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University of Cyprus

MAI643: Artificial Intelligence in Medicine

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Medical Image Informatics

(Some material drawn from Hersh, WR, 2022. Health Informatics: Practical Guide, 8th Edition, slides)

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Medical Image Informatics

1. Introduction to medical images and their use in health care
2. Medical Image Modalities
   - Photographic images
   - X-ray
   - MRI
   - CT
   - Nuclear images
3. Image Representation and Processing
4. Image Compression, Management and Interpretation
5. AI/DL in Medical Image Informatics
6. Challenges of AI in Medical Image Informatics

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INTENDED LEARNING OUTCOMES

Upon completion of this unit on Medical image informatics and interpretation, students will be able to:

1. Explain what medical images are, and how they are different from photographic images
2. Describe the main applications of medical images in clinical medical practice
3. Differentiate between the different image modalities
4. Overview the main tasks for image processing
5. Discuss the challenges and opportunities for interpreting medical images
6. Explain the role of AI in medical imaging
7. Appreciate the promising approaches and directions for AI in medical imaging?

Medical Images

- "Medical Imaging": techniques used to create images of the human body
- Images are used for a variety of purposes, not only in diagnosis, but also in:
  - Treatment planning and guidance
  - Communication
  - Education
  - Research

From Hersh, 2022

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Images in Medical Diagnosis

- Primary use of images in healthcare
- Like all diagnostic tests, radiologic images do not have 100% sensitivity or specificity
  - Must recognize their limitations and potential harms (from radiation)
- May also lead to “incidental” findings that require additional cost and exposure
- Diagnostic imaging is also expensive

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Assessment and Planning

- Can be used to assess a patient’s status
  - Heart size and motion via echocardiography
  - Fetal development via ultrasound
- Also used for planning
  - Use of CT scans or tomography to plan surgery or radiation therapy

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Education and Training

- Important part of medical education, taking the form of:
  - Demonstration of techniques
  - Case studies and libraries
- Increasingly important for educating patients

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Research

- Images are biological data like any other used in research, and their interpretation adds structured data
- Image archives and data sets can be valuable, e.g..
  - Cancer Imaging Archive – https://www.cancerimagingarchive.net/
  - Andrew Beam data for machine learning – https://github.com/beamandrew/medical-data
- Visualization of research data can provide views that tables and charts cannot, e.g.,
  - Structural modeling of DNA and proteins
  - Behavior of physiological processes
  - Functional mapping – e.g., connecting areas of brain to specific functions

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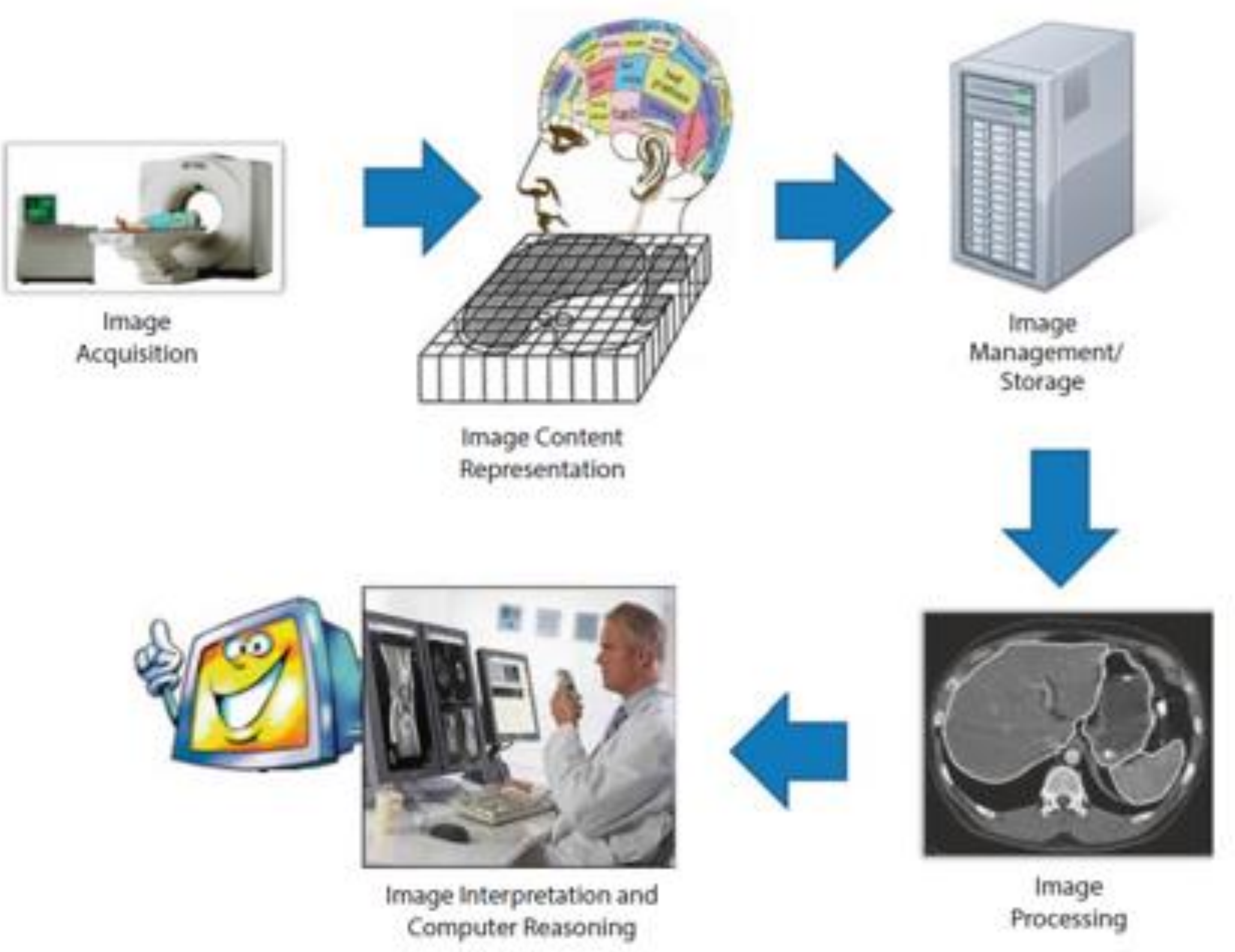
Tasks in Medical Image Informatics



