Biomechanics of the musculoskeletal system

Tissue and medical imaging

Vincent Stadelmann

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Personal introduction

Physicist / Orthopedic Bioengineer / Preclinical scientist / Clinical researcher
Consultant / Founder of EasyIPL


EPFL

UC Davis

NIBR

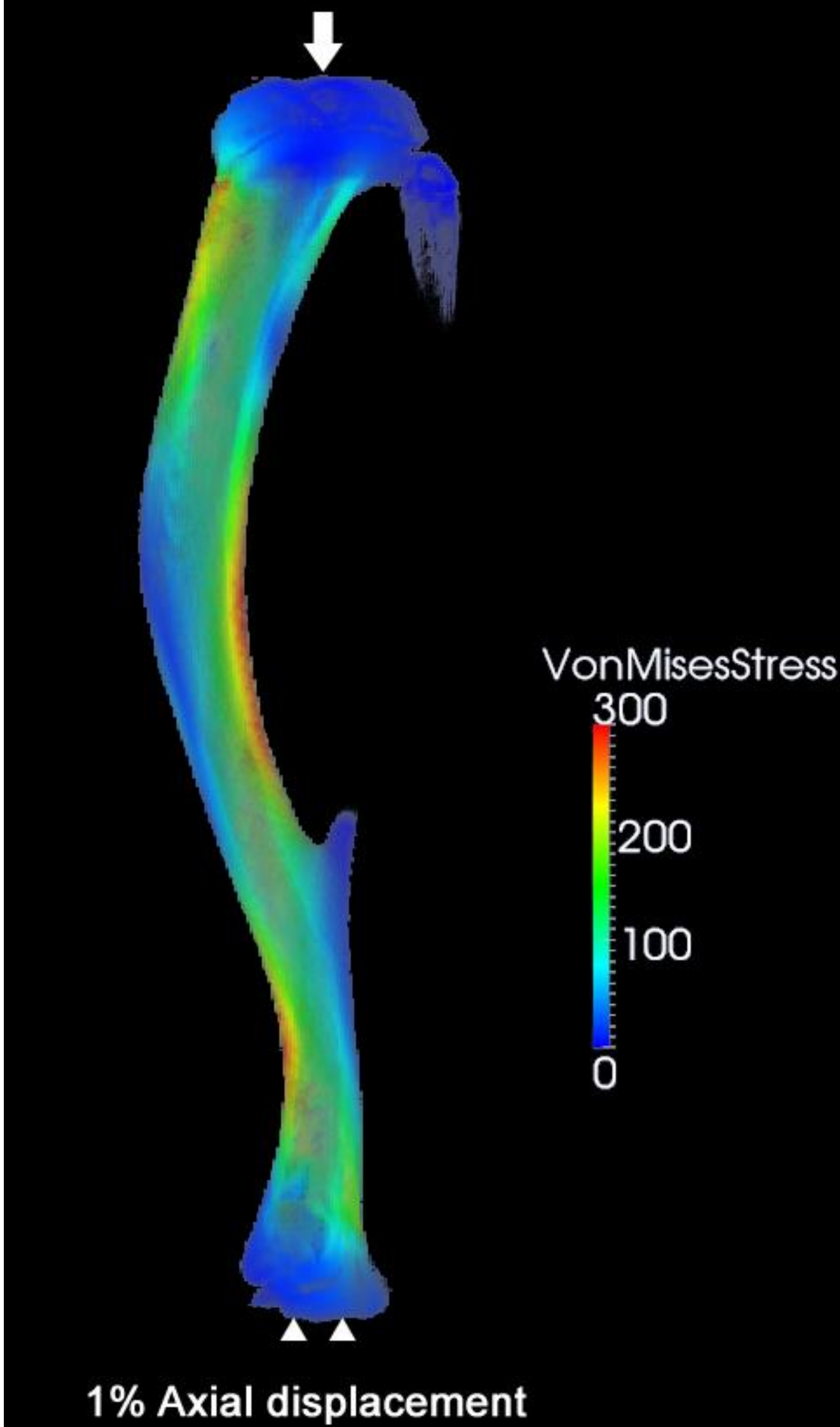

U of Calgary


AO Foundation

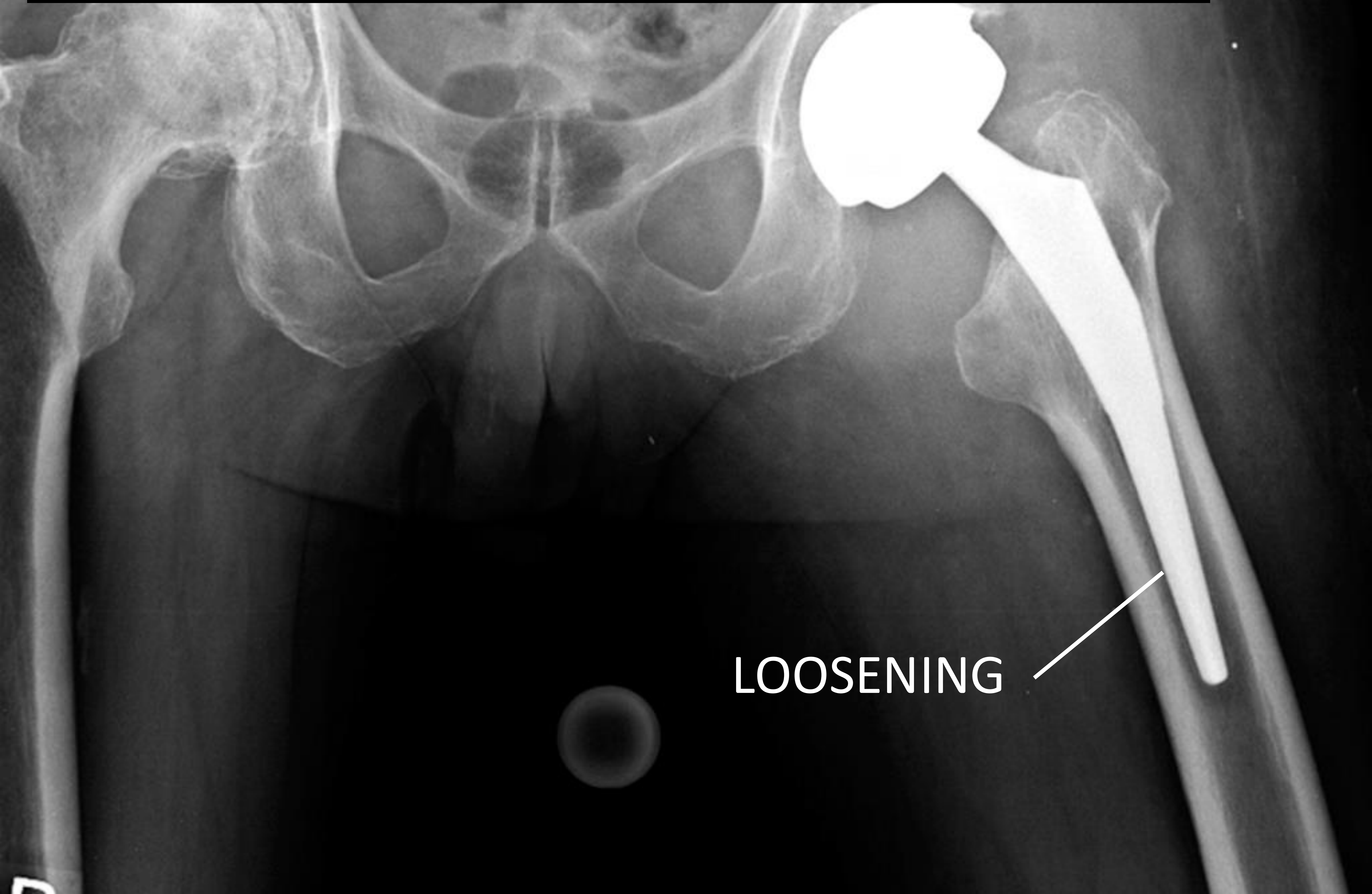
SCANCO Medical


Schulthess Klinik

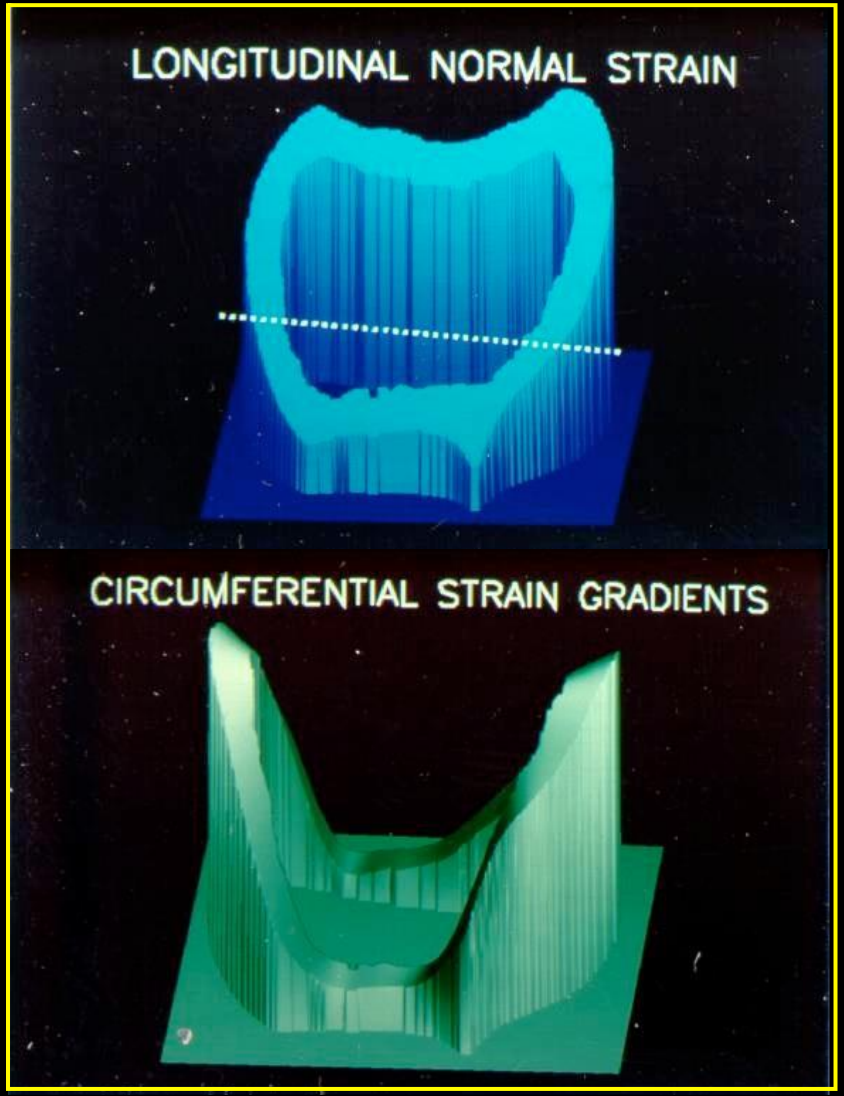
Why is there an "imaging" module in a biomechanics course??



Clinical:
Diagnostic imaging to identify biomechanical problems

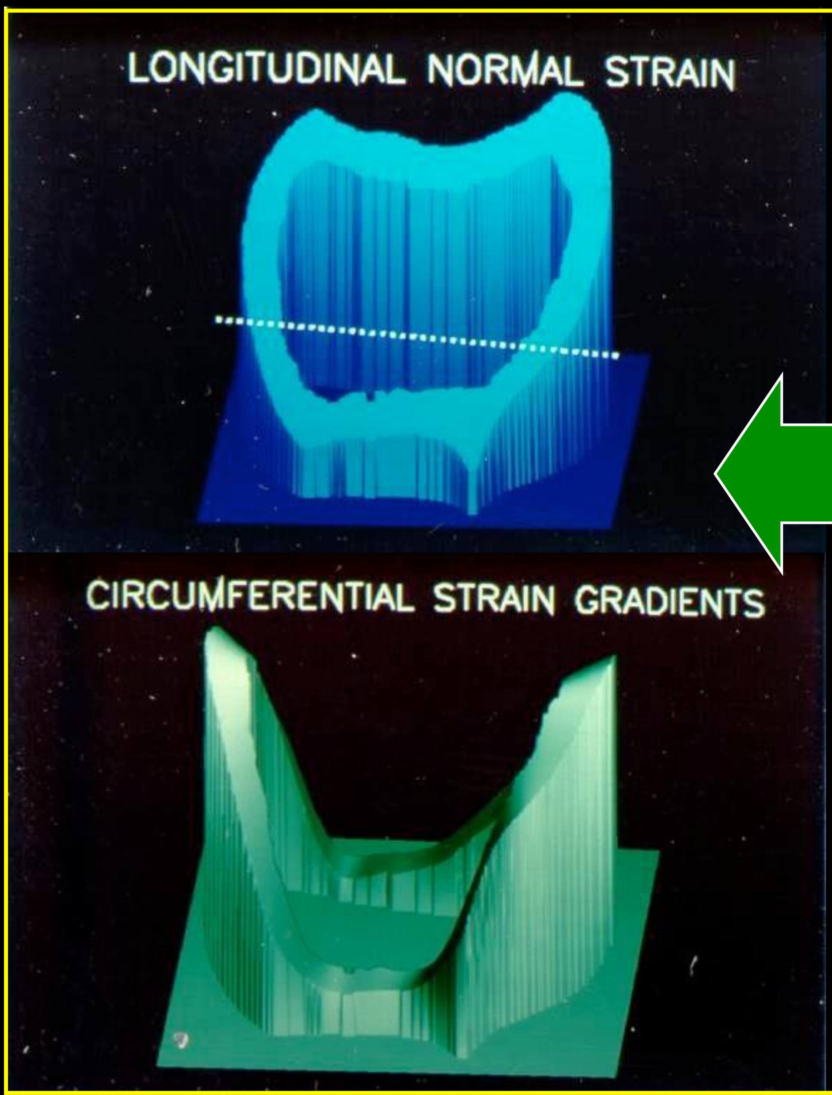


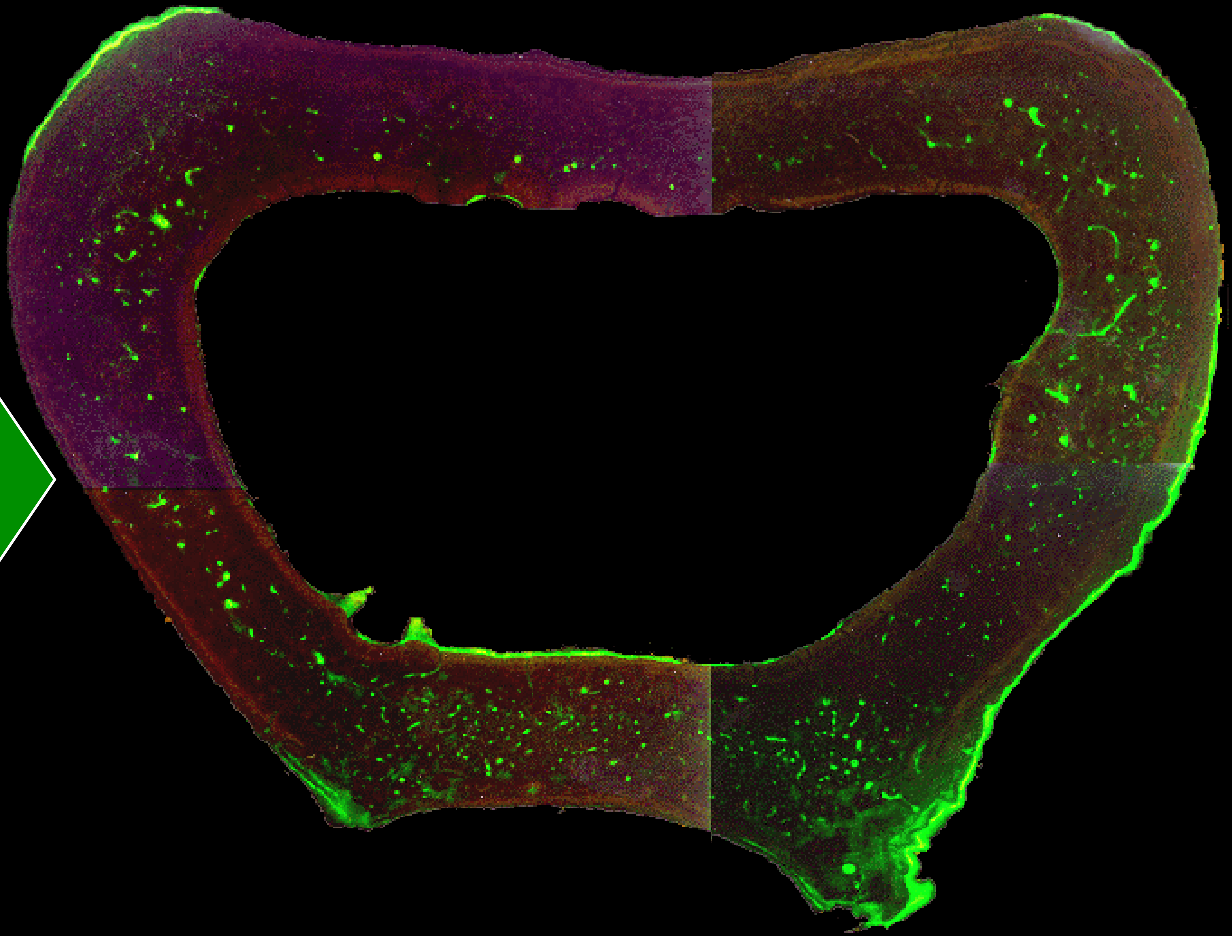
Experimental biomechanics:
correlate mechanics with biology



Zernicke, Judex et al.

