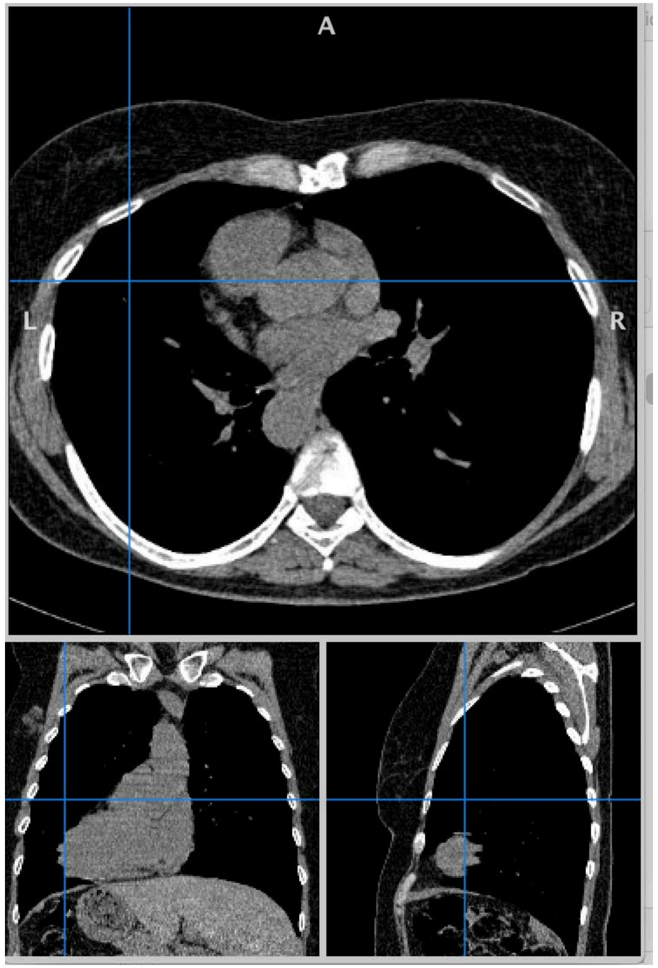
Mango software is copyrighted by the University of Texas. Mango is available for use, as is, free of charge, for educational and scientific, non-commercial purposes. The software and data derived from Mango software may be used only for research and may not be used for clinical purposes. If Mango software or data derived from Mango software is used in scientific publications, we request that the 'Research Imaging Institute, UTHSCSA' be cited as a reference. Use or incorporation of this software or data derived from this software in commercial applications or commercial publications requires a written consent from the RII-UTHSCSA.

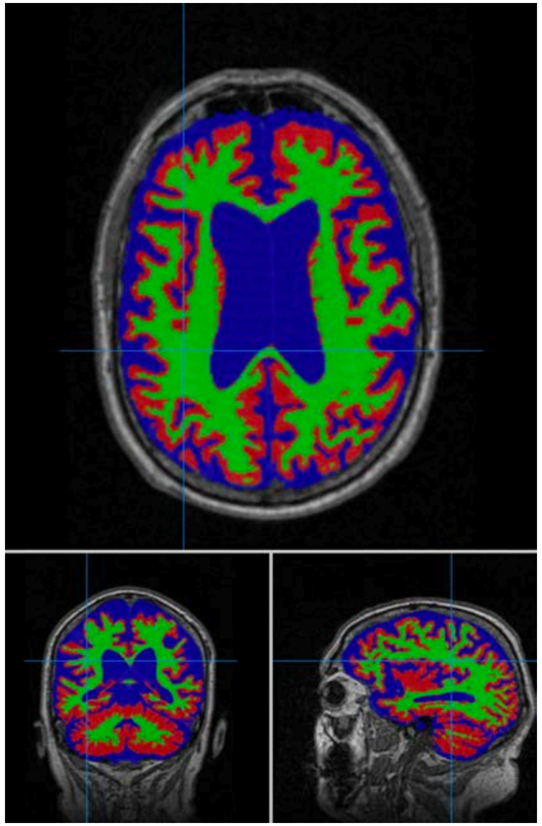
Let’s read real images with Mango …

- 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 sclice)
- 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 to be compliant to GDPR:
    - Anonymization: using the Hash function (non-reversible)
    - Pseudo-anonymization: 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://eugdpr.org
  - 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:
  http://doc.sid.unipi.it/Campus_Matlab
- Follow the link Come ottenere ed installare MATLAB and then “Istruzioni ad uso degli studenti (Installazione MATLAB Student)”

Current stable release is R2019a

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

- http://ric.uthscsa.edu/mango/index.html

System requirements and useful MATLAB toolboxes

- System requirements for installation:
  - Administrative rights
  - **Processors – Minimum**: any Intel or AMD x86-64 processor
  - **RAM – Minimum:** 3.3 GB. **Recommended:** 8 GB
  - **DISK – Minimum**: 3.3 GB of HDD space for **MATLAB** only, 5-8 GB for a typical installation. **Recommended**: An SSD is recommended

- During the installation 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 Statistics and Machine Learning toolbox, the Deep Learning toolbox)
  - Add wavelet toolbox and curve fitting toolbox we will use in exercises
- you can add more toolboxes whenever you need fro the Add-Ons drop down menu from the MATLAB desktop HOME tab.