From Shortliffe et al., 2021

Image Modalities

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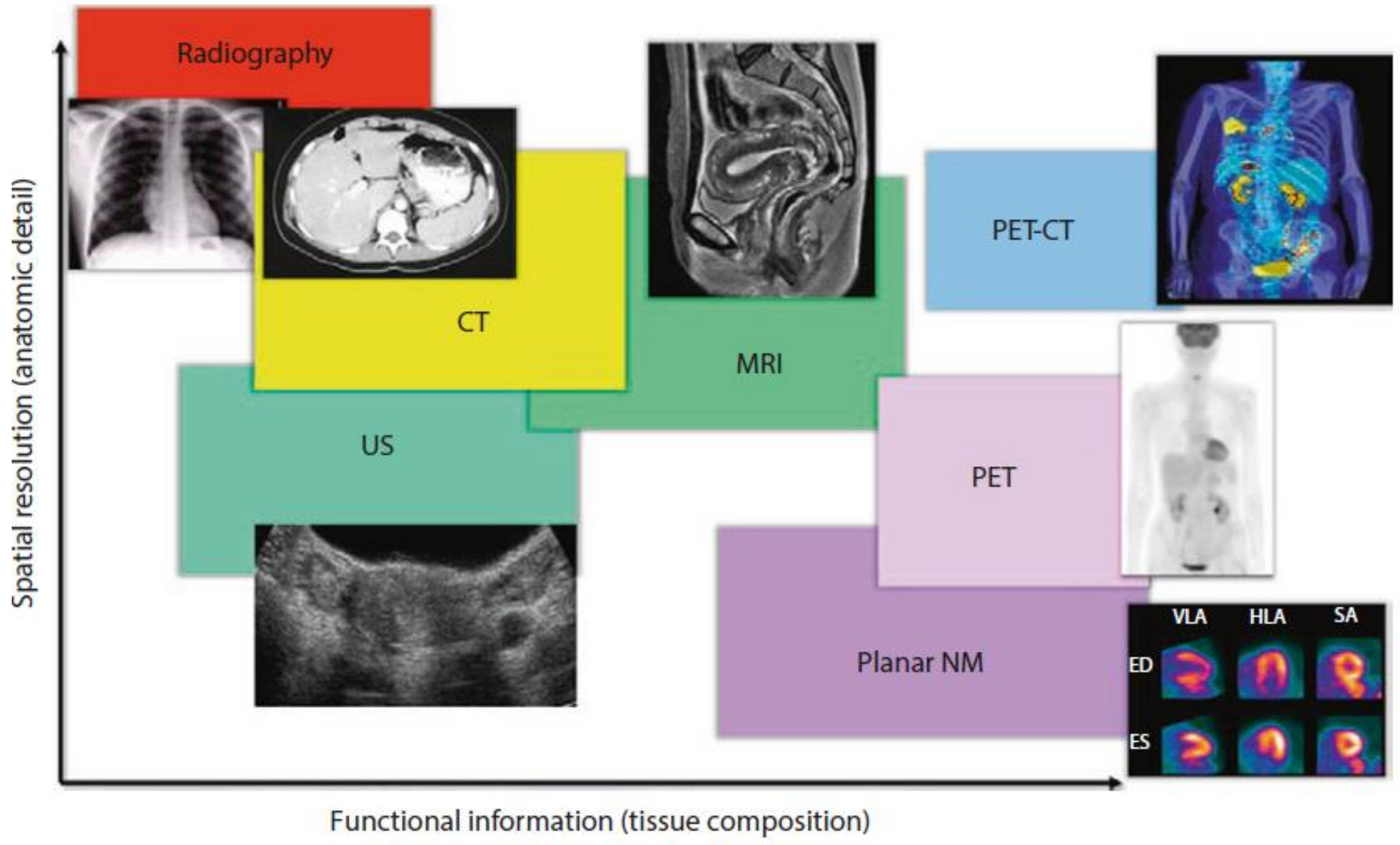
Image Acquisition

- Anatomic structure (anatomic/structural imaging)
- Determine tissue composition or function (functional imaging)
- The most employed imaging technique is conventional radiography—the use of X-ray radiation
- Image Intensities (matrix):
  - Radiation absorption in X-ray imaging
  - Acoustic pressure in ultrasound
  - Radio frequency (RF) signal amplitude in MRI



From Shortliffe et al., 2021

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Anatomic (Structural) Imaging

- Depict the structure of the body the size and shape of organs— and to visualize abnormalities clearly.
- High spatial resolution is required
- A combination of methods or modalities is used to derive both structural/anatomic information as well as functional information.

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Functional Imaging

- Observing changes of structure over time.
- Applications:
  - Ultrasound and angiography show the functioning of the heart by depicting wall motion, and ultrasound doppler can image both normal and disturbed blood flow.
  - Molecular images depict the expression of particular genes on structural images
  - Understanding the cognitive activity in the brain
- Functional brain imaging modalities can be classified as:
  - image-based
  - non-image based

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Functional Brain Imaging

- Positron emission tomography (PET)
- Magnetic resonance spectroscopy (MRS)
- Functional magnetic resonance imaging (fMRI)
- The output of most of these techniques is:
  - A low-resolution 3-D image volume in which each voxel value is a measure of the amount of activation for a given task.
  - The low-resolution volume is then mapped to anatomy guided by a high-resolution structural MR dataset, using one of registration techniques
- **Goal:** to observe the actual electrical activity of the neurons as they perform various cognitive tasks

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Parameters of Image Quality

- Spatial resolution
  - How well can distinguish close points
  - Related to the sharpness of the image;
  - For digital images, measured by pixels per image area
- Contrast resolution
  - How well can distinguish differences in intensity
  - For digital images, measured by bits per pixel
- Temporal resolution
  - Number of images per time sequence
  - Need 30 per second for real-time visualization

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Imaging Modalities

- Complex devices that acquire medical images
- **Visible light:**
  - Earliest medical images
  - Optical imaging, dermatological imaging, retinal imaging
  - It does not allow us to see more than a short distance beneath the surface of the body
- **More recent examples:**
  - Ultrasound Imaging Modality (1960)
  - Magnetic Resonance Imaging (MRI) (1970)
  - Computed Tomography (CT) (1972)
  - Nuclear Medicine Imaging

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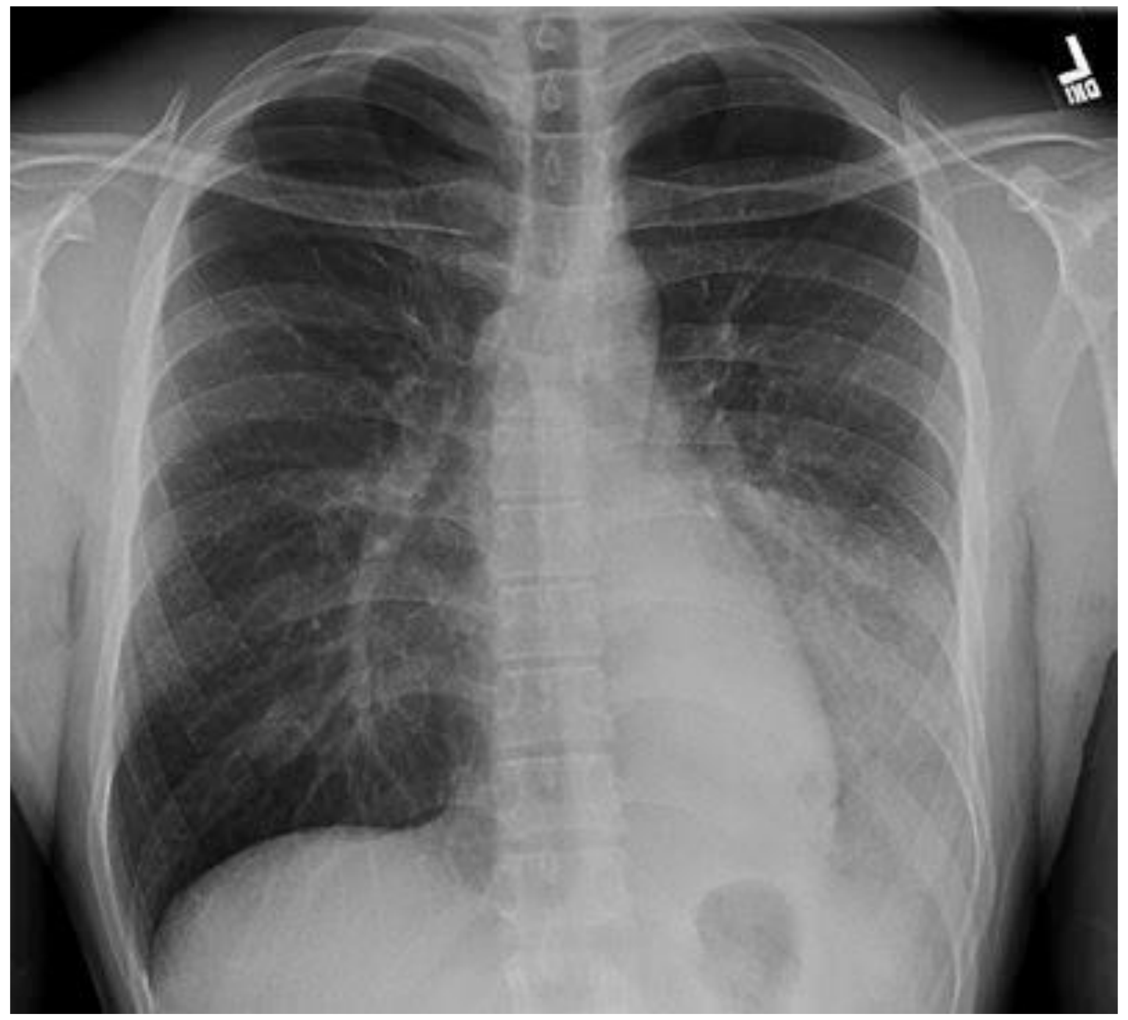
Radiography (or X-ray)