Bone cells activity colocalize with high strains

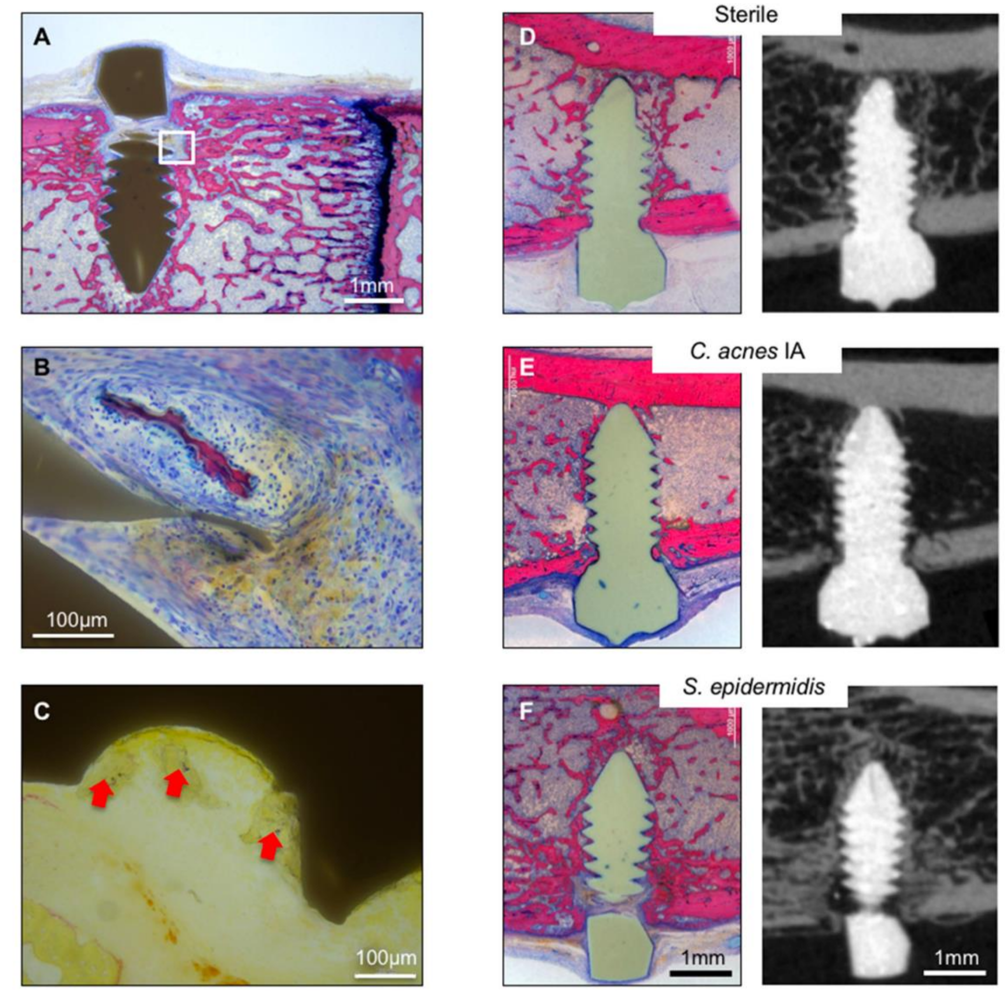


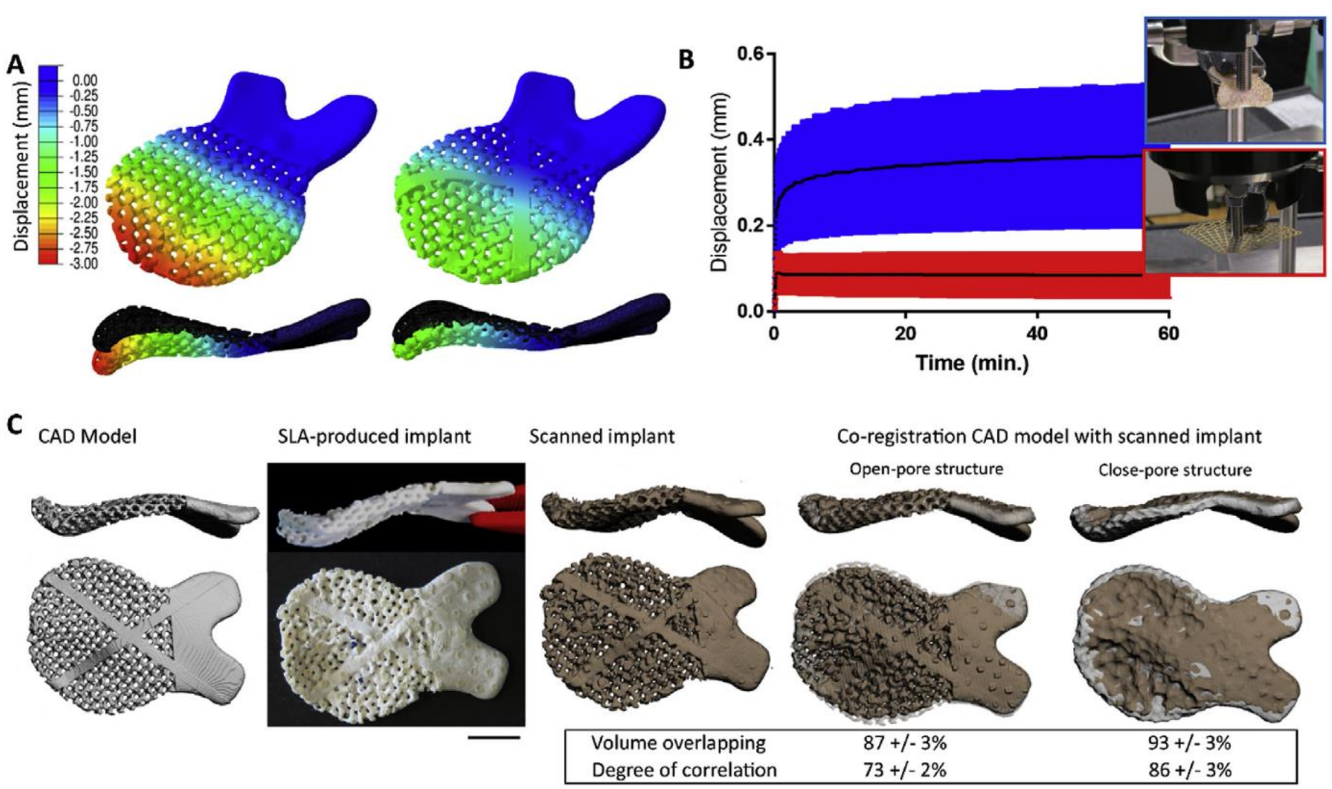


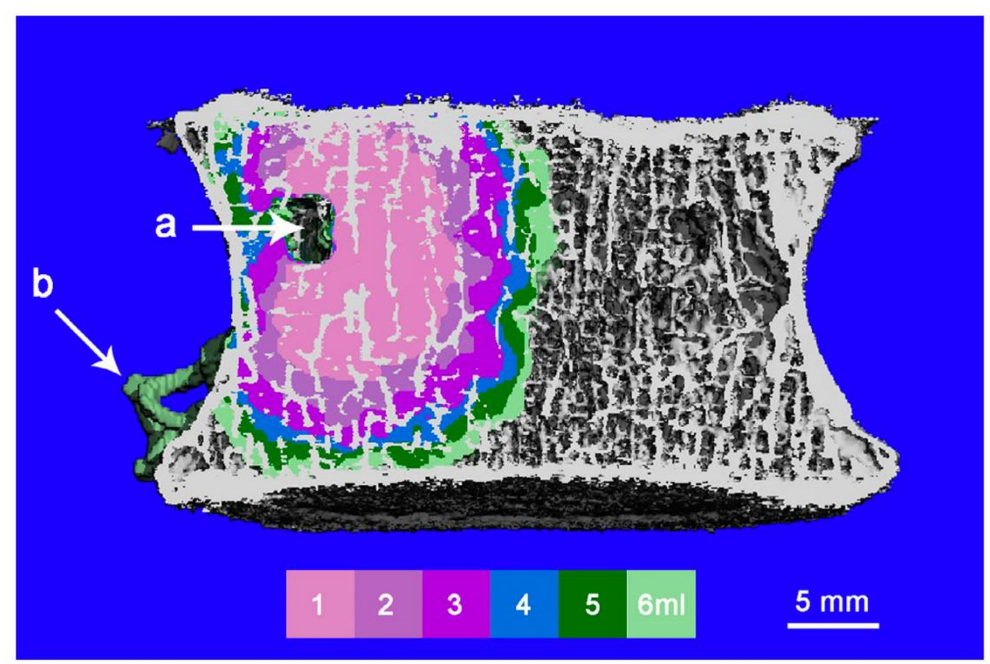
Mid diaphyseal section

Zernicke, Judex et al.

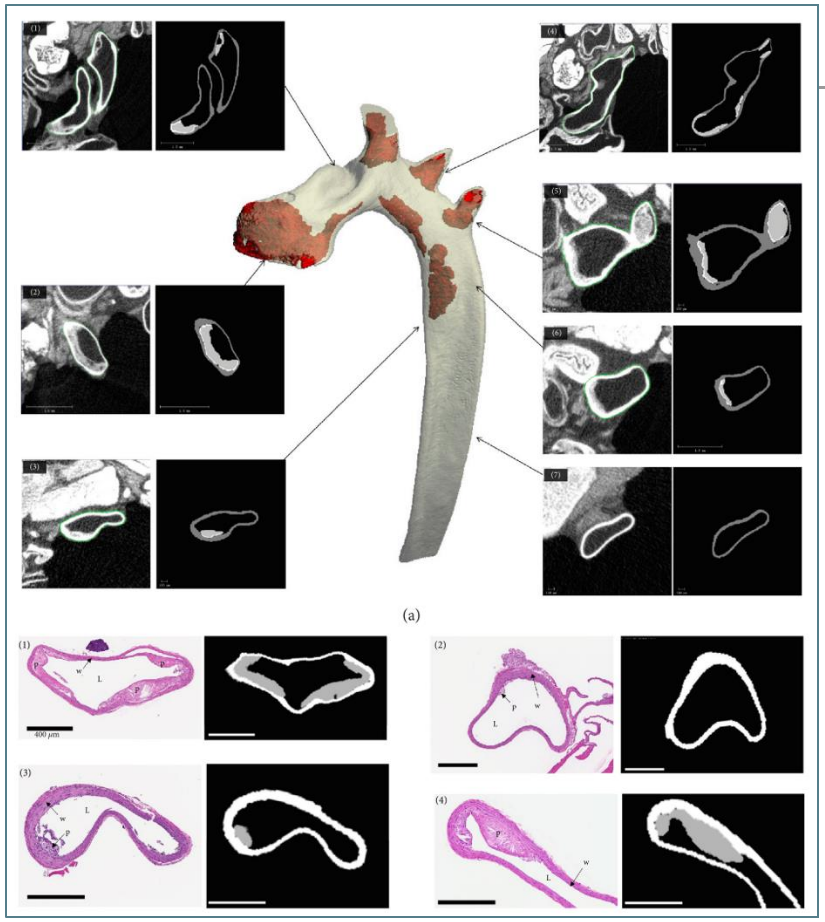
Life of a biomechanics researcher…

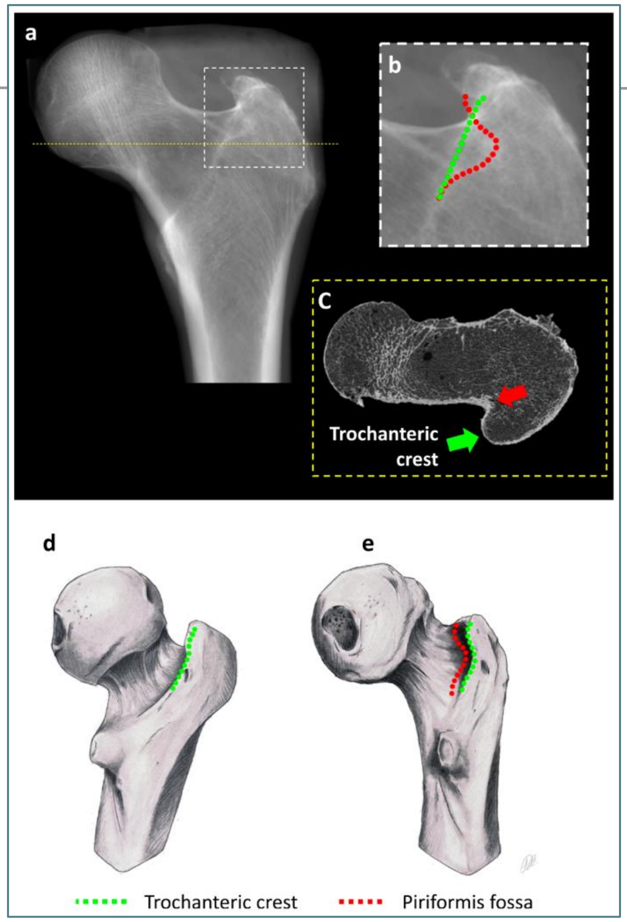


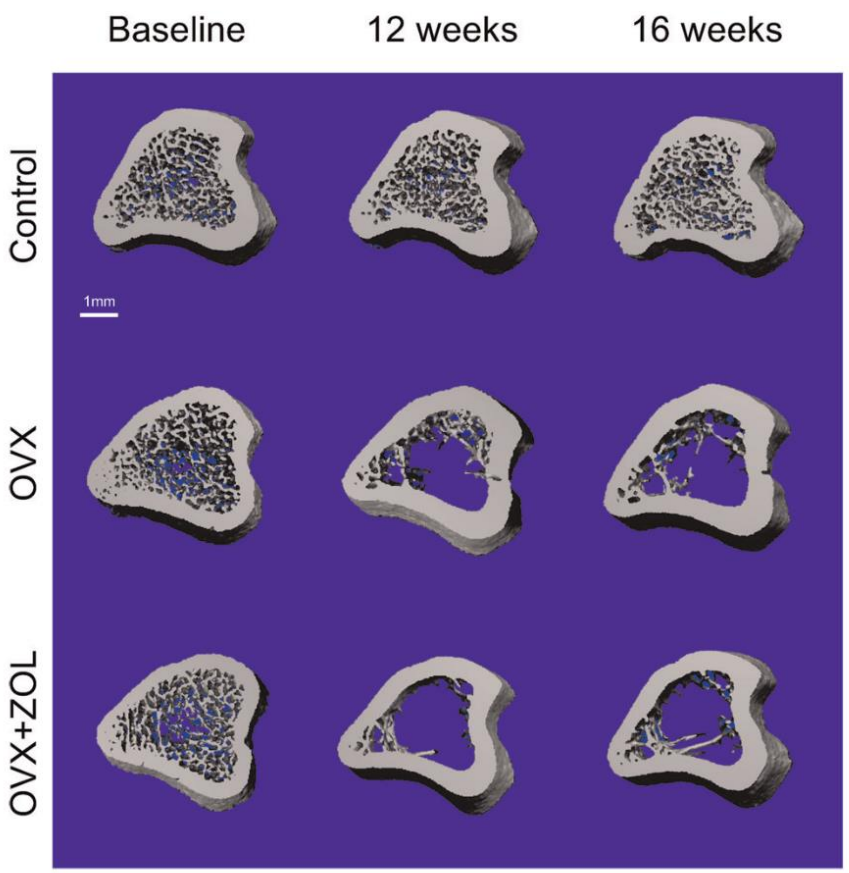


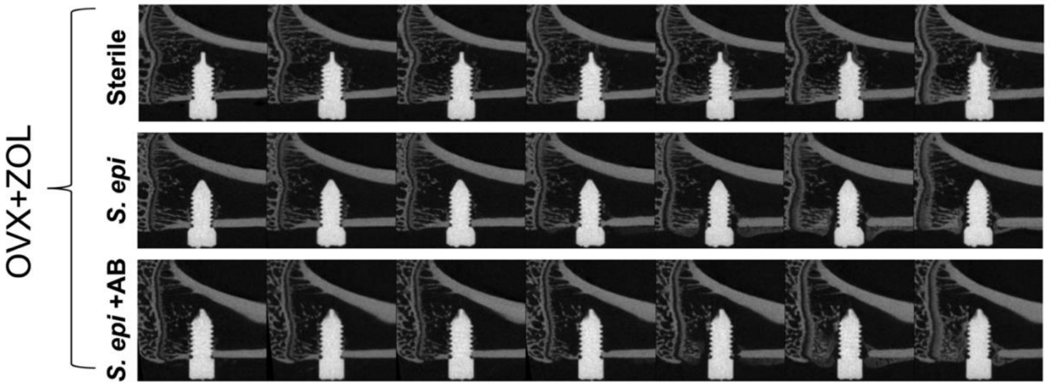


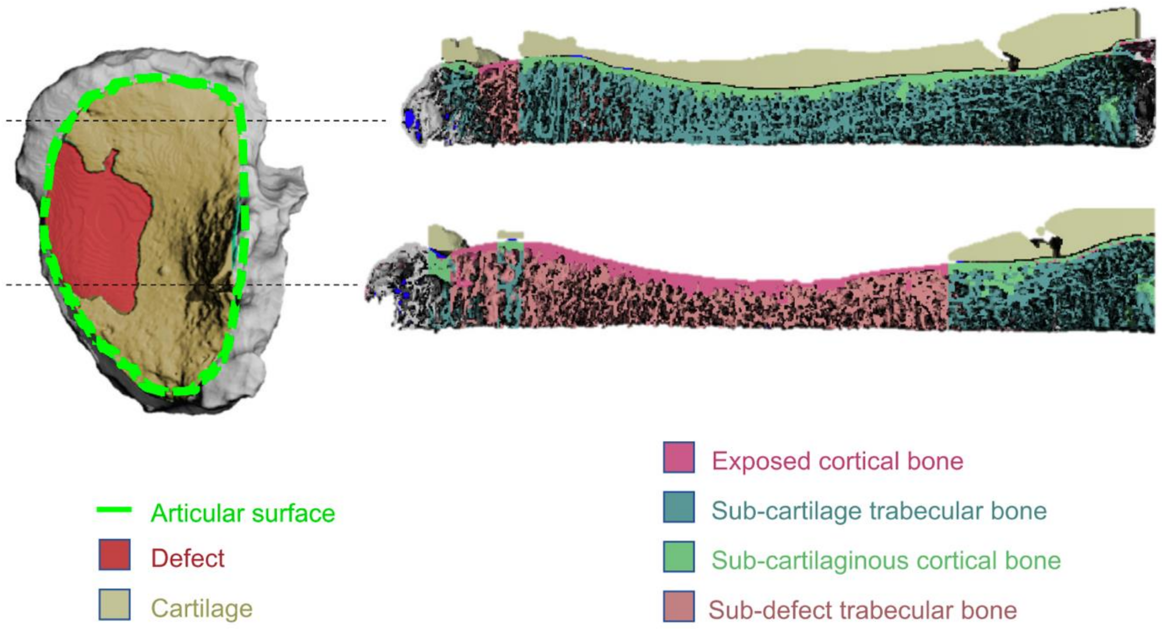
Life of a biomechanics researcher…











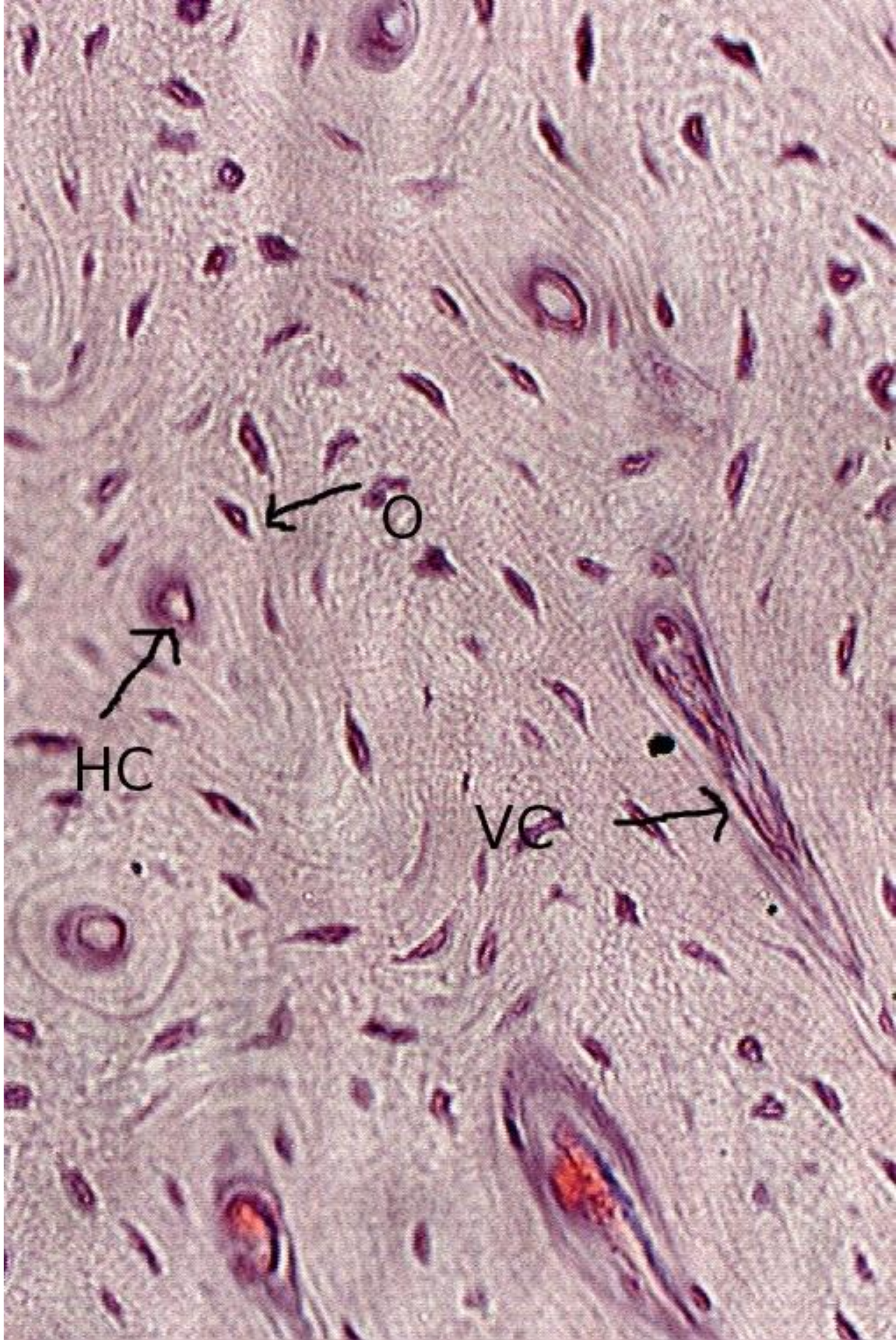
Content of this lecture

- Image acquisition
    - Light microscopy
    - X-ray radiography
    - Computed tomography
    - (MRI is outside the scope of this presentation)
- Limitations and artefacts
- Image evaluation and processing
    - Evaluation reliability / reproducibility
    - Image segmentation/transformations

Learning objectives

- Be able to
  - **Describe** different imaging modalities
  - **Describe** the acquisition systems
  - **List** the main limitations/artefacts of the different systems
  - **Compute** the x-ray projection of a generic image (a numerical matrix)
  - **Compute** back-projection algorithms of a generic image
  - **Describe** measurement reliability concept

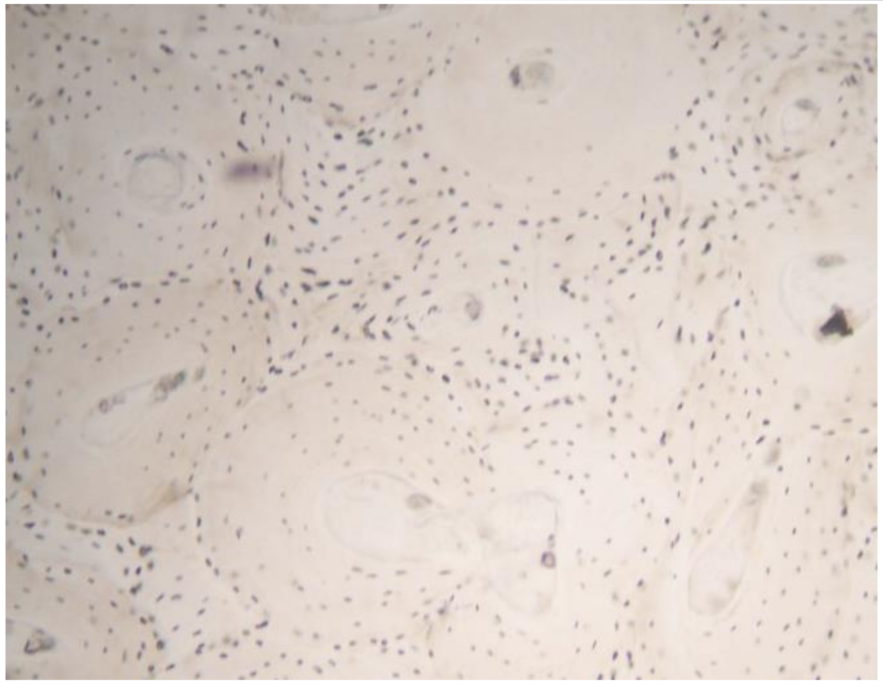
Microscopy/ Histology



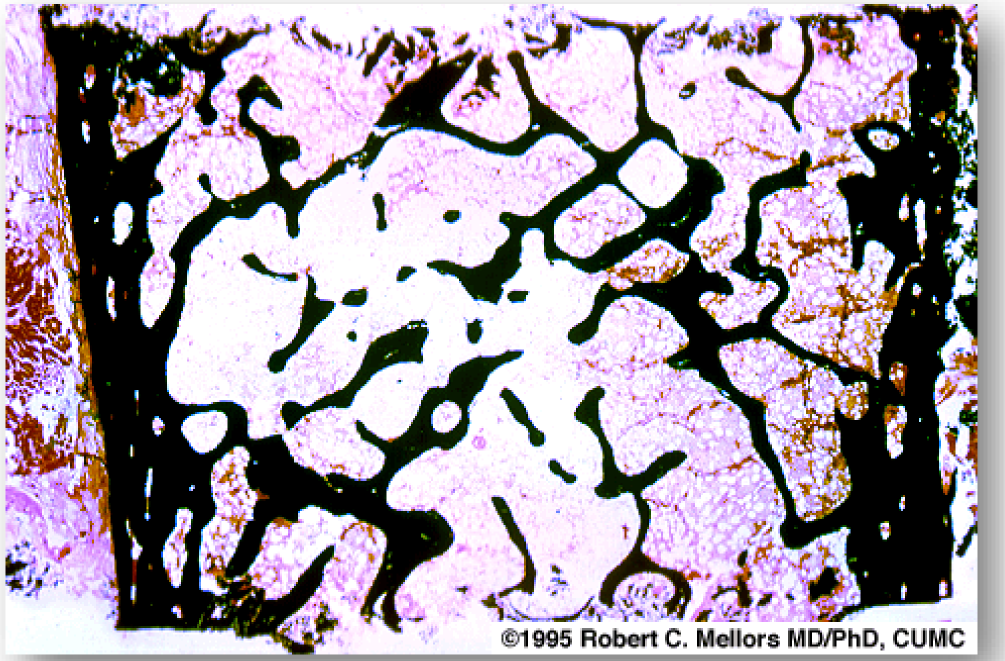
Thin bone section under light microscopy.