- The **primary modality** used in radiography both for static images and real-time video of the patient.
- X-rays produce different amounts of brightness and darkness – referred to as **image contrast**, the basis for recognizing anatomic structure.
- They have **very high spatial resolution**
- Limited ability to depict physiological function
- Currently analog images replaced with digital images.



A radiograph of the chest (Chest X-ray) taken in the frontal projection. The image is shown as if the patient is facing the viewer. This patient has abnormal density in the left lower lobe. From Shortliffe et al, 2021

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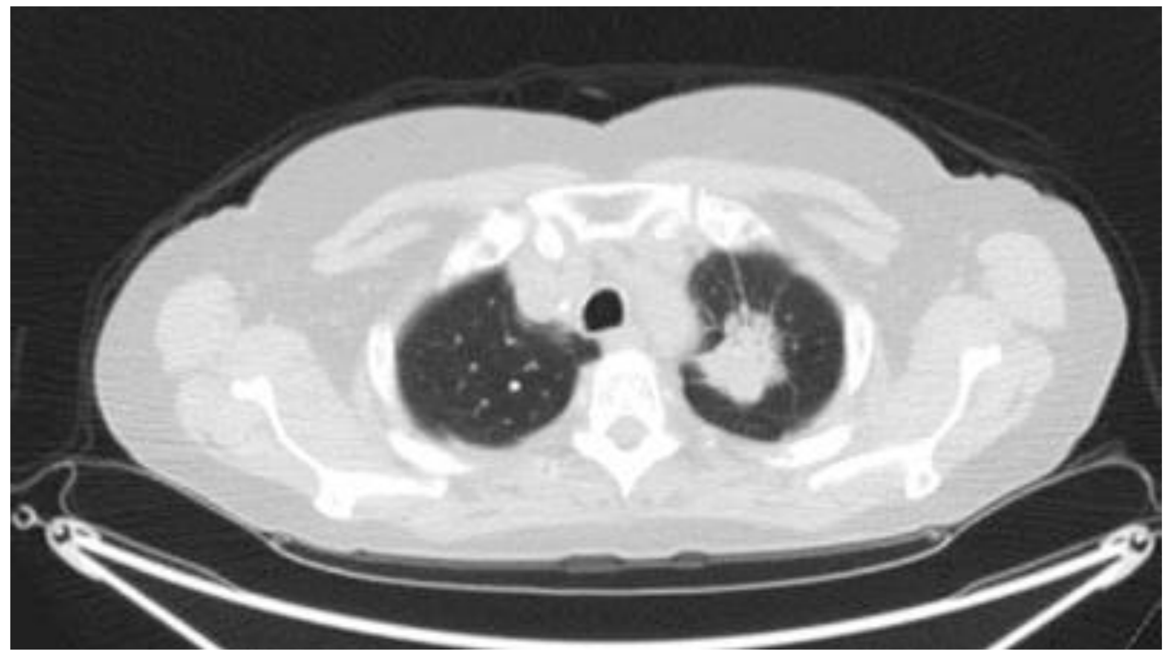
Computed Tomography (CT)

- Uses X-ray to produce cross sectional and volumetric images of the body.
- CT is a computed image **using reconstruction algorithms** to estimate the absolute density at each point of the body.
- The **contrast resolution** and ability to derive functional information of tissues in the body is **superior to radiography.**
- CT has wide applications in medicine, e.g., showing internal injuries and bleeding; locating a tumor, blood clot, excess fluid, or infection; detecting cancer, heart disease, emphysema, or liver masses; guiding biopsies, surgeries.



A radiograph of the chest (Chest X-ray) taken in the frontal projection. The image is shown as if the patient is facing the viewer. This patient has abnormal density in the left lower lobe