A slice of bone under light microscope

Uses visible light
Lenses to magnify images
Resolution of 200nm possible
Specimen must let light transmit



No staining



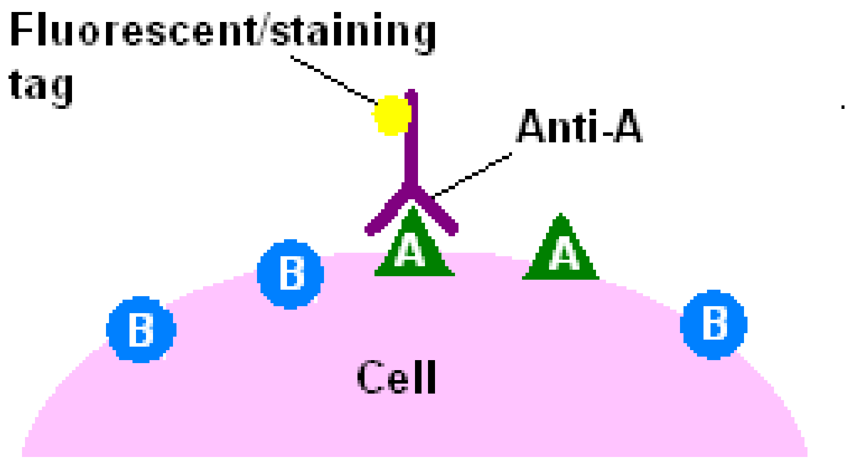
Von Kossa staining

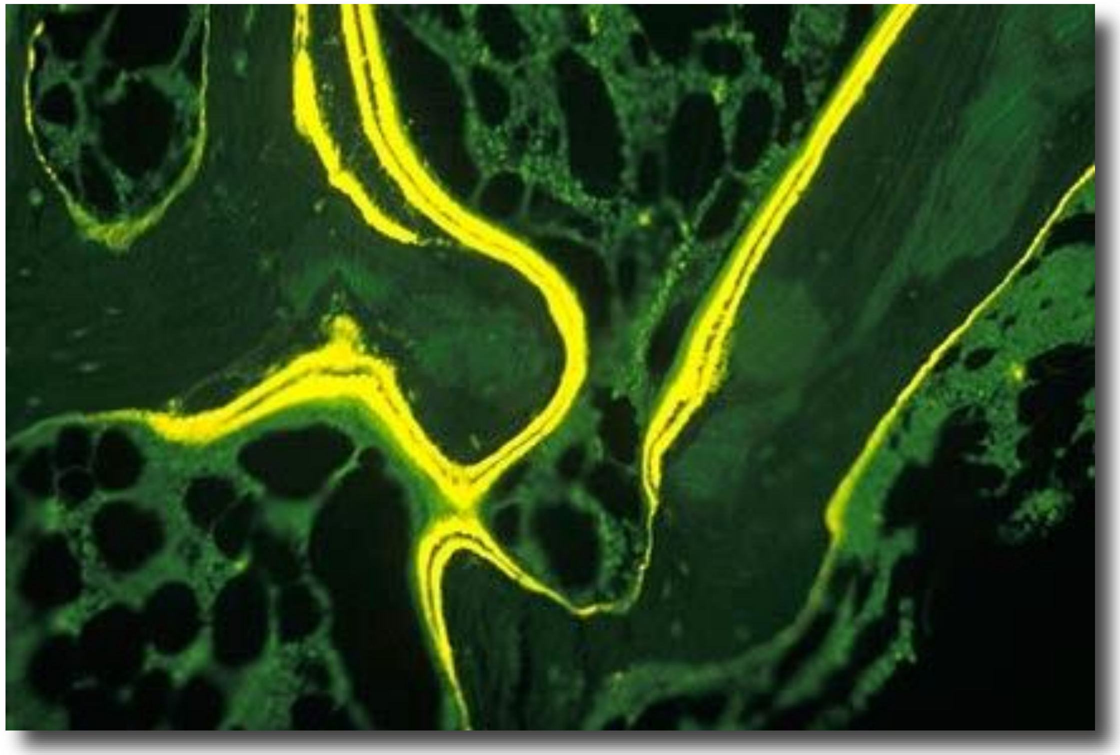
Structures and cells are revealed by **stains**

- Stain choice depends on objectives!
- Staining is applied on slides

Labelling

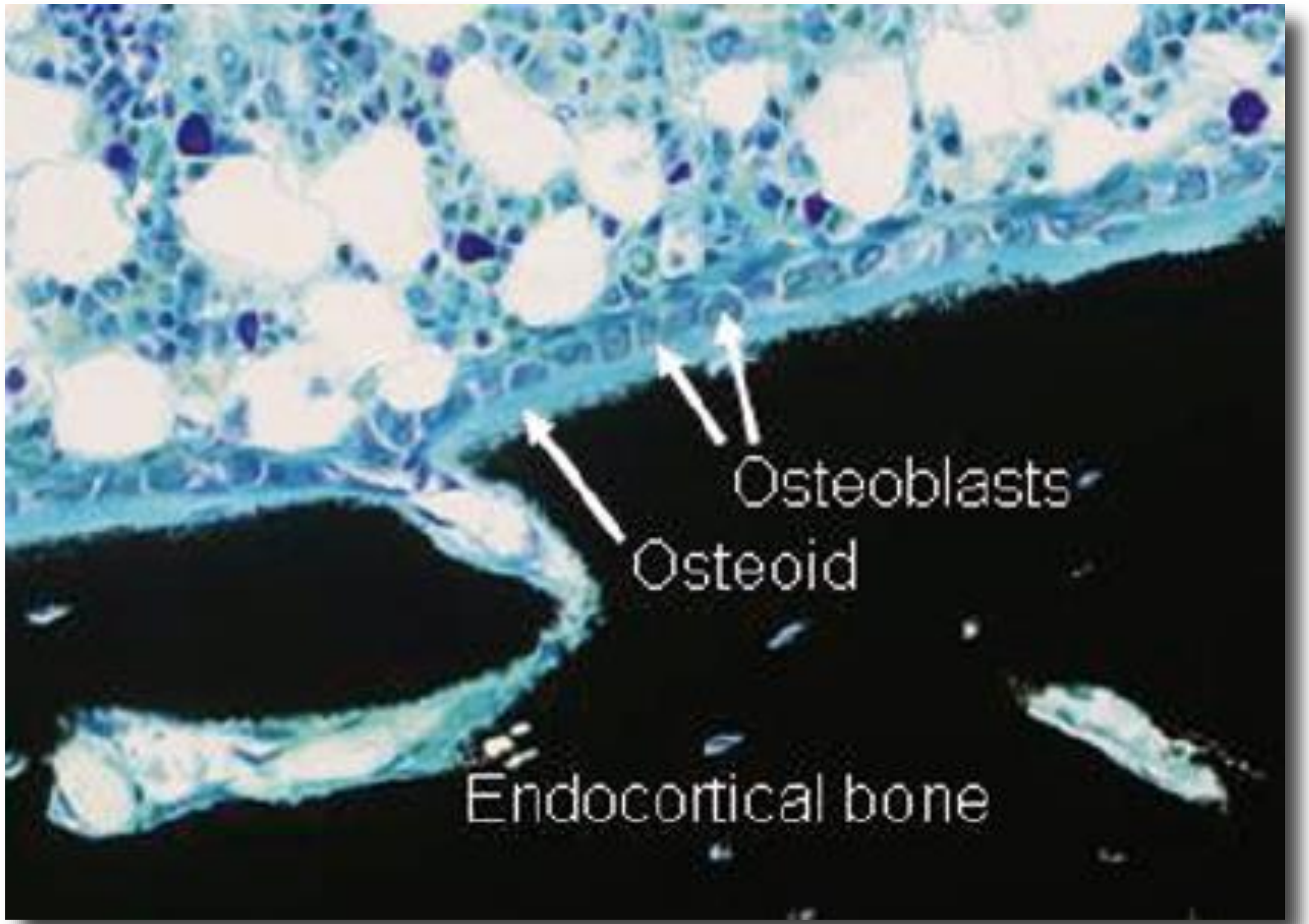
- Cellular activity is revealed by **fluorescent labels** (tetracycline, calcein)
- Labels are administred prior to biopsy or harvesting on a precise schedule

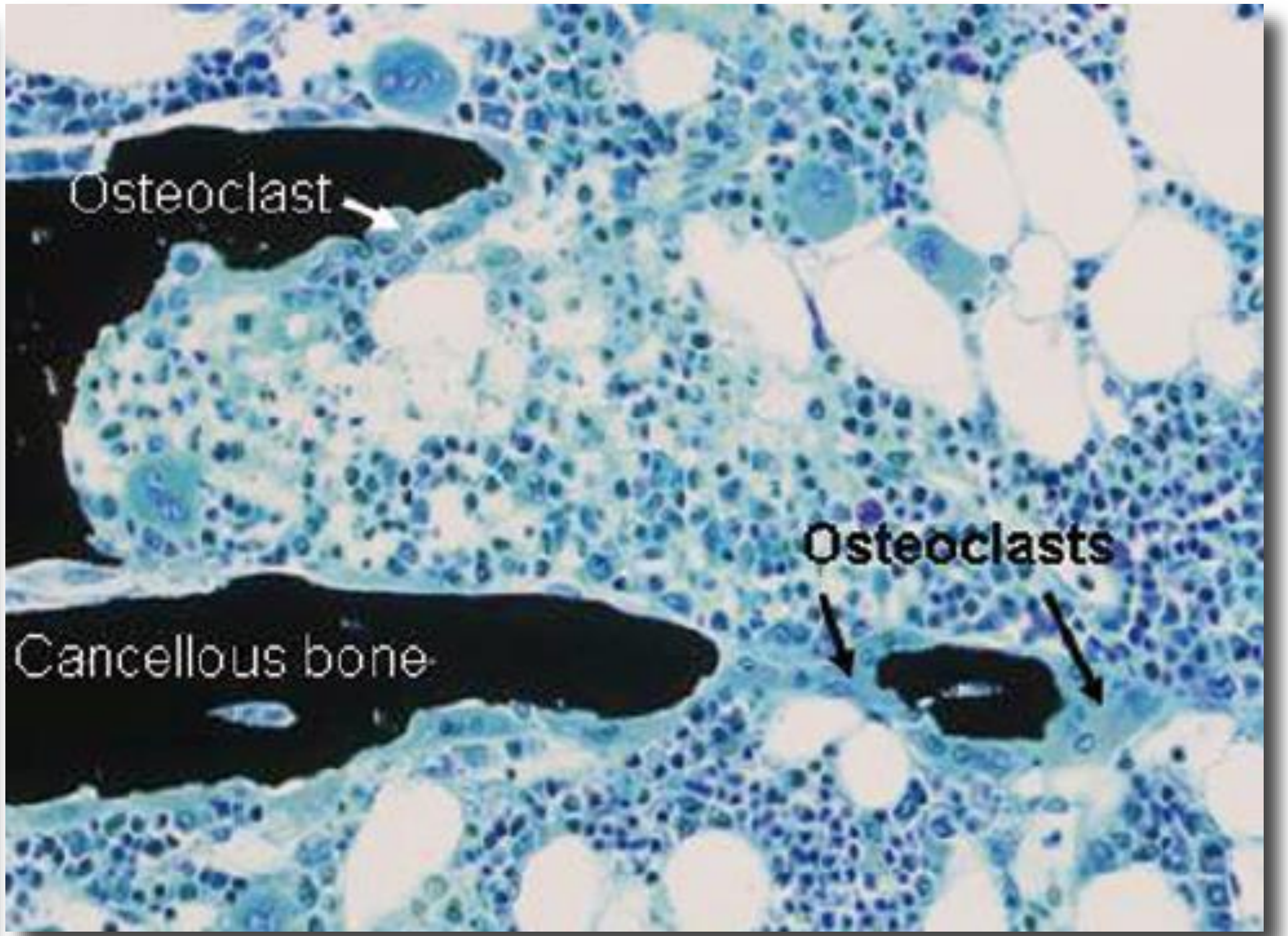




Histology

Histology is the study of the microscopic anatomy of cells and tissues of plants and animals.





Histomorphometry:

Quantitative measurements on histology slices

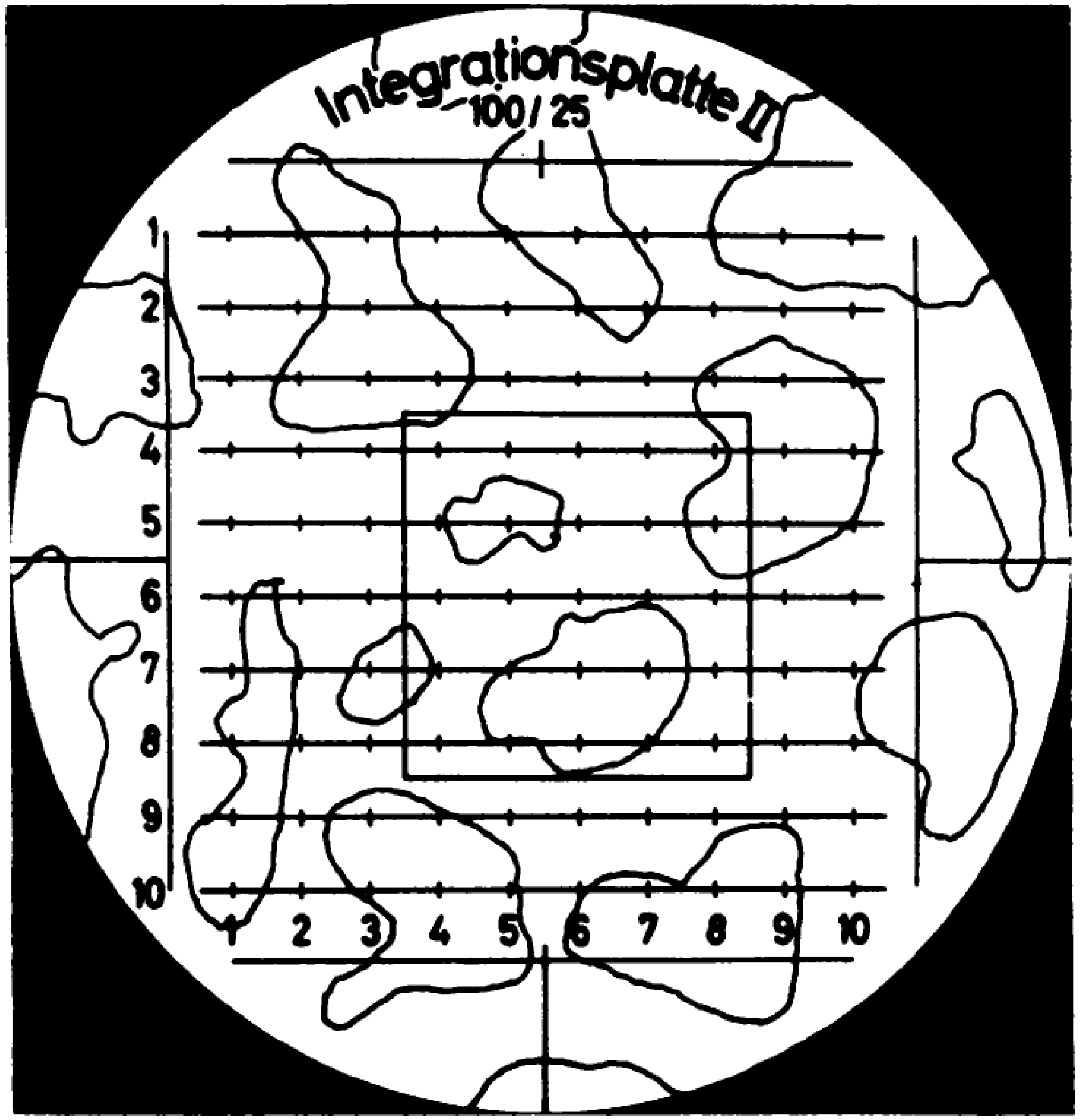
Bone histomorphometry, primary indices:

Referent (3D/2D)	Abbreviation (3D/2D)
Bone surface/perimeter	BS/B.Pm
Bone volume/area	BV/B.Ar
Tissue volume/area	TV/T.Ar
Core volume/area	CV/C.Ar
Osteoid surface/perimeter	OS/O.Pm
Eroded surface/perimeter	ES/E.Pm
Mineralizing surface/perimeter	Md.S/Md.Pm
Osteoblast surface/perimeter	Ob.S/Ob.Pm
Osteoclast surface/perimeter	Oc.S/Oc.Pm

Histomorphometry:

Name	Abbreviation	Unit
Bone area	B.Ar/T.Ar	%
Osteoid area	O.Ar/T.Ar or O.Ar/B.Ar	%
Osteoid perimeter	O.Pm/B.Pm	%
Osteoid width	O.Wi	μm
Osteoblast perimeter	Ob.Pm/B.Pm	%
Wall width	W.Wi	μm
Mineralizing perimeter	M.Pm/B.Pm	%
Mineral apposition rate	MAR	μm/d
Eroded depth	E.De	μm
Eroded cavity area	E.Ar	μm^2
Eroded perimeter	E.Pm/B.Pm	%
Osteoclast perimeter	Oc.Pm/B.Pm	%
Erosion length	E.Le	μm
Cavity number	N.Cv/B.Pm or /T.Ar	No./mm or /mm^2
Osteoclast number	Oc/T.Ar	cells/mm^2

Historic example:
Evaluation of bone area with a graticule



Point counting with the graticule
(Zeiss Integration Plate II)

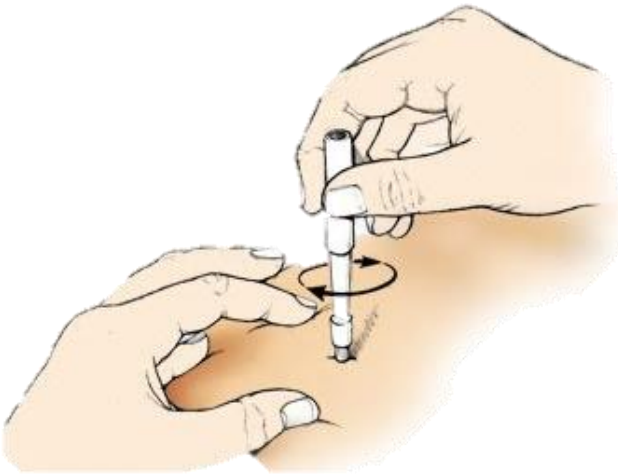
- A measure of bone density is bone area: Bone area = B.Ar/T.Ar [%]
- A graticule is a grid that fits on the eyepiece of the microscope to help counting features.
- Example: If the islands are considered to be bone trabeculae, then in the small central square there are 8 out of 25 points falling on bone; that is 32 % of total tissue is bone, i.e. B.Ar/T.Ar = 32%

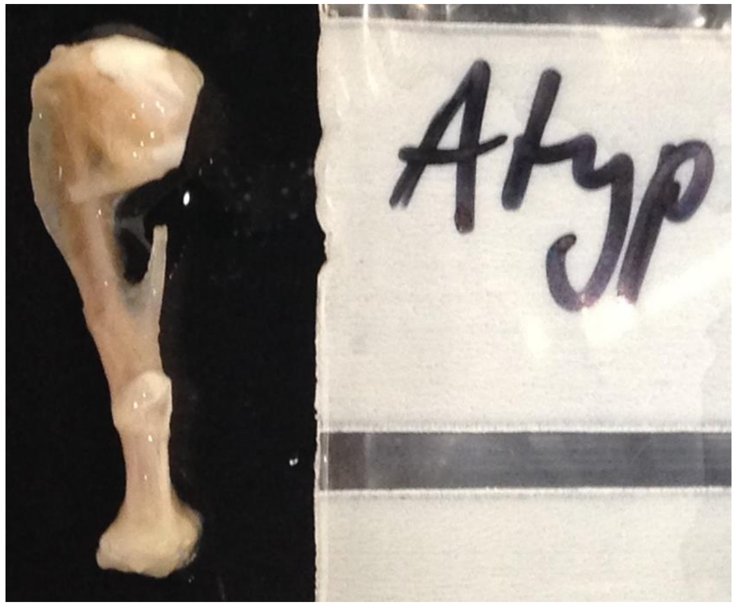
Revell, J Clin Pathol 1983;36:1323-1331

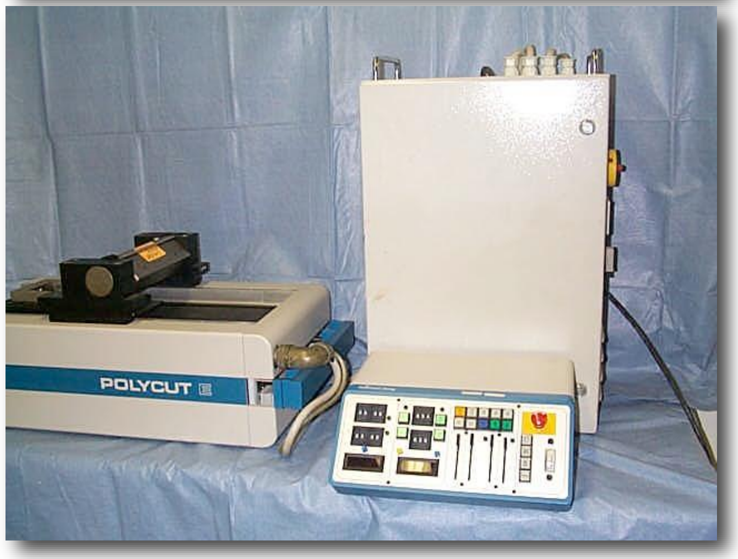
Exercise 1…

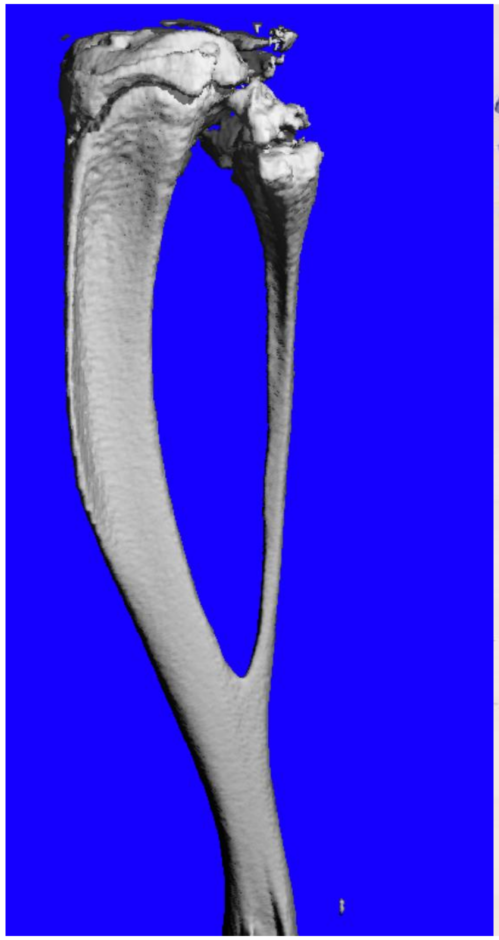
Limitations

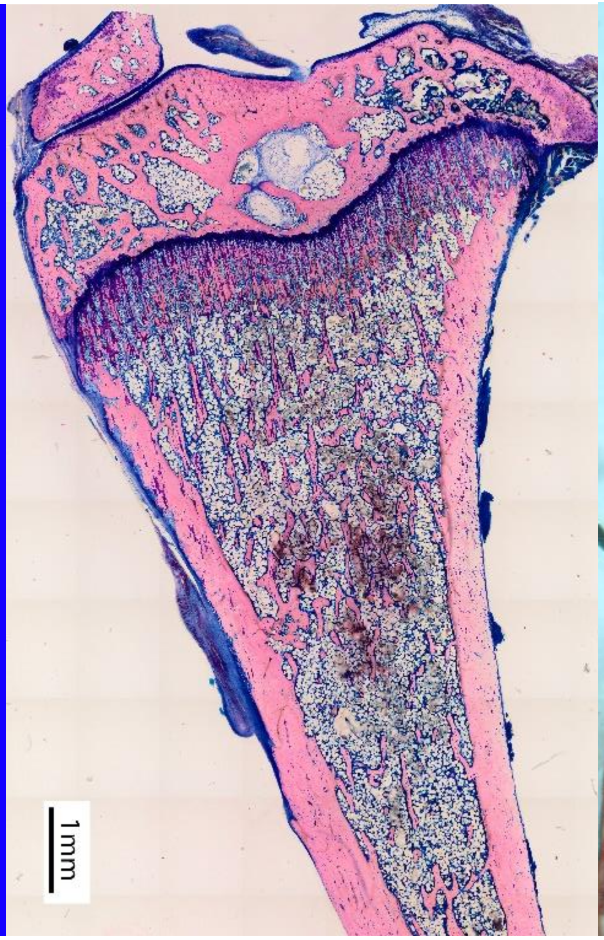
- Long & technical preparation
- Invasive + Specimen destruction
- (Stilll) relies a lot on human expertise
- Limited ROI & 2D