From Shortliffe et al.,2021

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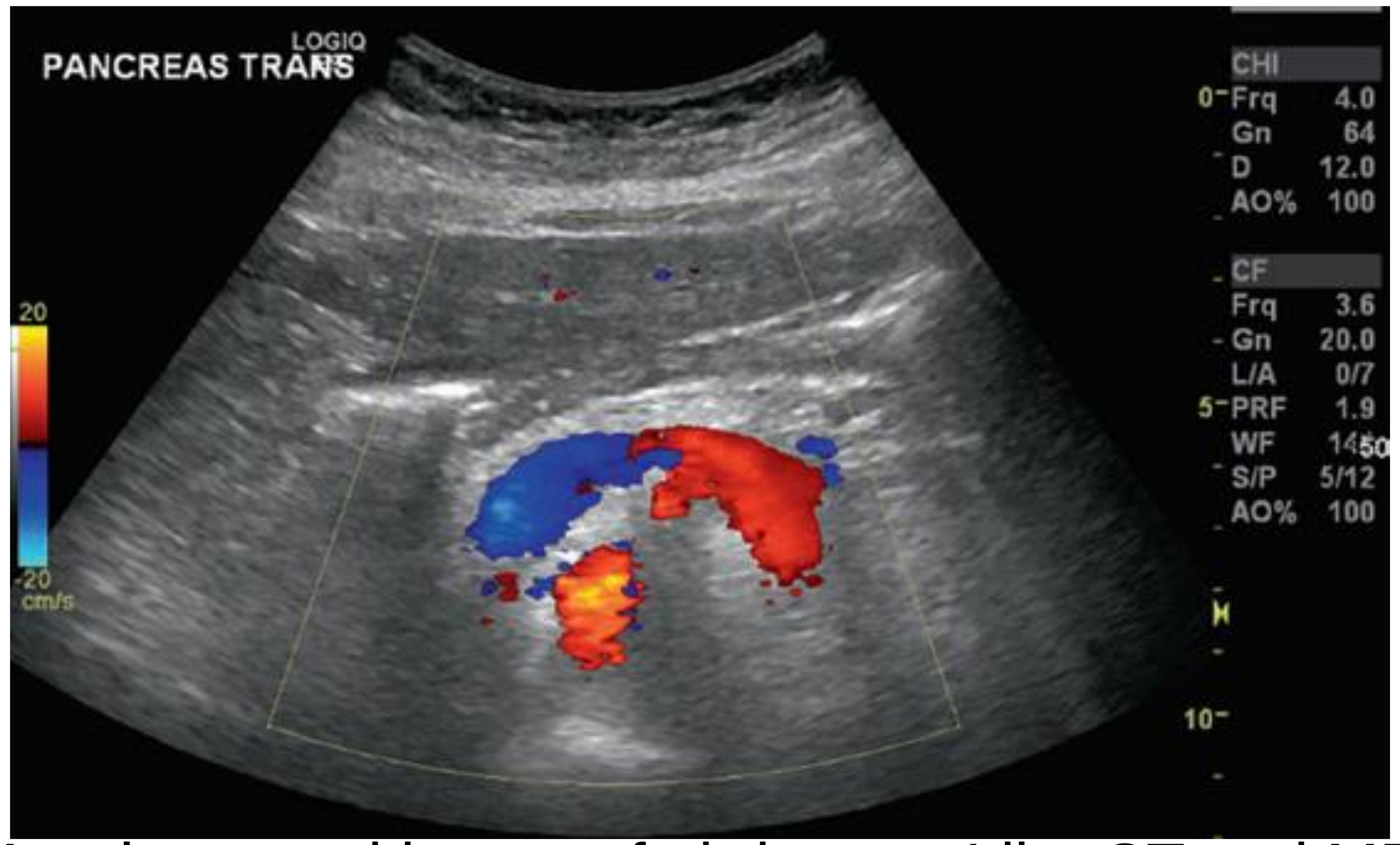
Ultrasound Imaging Modality

- Uses pulses of high-frequency sound waves
- 2D images but recently 3D images can be constructed
- **Low-dimensionality images in contrast to other imaging modalities.**
- **Provides both structural and functional information** (e.g. tissue composition and blood flow)



An ultrasound image of abdomen. Like CT and MRI, ultrasound images are slices of a body, but because a user creates the images by holding a probe, any arbitrary plane can be imaged (so long as the probe can be oriented to produce that plane). This image shows an axial slice through the pancreas, and flow in nearby blood vessels (in color) is seen due to Doppler effects incorporated into the imaging method.

From Shortliffe et al., 2021

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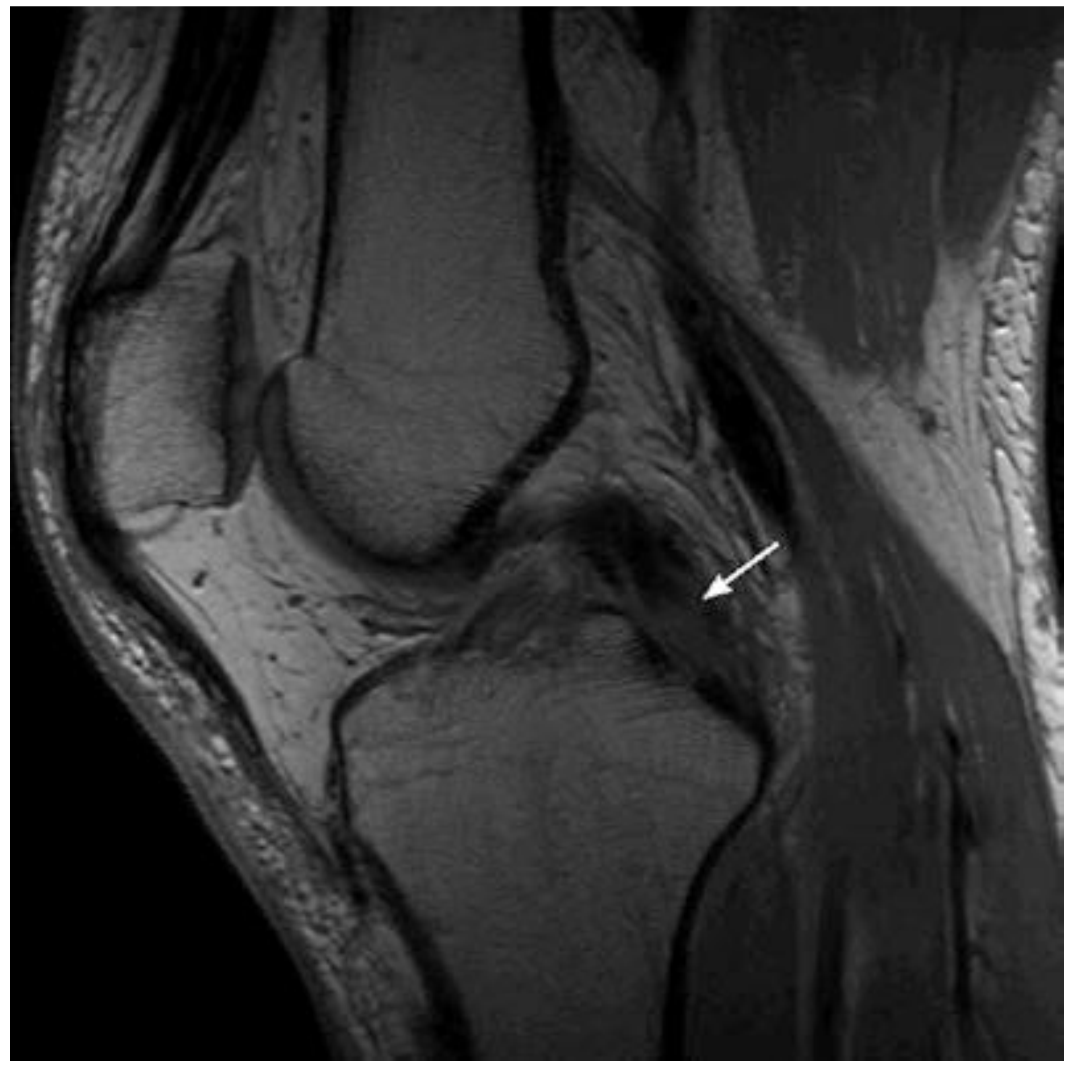
Magnetic Resonance Imaging (MRI)

- Medical images created from nuclear magnetic resonance (NMR) signals using reconstruction algorithms.
- Provides **detailed functional information about tissue** and can be valuable in clinical diagnosis.
- **High spatial resolution**
- MRI has been widely applied to differentiate between white matter and grey matter in the brain and can also be used to diagnose aneurysms and tumors.



An MRI image of the knee. Like CT, MRI images are slices of a body. This image is in the saggital plane through the mid knee, showing in a tear in the posterior cruciate ligament (arrow) From Shortliffe et al., 2021

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Nuclear Medical Imaging

- Usually acquired as projections (detector positioned outside of the patient and collects a projected image).
- **High functional information and low spatial resolution**.
- **Positron Emission Tomography (PET)** computes a cross sectional slice through the patient.
- PET/CT integrates PET scanner and CT with image fusion -> **functional information in PET image and spatial localization of the abnormality in the CT image**.

A PET image of the body in a patient with cancer in the left lung. This is a projection image taken in the frontal plane after injection of a radioactive isotope that accumulates in cancers. A small black spot in the left upper lobe is abnormal and indicates the cancer mass in the upper lobe of the left lung.

From Shortliffe et al., 2021

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Characteristics of Medical Images

- **Images are created by modalities**
- **Medical images possess high dimensionality**. Techniques, such as CT and MRI, produce three-dimensional images, and when dynamic imaging is performed, a fourth dimension—time—is added
- **Medical images vary in quality**
- **Medical images convey physical meaning** (i.e. by measuring the density of human tissue, enables human experts to identify potential abnormalities in human anatomy)
- **Medical images encode relative location and orientation**. Improves the accuracy of disease detection and segmentation.
- **Medical images encode both scale and distance**. Computer-aided diagnosis because the physical size of a lesion influences disease stage, treatment options, and prognosis.

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Characteristics of Medical Images (ctd.)

- **Medical images have sparse and noisy labels**. Partially-annotated dataset
- **Medical images contain quantitative image characteristics:**
  - Intensity value
  - Physical size of pixels—that can be used as additional information to enhance AI/DL performance.
- **Medical images also present qualitative imaging characteristics:**
  - consistent and predictable anatomical structures with great dimensional details—that can provide an opportunity for comprehensive model training.
- **Several characteristics unique to medical images create new challenges, such as:**
  - Data discrepancy: when two or more comparable data sets don't align.
  - Partial, noisy labels, that must be addressed through additional investigation.

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Medical Image Tasks

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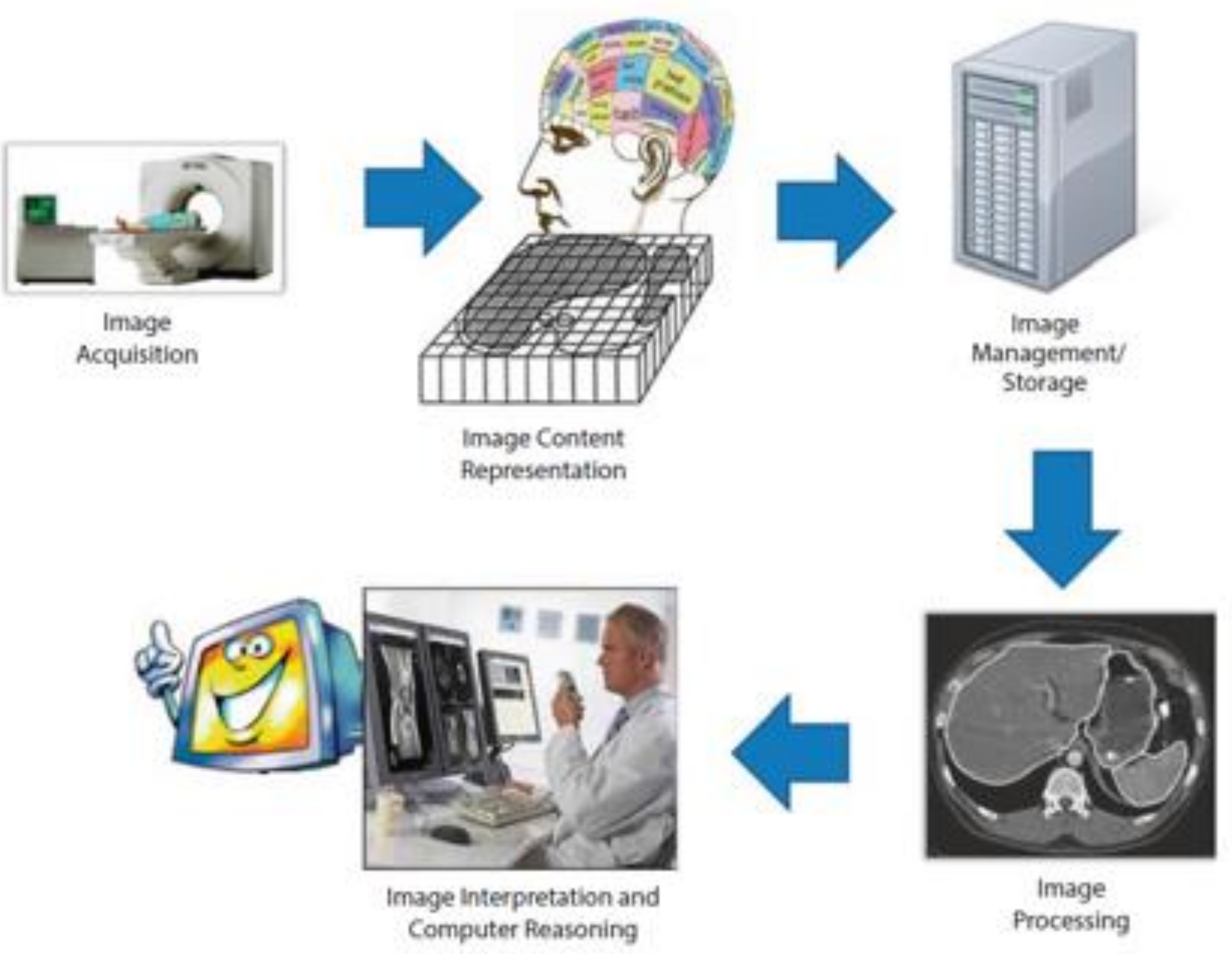
Tasks in Medical Image Informatics



From Shortliffe et al., 2021

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Representations of Image Content

- The visual content of digital images typically is represented:
  - by a 2D-array of numbers
  - each element of the array represents a pixel and
  - each pixel corresponds to a volume element (vexel) in the image
  - 3-D array is required to represent the volume
- Multi-modality data are required for the diagnosis (combination of modalities)
  - A feature vector is combined in a multi-dimensional space to represent the spectrum of image content.
  - Any imaging performed over time (e.g., cardiac echo videos) can be represented by the set of values at each time point.