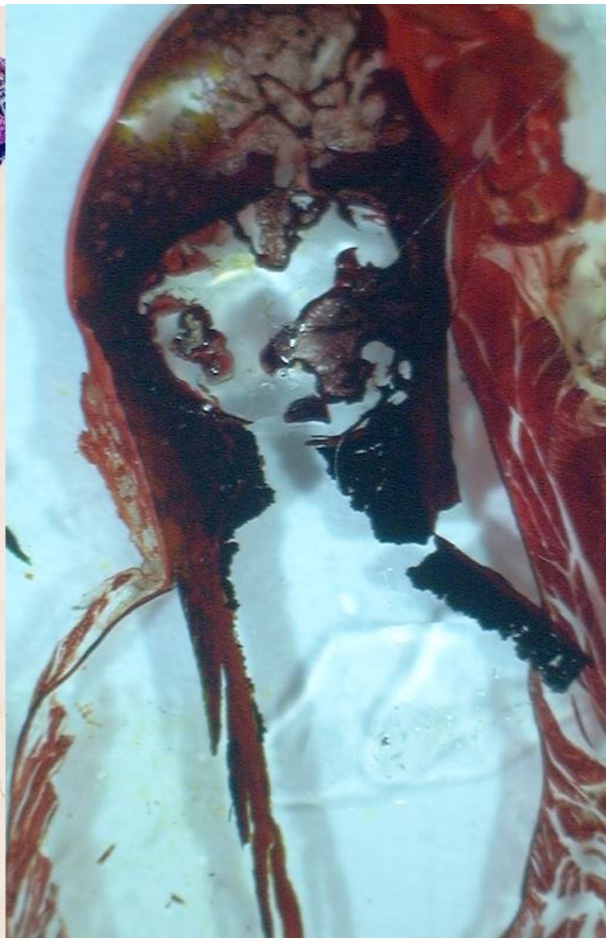




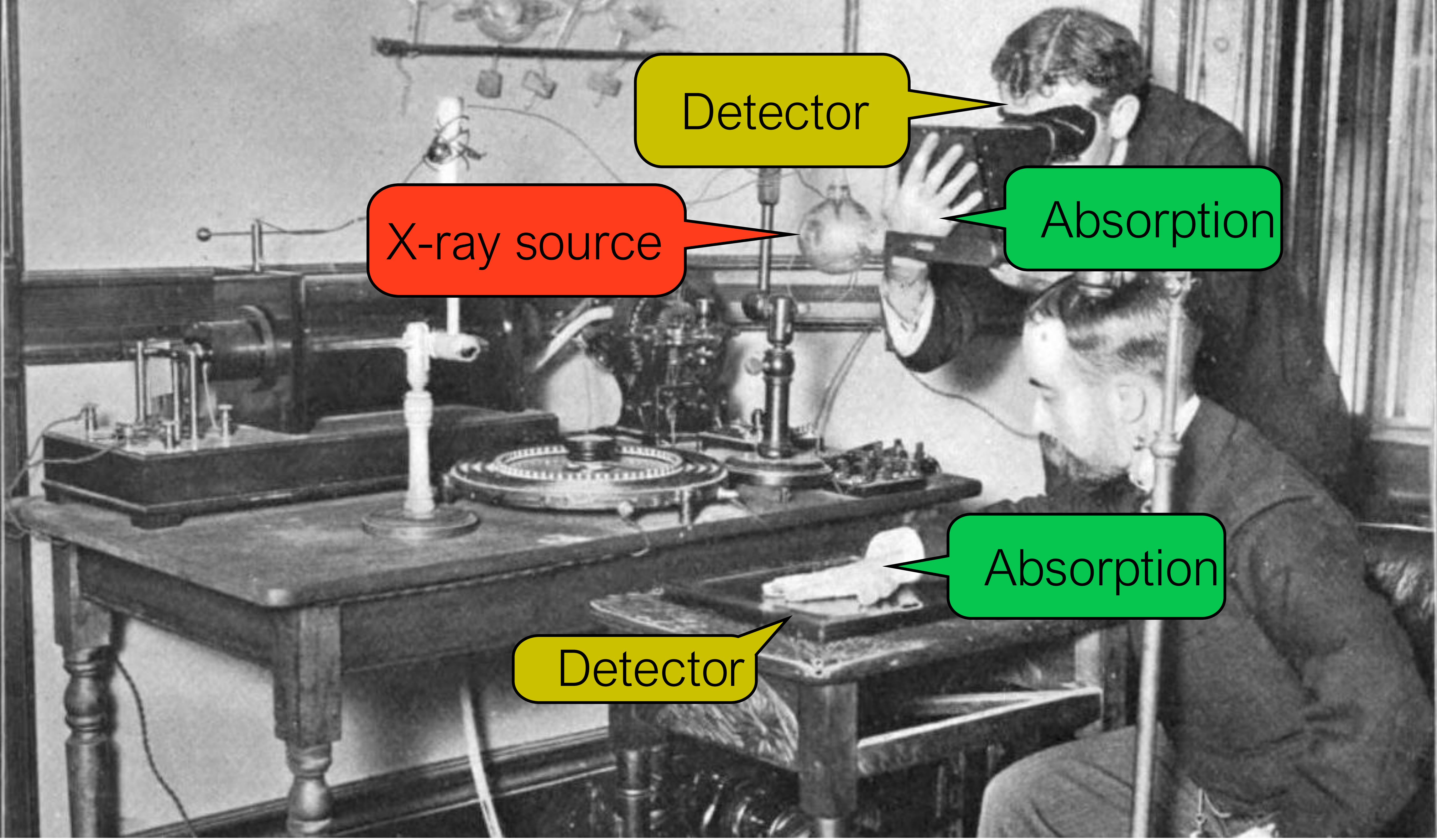








X-ray radiography

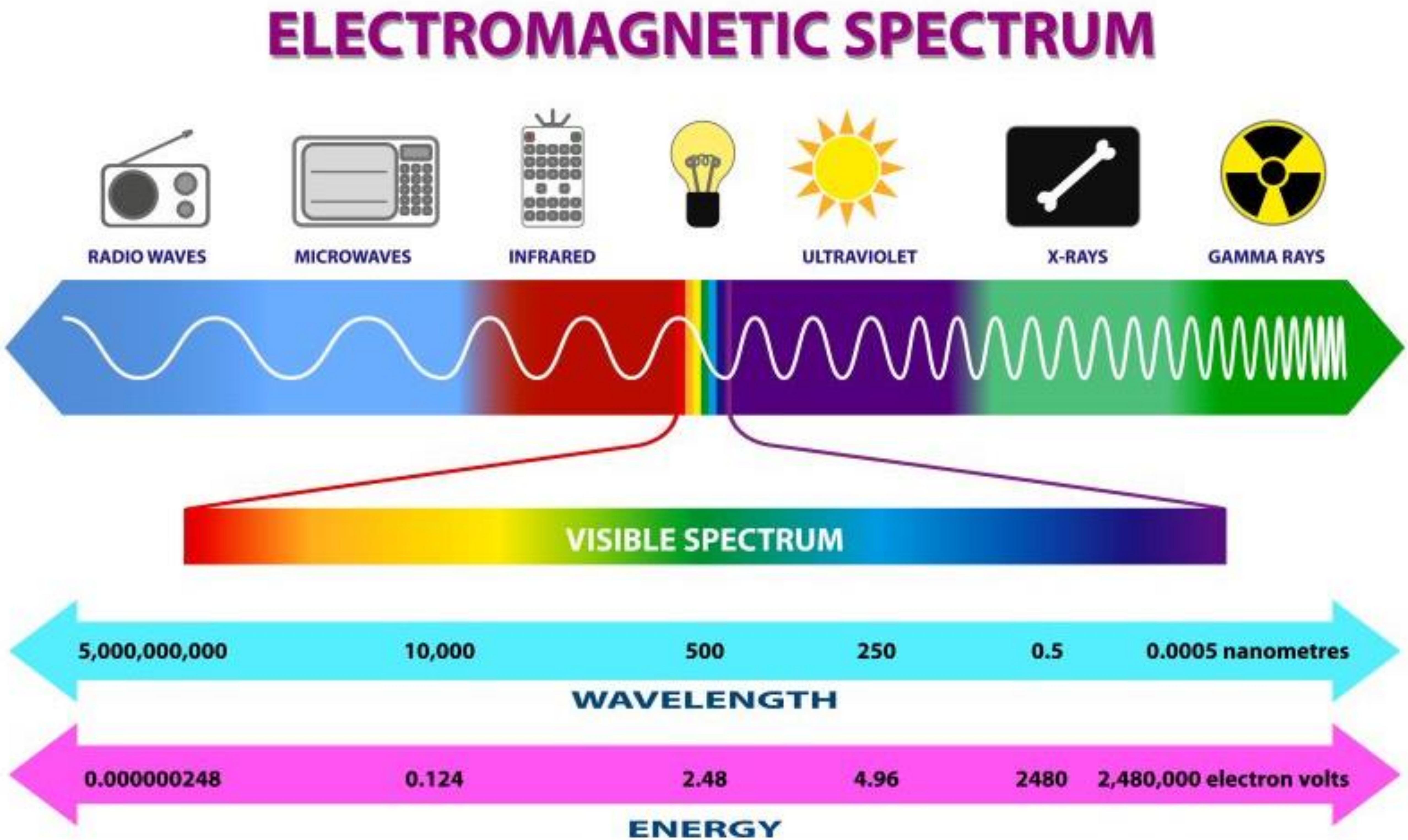


X-ray radiography

First known medical radiography

Hand mit Ringen:
print of Wilhelm Röntgen's first "medical" X-ray, of his wife's hand, taken on 22 December 1895

https://en.wikipedia.org/wiki/X-ray#cite_note-22

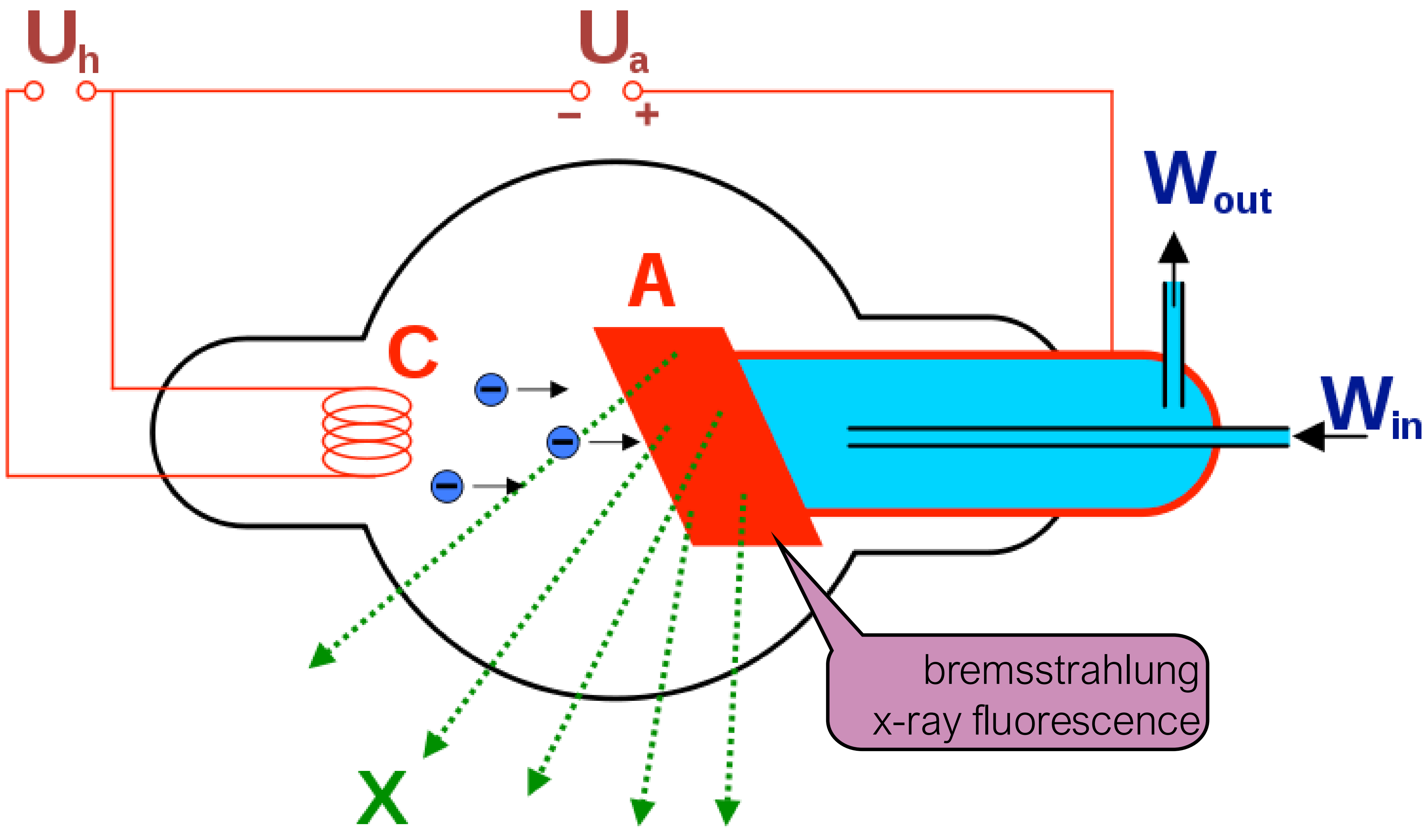


X-rays

X-ray is a high-energy electromagnetic radiation

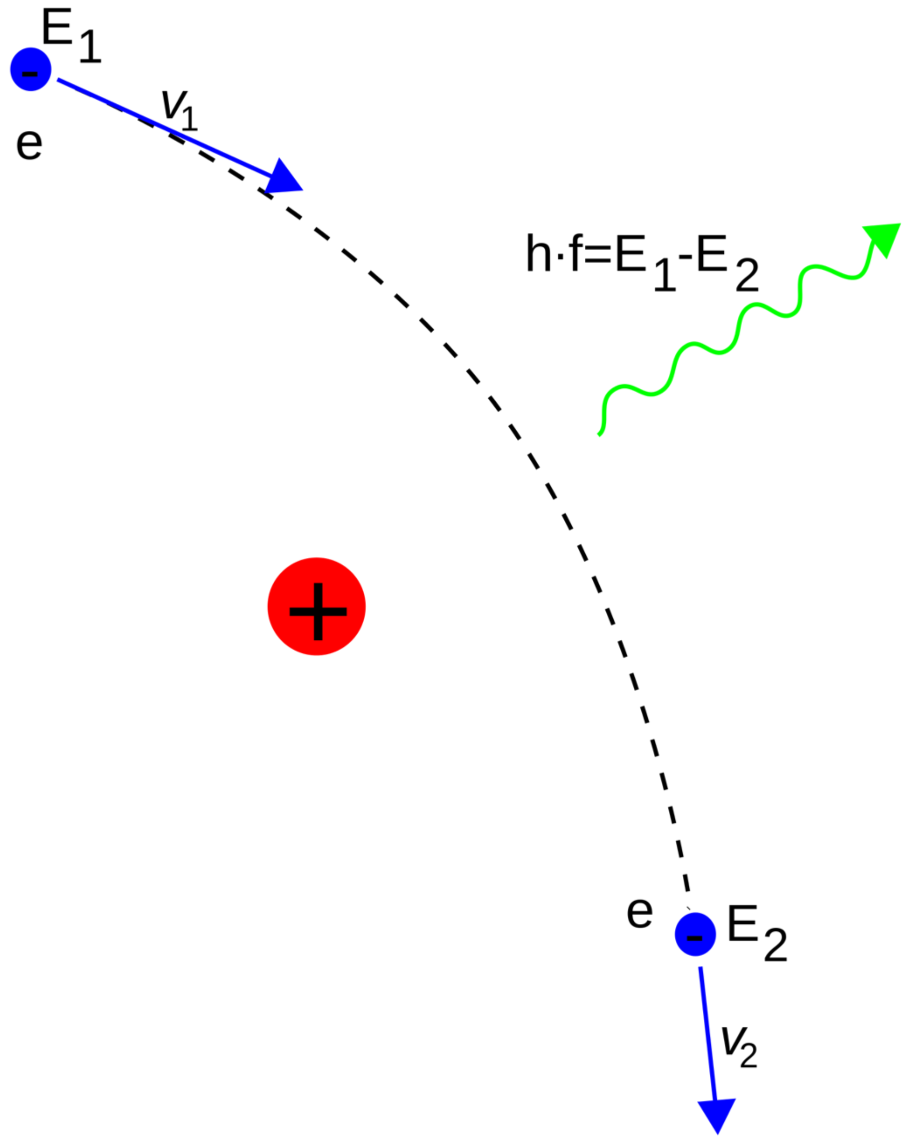
X-rays have a wavelength ranging from 10 nanometers to 10 picometers

X-ray tubes generate x-rays

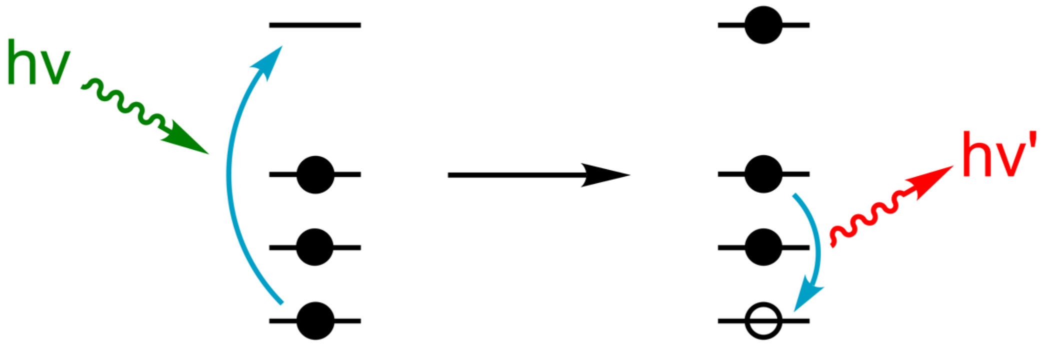


Generation of x-rays

Bremsstrahlung
("deceleration radiation")



X-ray fluorescence
("secondary" emission)



Absorption of x-rays

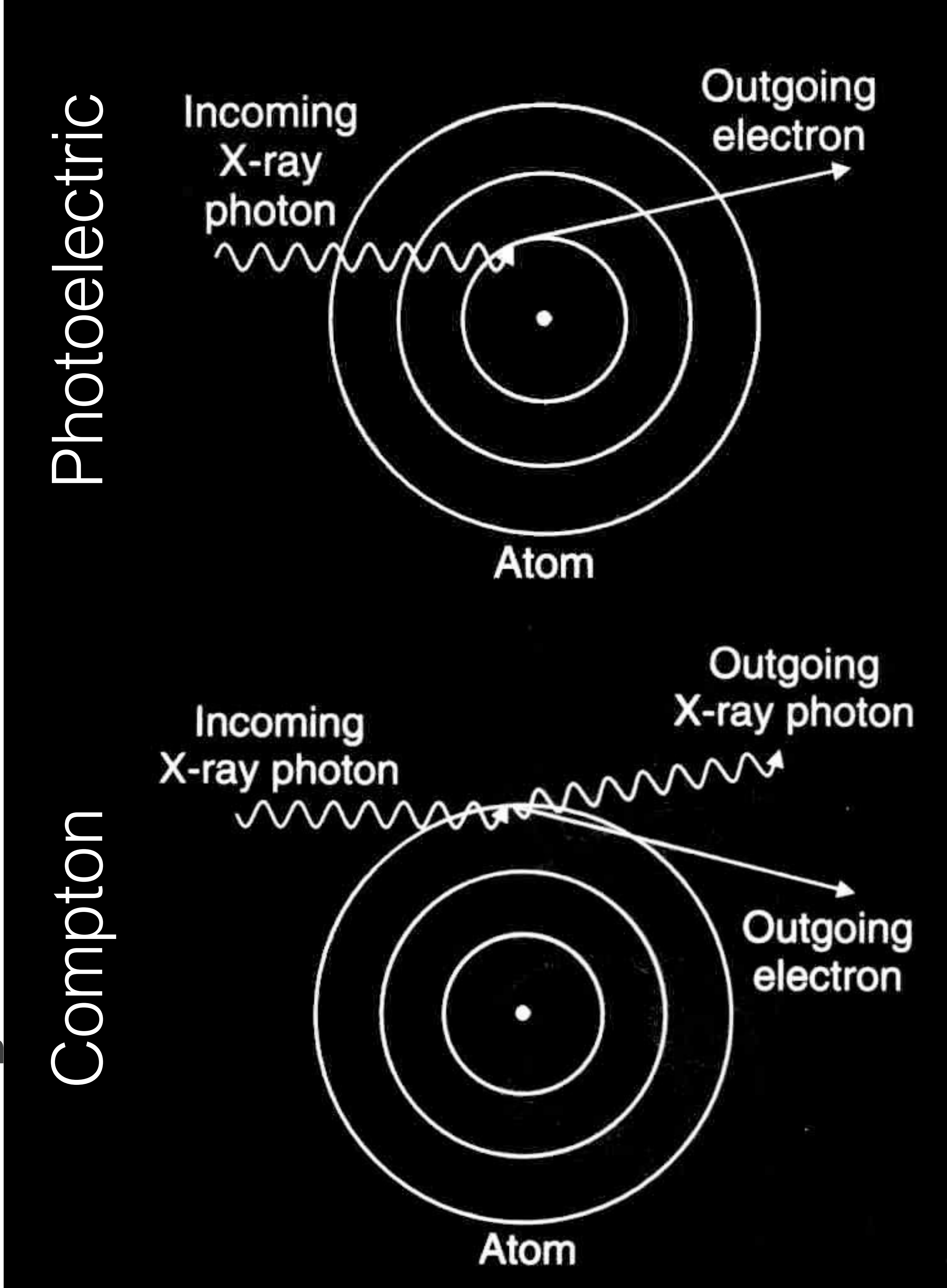
In the energy range used in radiology (30-200keV) two effects dominate x-ray absorption:

- Photoelectric effect (dominates < 100keV)
- Compton effect (dominates > 100keV)