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Image Compression

- Two categories:
  - Lossless – No resolution lost upon reconstruction
    - Best achievable compression around 2:1-3:1
  - Lossy – Eye less sensitive to certain changes (e.g., hue or color), so can lose some depth of hue with little or no notice
    - Higher levels of compression possible, up to 20:1-30:1 for x-rays and 6:1 for CT scans
    - Also used in common computer images, e.g., JPG

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Image Management

- A key aspect of imaging, especially for those concerned with informatics
- Increasingly fewer centers store images on film
  - Conventional x-rays taken on celluloid film
  - Digital studies, e.g., CT and MRI, optimized for viewing and stored on film
  - Other modalities, e.g., ultrasound and nuclear medicine, also stored on film
- Film storage requires large amount of space

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Picture Archiving and Communications Systems (PACS)

- Systems dedicated to digital radiologic image management
- PACS have substantial system requirements
  - High-resolution acquisition
  - High-capacity storage
  - High-bandwidth networking
  - High-resolution displays

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Messaging Standards for Digital Images

- Digital Imaging and Communications in Medicine (DICOM) standard allows transmission of images across various devices, such as:
  - Acquisition devices
  - Archival systems
  - Interpretation stations
- https://people.cas.sc.edu/rorden/dicom/

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Image Processing and Interpretation

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Image Processing Methods

- Most image processing pipelines and applications generalize from two-dimensional to three-dimensional images.
- Image processing methods:
  - global processing,
  - image enhancement,
  - image rendering/visualization,
  - image quantitation,
  - image segmentation,
  - image registration,
  - image reasoning (classification)

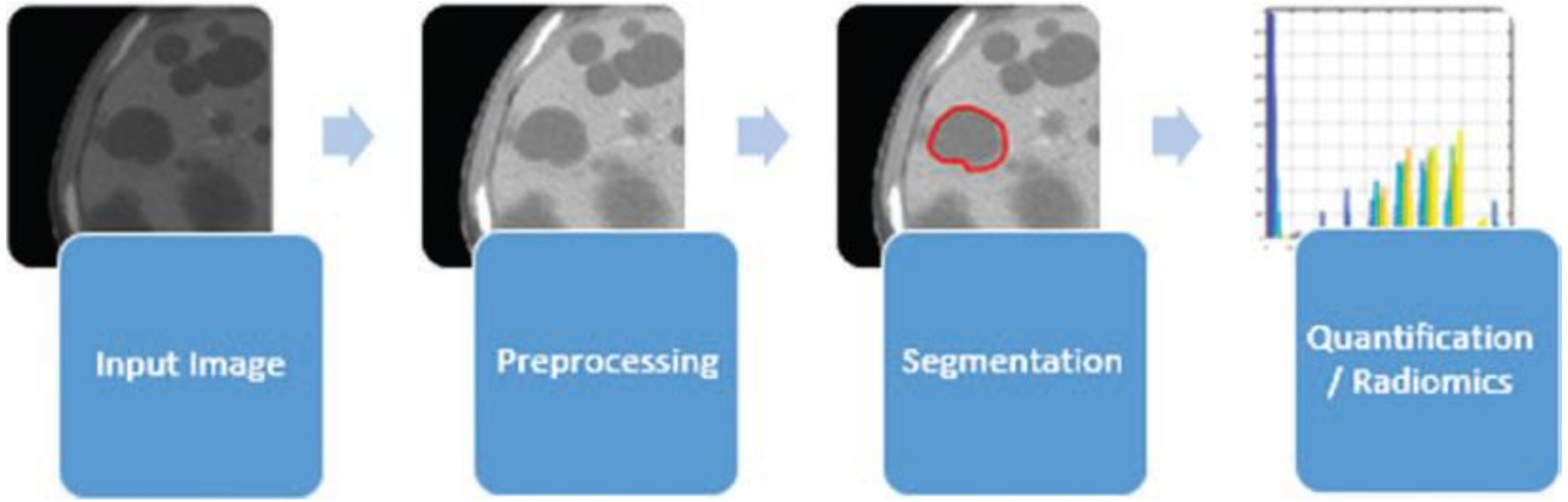

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Image Pre-Processing

- **Global Processing:** involves computations on the entire image
- Change the pixel values to produce an overall enhancement or desired effect on the image:
  - histogram equalization
  - convolution and filtering
- **Image Enhancement:** use global processing to improve the appearance of the image for human visualization or for further analysis by the computer.
- **Image Quantitation:** the process of extracting useful numerical parameters or deriving calculations from the image
  - used as features in automated classification methods

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Image Segmentation

- Automatically partition the image into different regions that might correspond to:
  - anatomically meaningful structures, such as organs or parts of organs
  - an abnormal change in the structure of an organ
- Popular segmentation techniques can be:
  - region-based Vs. edge-based methods
  - knowledge-based Vs. data-driven methods
  - combined methods.
- Segmentation can be regarded as an unsupervised clustering task in the high-dimensional feature space.

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Image Registration

- Process of transforming different sets of data into one coordinate system
- Image registration algorithms
  - **Intensity-based:** Compare intensity patterns in images via correlation metrics
  - **Feature-based:** Find correspondence between image features such as points, lines, and contours.
- Single or multi-modality registration
  - Multi-modality registration register images coming from different scanners
- Image similarity measures are used in medical images registration
  - Depends on the image modality
  - Quantifies the degree of similarity between intensity patterns in two images
  - Similarity of images of the same patient at different time points

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Radiomics/Quantification

- Extract a set of quantitative features from radiology images
- Based on computer vision techniques
- Used as input features in ML classifiers
- Clinical outcome labels are available in supervised learning
- Identification of quantitative imaging indicators that predict important clinical outcomes, e.g. prognosis and response or resistance to a specific cancer treatment.

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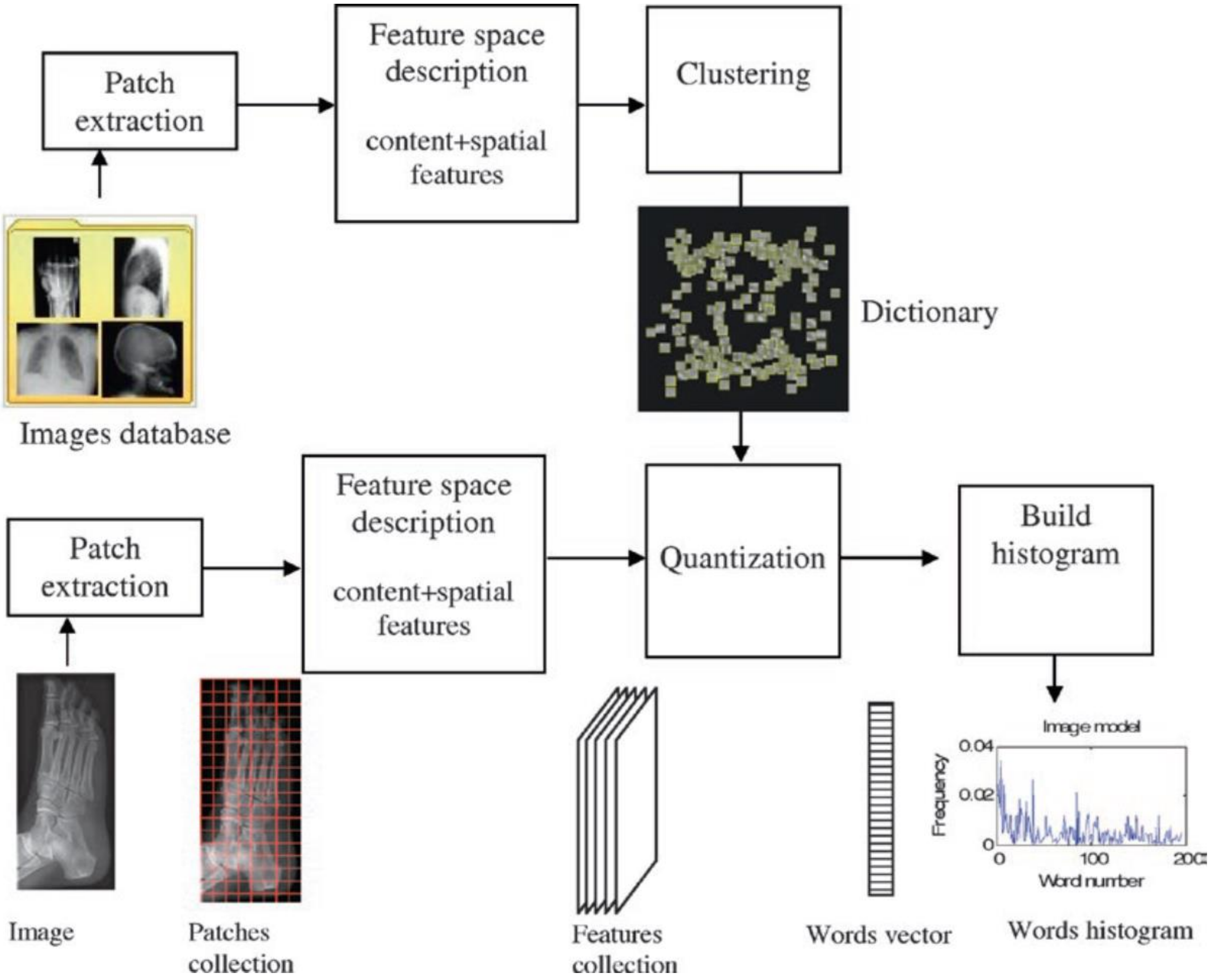
Unit 6



A block diagram of the patch-based image representation. A radiographic image is shown with a set of patches indicated for processing the image data. Subsequent image processing is performed on each patch, and on the entire set of patches, rather than on individual pixels in the image. A dictionary of visual words is learned from a large set of images, and their respective patches. Further analysis of the image content can then be pursued based on a histogram across the dictionary words.

From Shortliffe et al.,2021

Image Interpretation

- The physician has direct impact on the clinical care process
  - by rendering a professional opinion as to whether abnormalities are present in the image and the likely significance of those abnormalities.

- Decision-support systems (reasoning –inference)
  - Probabilistic methods i.e. Bayesian networks
  - Knowledge-based computer reasoning using ontologies as the knowledge source to process the image content and derive inferences from them
  - Disease prediction without or with additional clinical data

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AI/ML in Medical Images

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AI on Medical Images – Main Steps

- Feature Extraction
- (Feature Selection)
- Decision Making

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Deep Learning in Medical Images

- Since 2012, tremendous progress due to the high-performance and computational power resurrected deep learning in image recognition.
- One of the greatest obstacles is the **lack of annotated datasets**.
  - ➢ Annotating medical images is time-consuming and requires limited and costly specialized skills.
- A breakthrough occurred in 2016 when **transfer learning** was first utilized to mitigate the data requirements.
  - ➢ The idea was to transfer the knowledge from a source domain (with a large-scale image dataset) to a target domain (where only limited images are available).
- In 2019, Zhou et al., developed generic pre-trained models, enabling models to learn visual features directly from 3D volumetric medical images without any human annotation.

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Convolutional-Neural Networks (CNN) for Medical Imaging Classification

The convolution filters automatically detect relevant image features:

- lines or circles that may represent straight edges (such as for organ detection)
- circles (such as for round objects like colonic polyps), and then
- higher order features like local and global shape and texture.

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AI/DL Applications in Medical Image Informatics

Organ System	Applications
Breast	Detection of cancer: breast density assessment
Neurologic	Detection of hemorrhagic brain confusion, white matter lesion tracking in multiple sclerosis, tumor identification
Pulmonary	Lung nodule detection Pulmonary embolism detection Pneumonia detection Chronic Obstructive Pulmonary Disease Quantification
Head	Interpretation of CT and MRI brain images
Abdominal	Colonic polyp detection

From Shortliffe et al, 2022, Chapter 12

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Computer-aided Diagnosis (CAD) for Pulmonary Embolism

- Provides illustrative example of how these methods have been integrated into clinical image interpretation..
- Pulmonary embolism (PE) is a condition in which a thrombus travels to the lungs, often from a lower extremity venous source, producing a blockage of the pulmonary arteries within the lungs.
- Computed tomography pulmonary angiography (CTPA) is the primary modality used to detect PE.

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Computer-aided Diagnosis for Pulmonary Embolism (ctd.)

- Image interpretation by radiologists is time-consuming
- Pulmonary nodules are commonly encountered using chest imaging
- Early detection of lung cancer from chest CT images using AI/DL methods has been shown to reduce cancer-related mortality.

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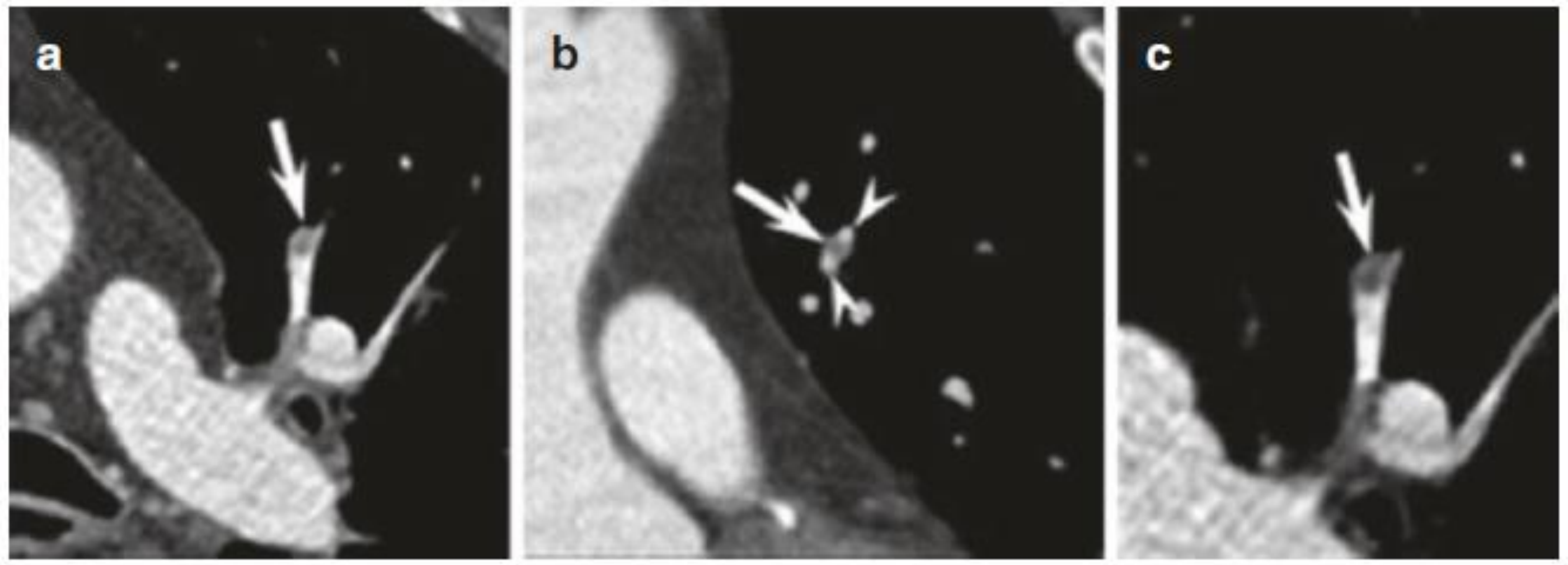
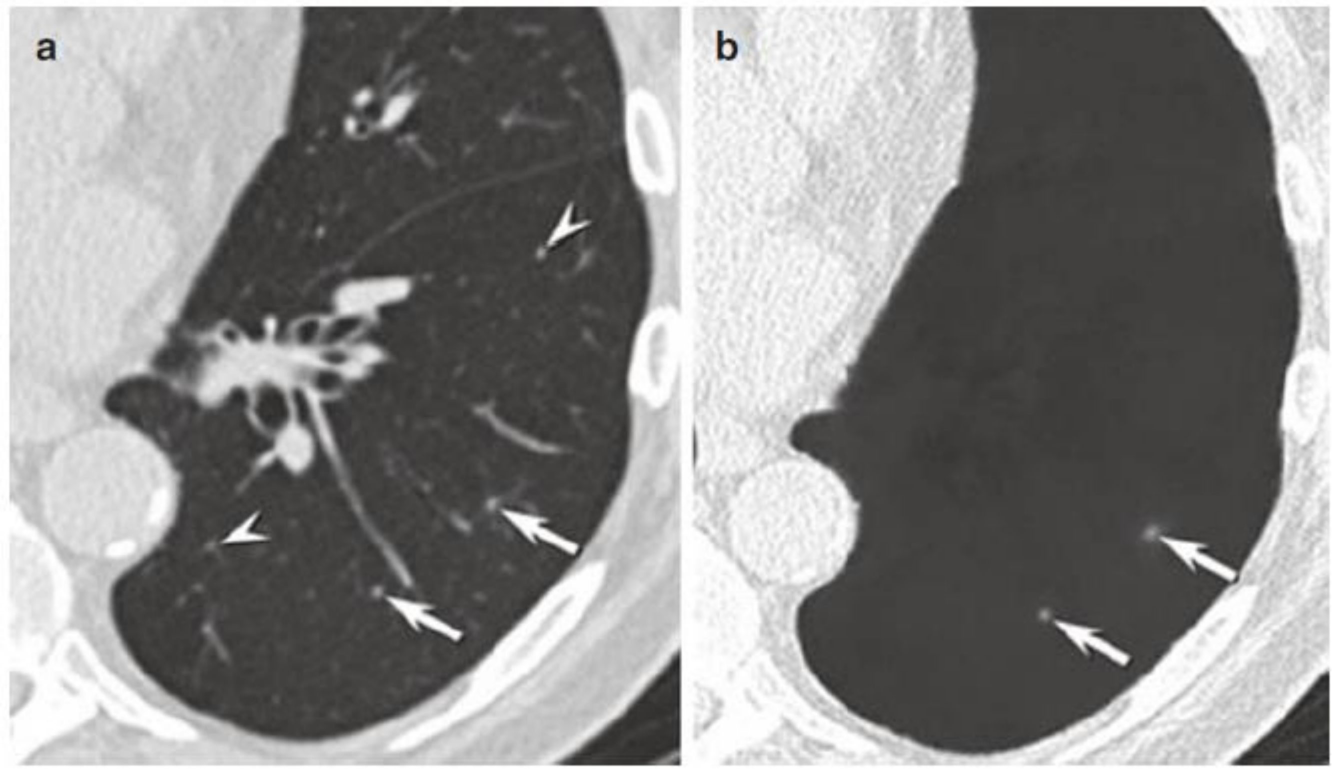
Computer-aided Diagnosis for Pulmonary Embolism



False-positive pulmonary embolism detection by an AI/DL model. (a) Axial enhanced CT image shows a “filling defect” (arrow) immediately adjacent to a left upper lobe pulmonary artery, closely resembling PE. (b) Coronal CT image (orientation of this image as if the observer is facing directly at someone) shows the apparent filling defect (arrow) is positioned between two pulmonary arteries (arrowheads)- this location and appearance are typical of lymph node tissue. (c) The output of the automated PE detection by the AIDOC medical system shows that the finding was flagged by the system as PE, representing a false-positive diagnosis



(**a**) The axial unenhanced chest CT displayed in lung windows shows two small left lower lobe pulmonary nodules (arrows). Note how these small nodules very closely resemble pulmonary vessels (arrowheads); this close resemblance can easily result in diagnostic errors, particularly inadvertently overlooking small nodules that could reflect potentially precancerous or cancerous lesions. (**b**) The output from AI/ML algorithm (ClearRead CT, Riverain Technologies, Miamisburg, OH) shows that the normal pulmonary vessels have been “suppressed” and are no longer visible, which clearly exposes the two small pulmonary nodules (arrowheads)

From Shortliffe et al., 2022

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Technical Barriers

- Medical image annotation is performed primarily by human experts, who manually annotate the existence, appearance, and severity of diseases in each medical image using appropriate software tools.
- Without large, annotated datasets, deep learning often results in algorithms that perform poorly and lack generalizability for new data.
  - perfectly-sized and carefully-annotated datasets are rarely available for training deep learning models, especially for medical images.
- The lack of clinical context other than images, and the non-standardized acquisition of images and annotations across hospitals.

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Emerging Techniques

- **Continual learning** capability of AI/DL incrementally improves the algorithm through fine-tuning.
  - ➢ Learners adaptively use new data to update their knowledge sets.
- **Active learning** – a human-in-the-loop procedure. Rather than randomly sampling, active learning aims to find the most representative data and annotate them first.
- The **representation learning** capability of AI/DL alleviates automatic feature engineering for specific medical conditions.
  - ➢ The consistent and recurrent anatomy embedded in medical images empowers AI/DL with a generic visual representation.

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Conclusions

- Computer-aided diagnosis aims to develop automated algorithms for gleaning clinically useful information from images to support clinical decision-making and to facilitate precision medicine.
- Physicians should become familiar with the principles and potential applications of AI/DL methods,
- The output from CAD systems should be used as a “second opinion”, at the end, the physicians will eventually must make the final decisions.

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SUMMARY

- Imaging modalities differ based on the image source (scanner):
  - X-ray, MRI, CT, Ultrasound and Nuclear images
  - The characteristics of image quality i.e. spatial resolution, contrast resolution and temporal resolution vary between different modalities.
- Different pre-processing methods are used such as image segmentation, image compression and image registration.
- Some of the modalities produce 2-D images where most of them produce 3D images.
- AI/DL methods have many applications in medical informatics in different medical domains.
- After pre-processing, set of features is extracted using different computational methods:
  - In radiology images, radiomics is the set of computational features
  - The extracted features are the input training data for a ML classifier
  - Deep Learning automatically extract medical image features

SUMMARY

- One of the main challenge for applying AI/DL methods in medical image informatics is the lack of annotated data.
- Annotating medical images needs human specialized expertise and it is time-consuming and costly.
- Transfer learning has been used in DL to learn from semi-annotated data

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Discussion

- What constitutes reliable evidence that computers outperform humans in image medical informatics?
- Do you think that a CAD system can eliminate the need for a radiologist? Consider the advantages/challenges of applying AI/DL in medical image informatics to answer this question.
- How can someone choose the best image modality for an application domain?

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