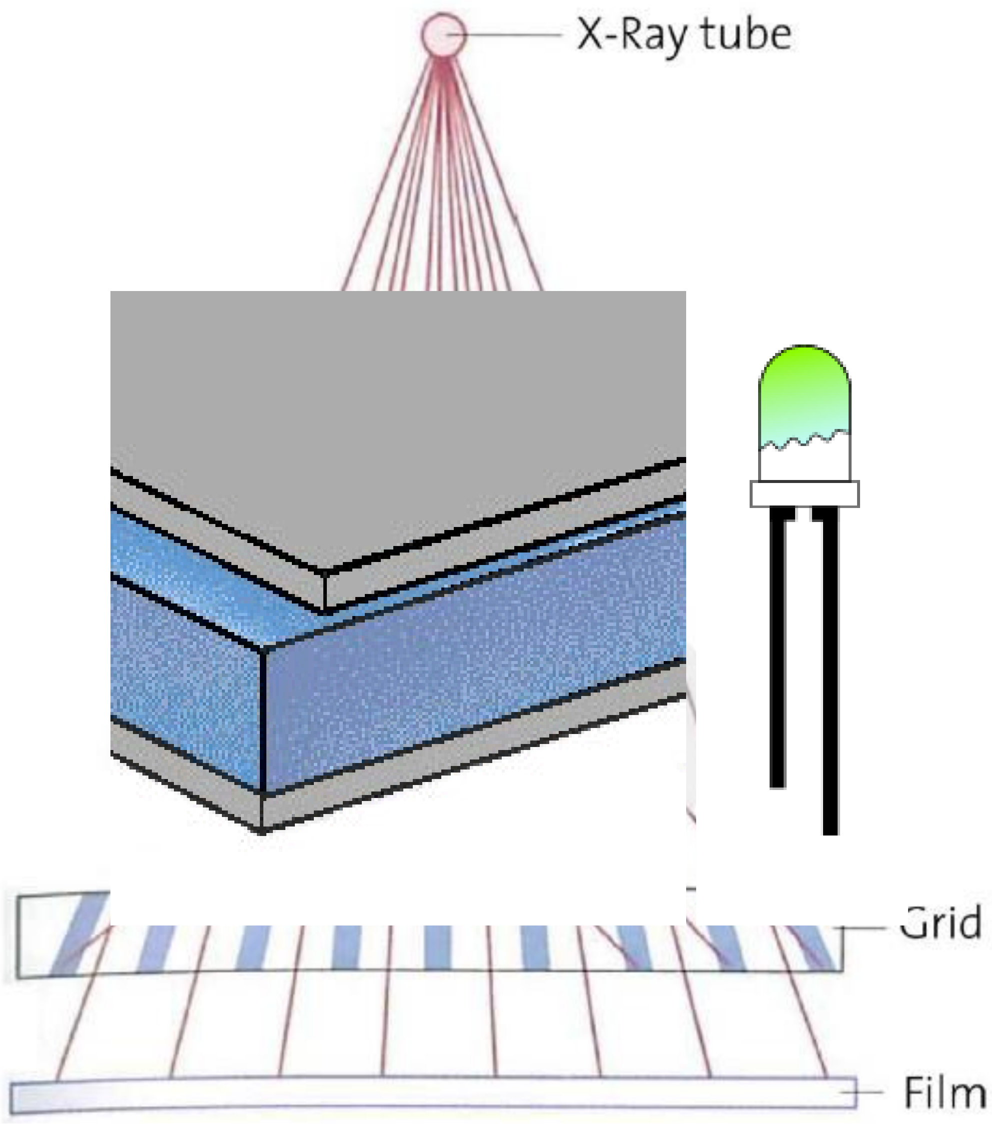
Other x-ray weakening effects like
- scattering
- reactions with nucleus

have no significant impacts.

Attenuation of x-rays depends on material density!



Radiographic image



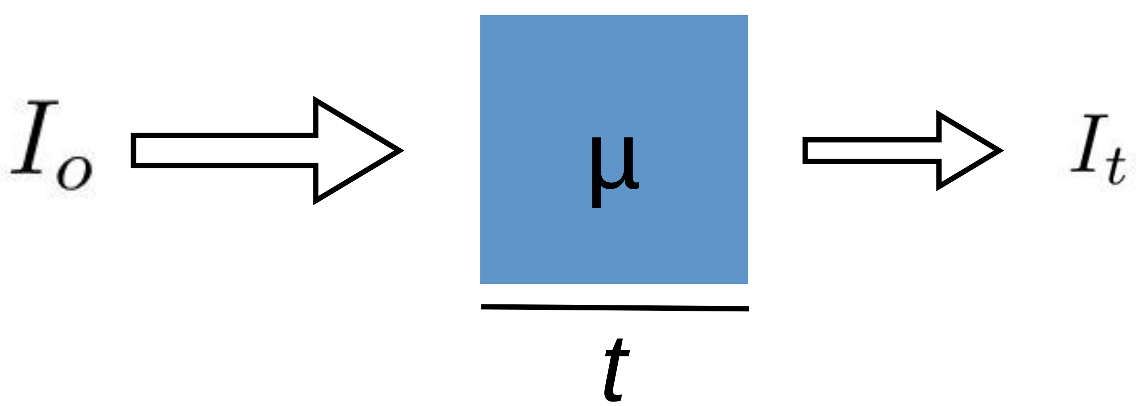
Acquisition:

- Film: standard photo film, with a layer of scintillographic material
- Indirect detector: CCD with fluorescent material
- Direct: flat panel detectors with semiconductors (Amorphous selenium)

X-rays absorption

An x-rays beam loses intensity as it passes through matter according to the **exponential law of absorption** where μ is the **absorption coefficient**:

For example, if a beam of intensity I_o passes through an homogenous material (a.c. μ, thickness ***t***), the intensity becomes:



$$\frac{dI}{I} = -\mu \, dx$$

$$I_t = I_o \, \mathrm{e}^{-\mu t}$$

X-rays absorption

For an inhomogenous material the absorption coefficient is variable: $\mu(\mathbf{x})$

If a beam of intensity I_o passes through an inhomogenous material (a.c. $\mu(\mathbf{x})$), along a ray path s the intensity becomes:

$$I_t = I_o \mathrm{e}^{-\int_s \mu(\mathbf{x}) ds}$$

The **ray-integral** $p(\mathbf{s})$ is defined as:

$$p(\mathbf{s}) = -log(\frac{I}{I_o}) = \int_s \mu(\mathbf{x}) ds$$

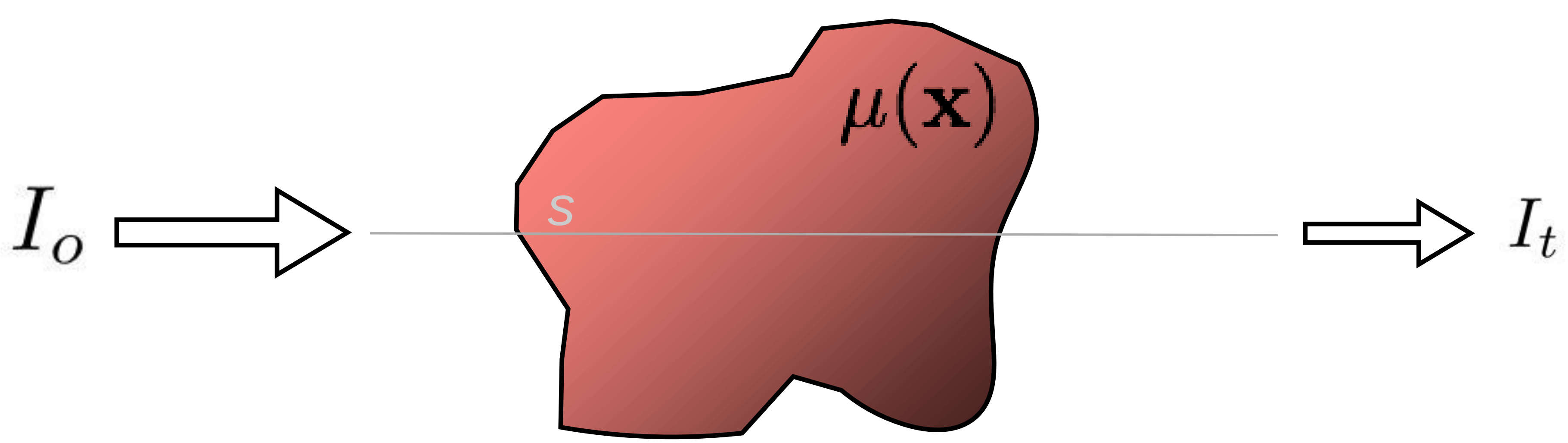
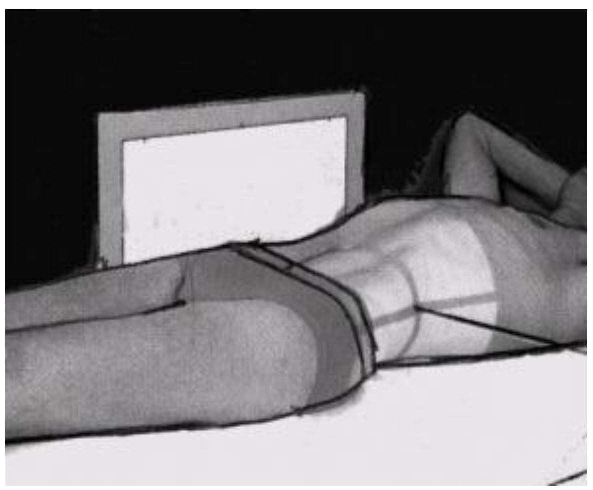
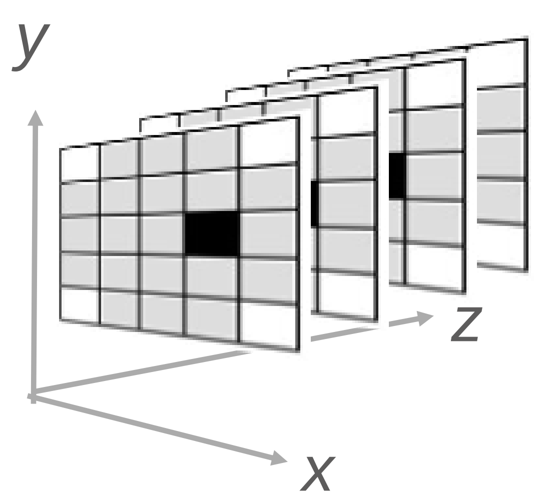
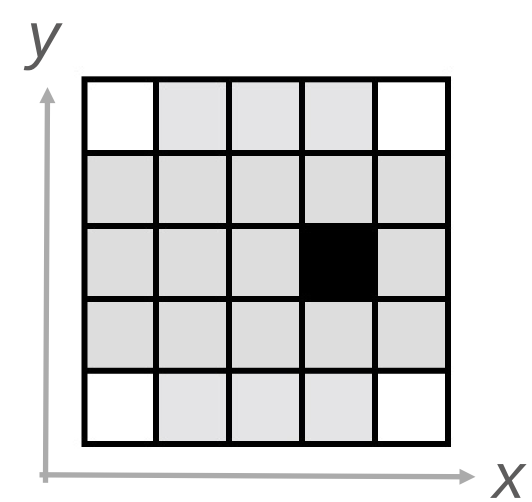
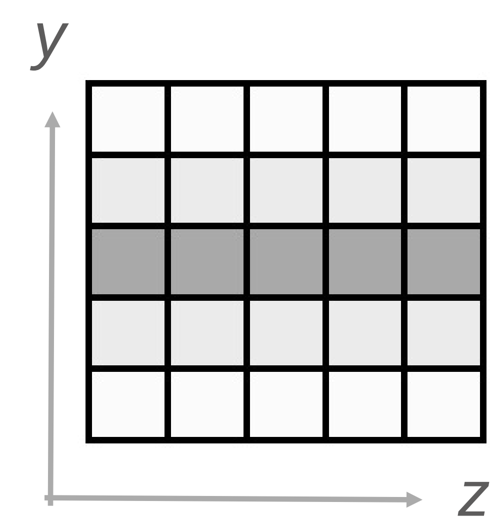


Image representation (rendering)









Physical model

Continuous
3-dimensional

"Patient"

Discrete model

Discrete
3-dimensional

Single slice

Discrete
2-dimensional

Projection

Discrete
2-dimensional

"Radiograph"
"X-ray"

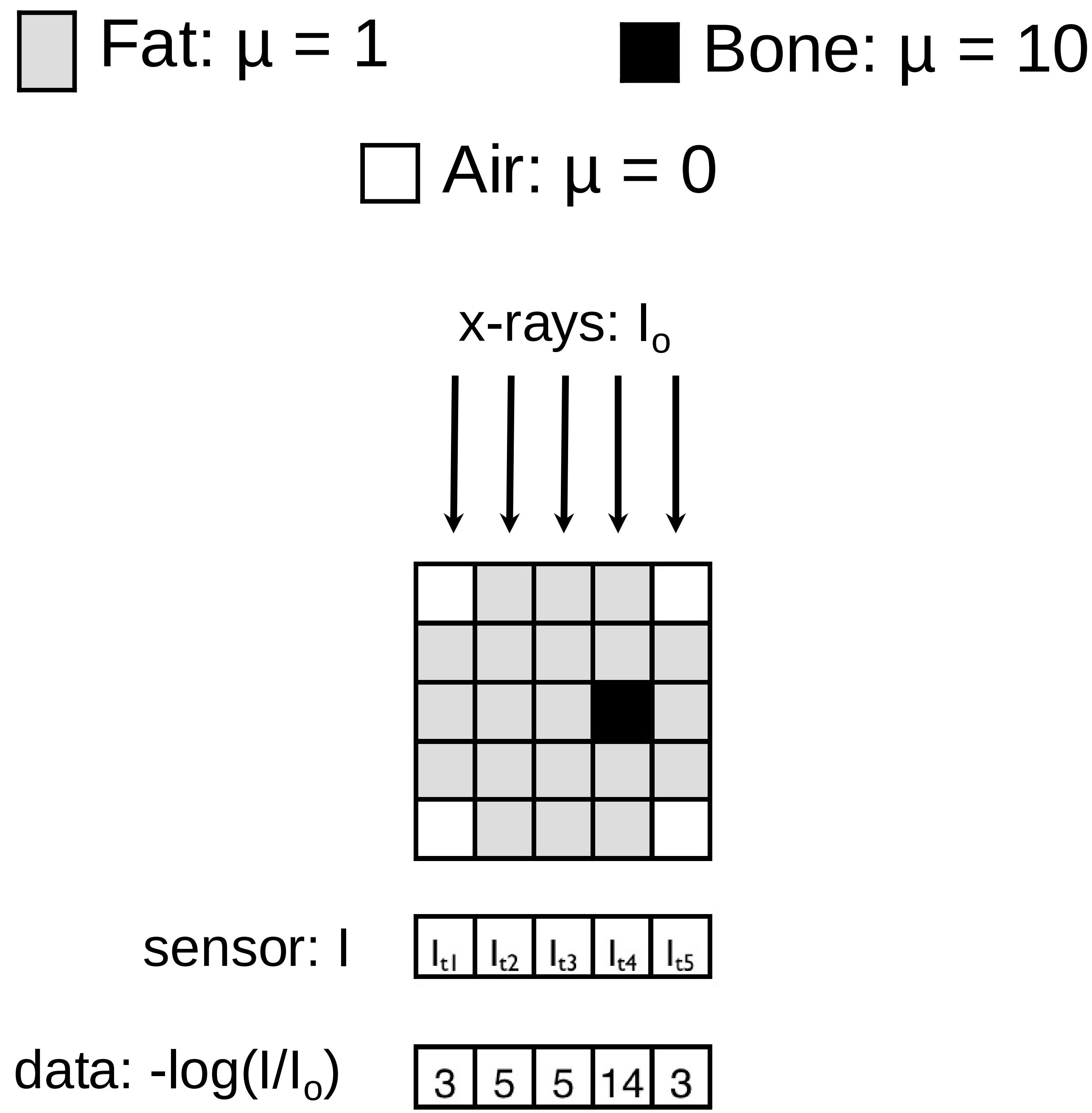
Radiography concept

ray integral:

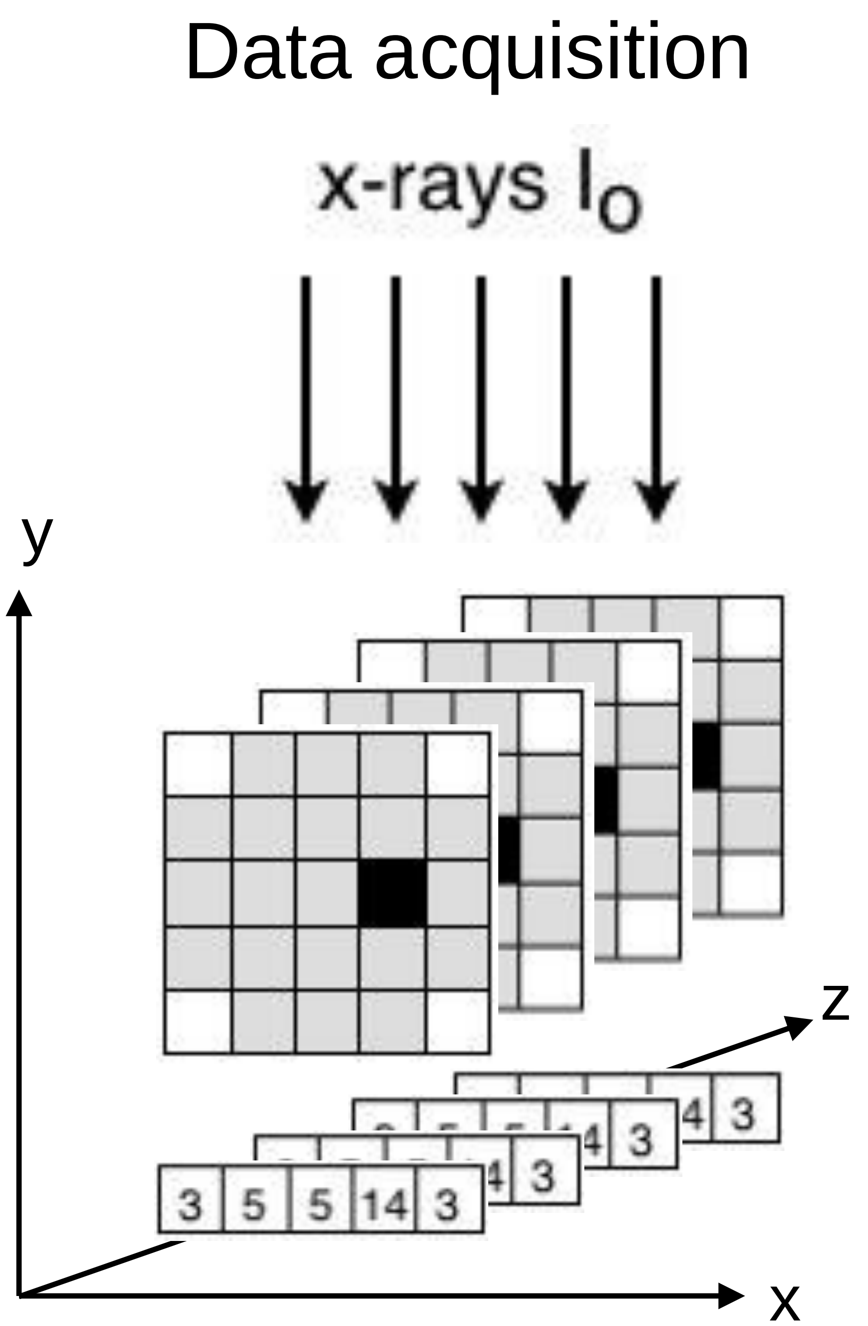
$$-log(I/I_o) = \int_s \mu(\mathbf{x})ds$$

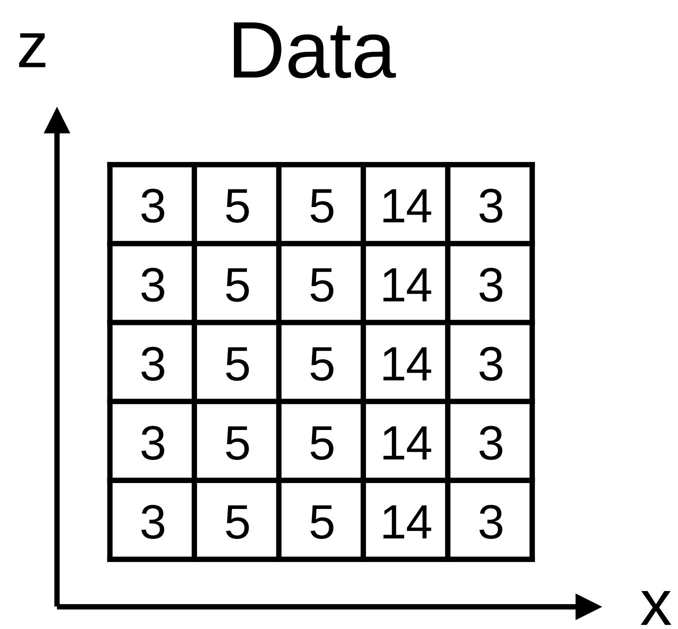
in a discrete space:

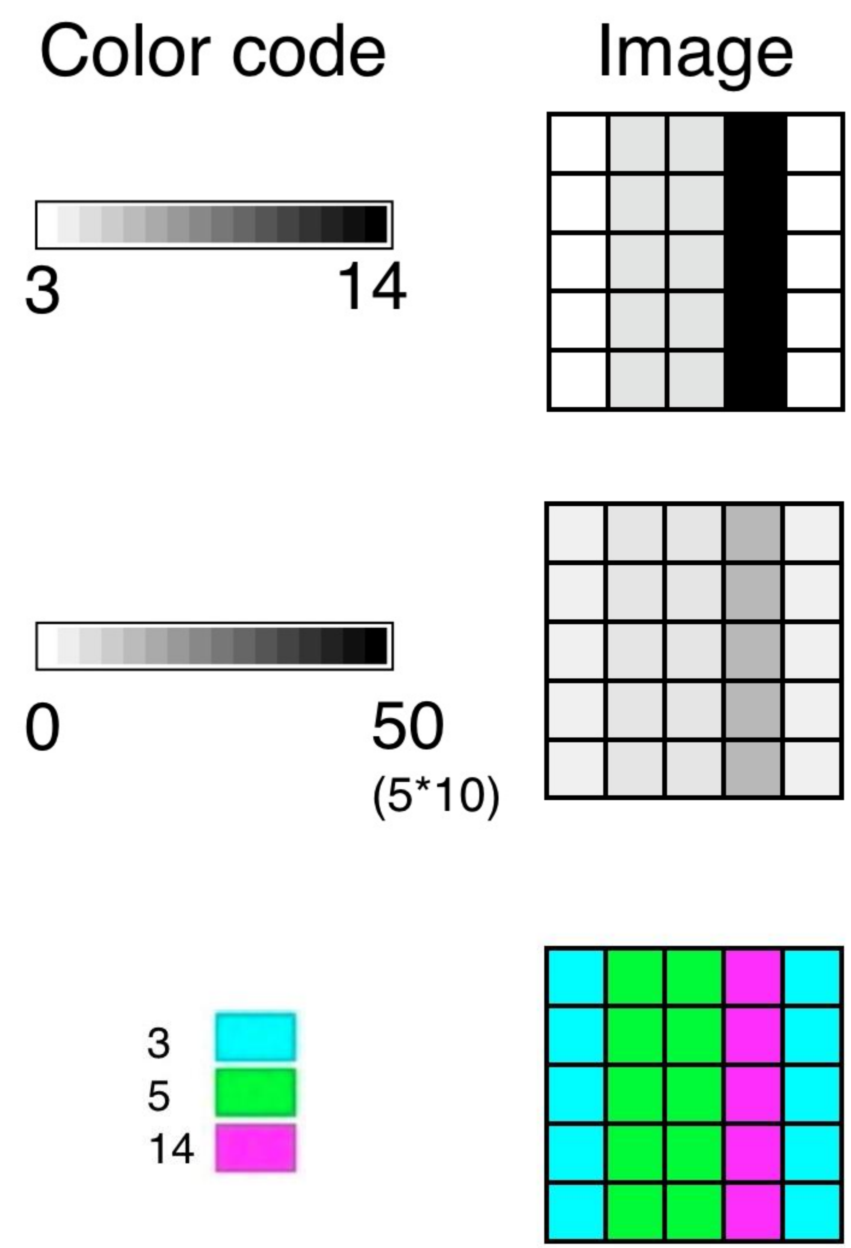
$$-log(I/I_o) = \sum_i \mu_i$$



From x-rays to images

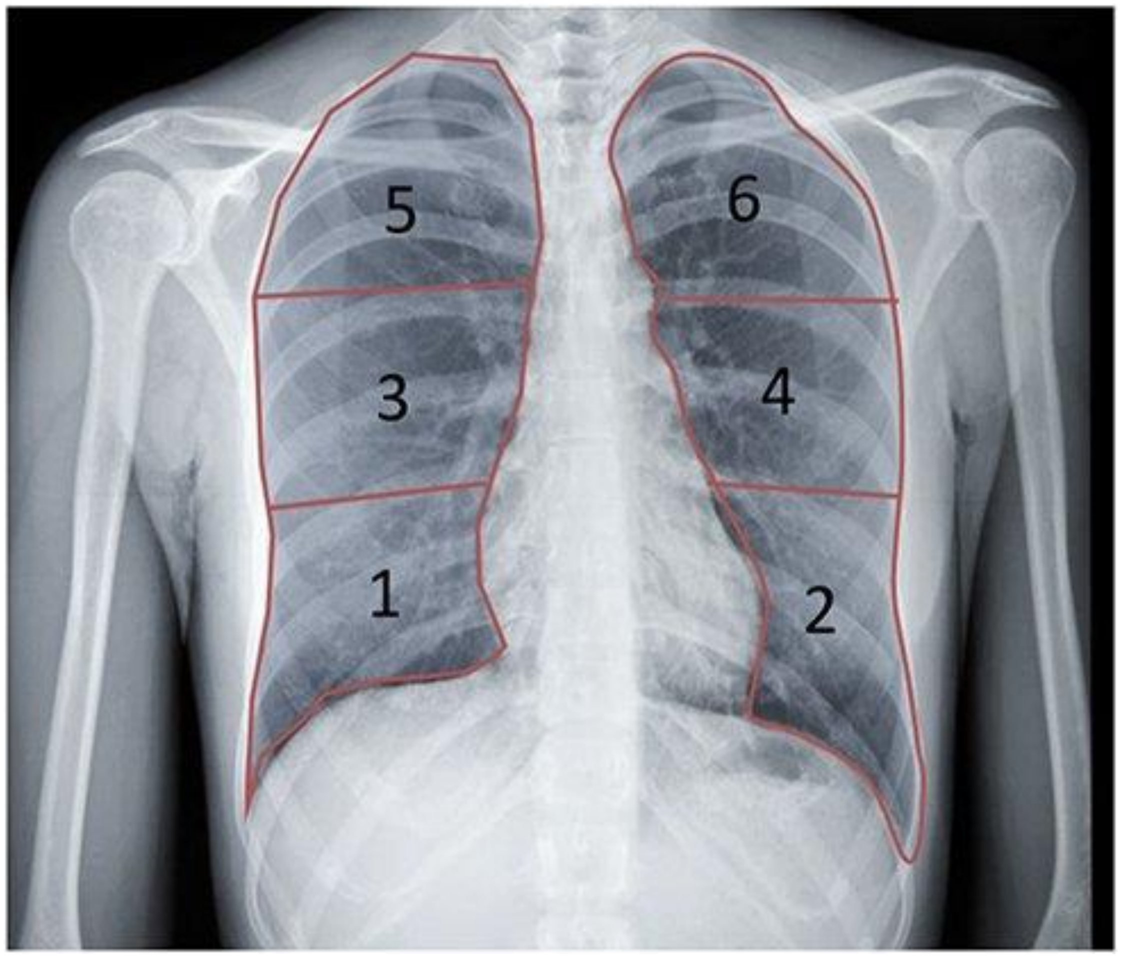




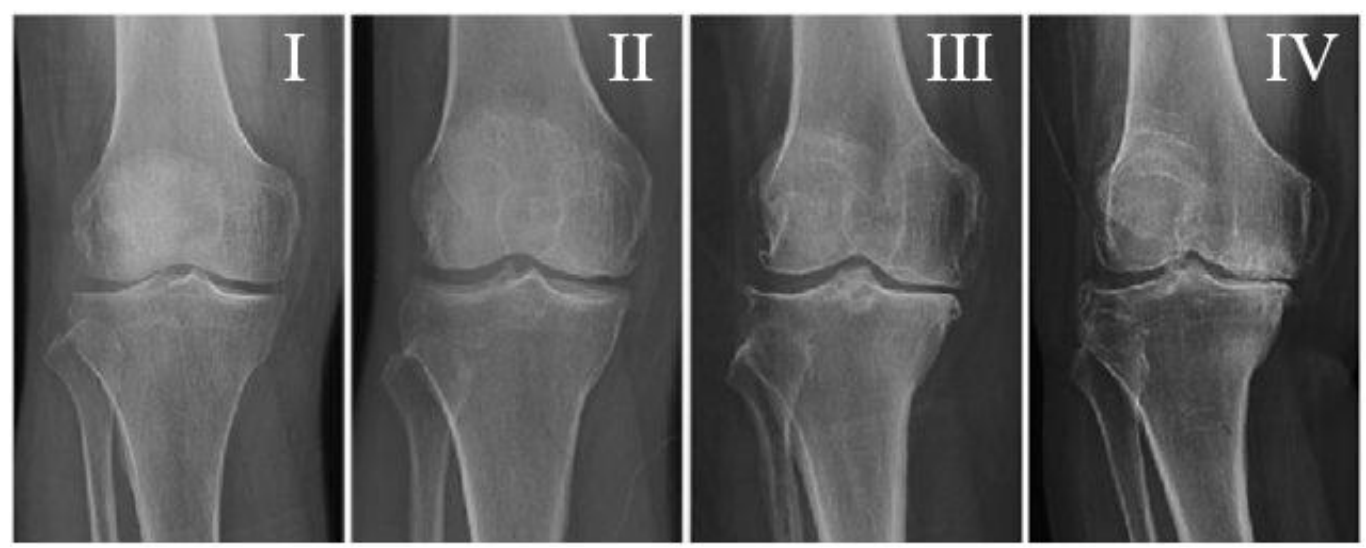


Exercise 2

Radiographic readouts: scoring systems



Grade	Radiologic Findings
0	No radiological findings of osteoarthritis
I	Doubtful narrowing of joint space and possible osteophytic lipping
II	Definite osteophytes and possible narrowing of joint space
III	Moderate multiple osteophytes, definite narrowing of joint space, small pseudocystic areas with sclerotic walls and possible deformity of bone contour
IV	Large osteophytes, marked narrowing of joint space, severe sclerosis and definite deformity of bone contour



Kellgren, J. H. et al. Ann. Rheum. Dis. 16, 494–502 (1957)

Radiographic readouts: scoring systems

- A scoring system is a set of “grades” or “scores”
- Usually categorical (1,2,3… or I,II,III, … or A,B,C,…)
- Each grade defined by a list of specific features in the image
- Features can be qualitative or quantitative

Grade	Radiologic Findings
0	No radiological findings of osteoarthritis
I	Doubtful narrowing of joint space and possible osteophytic lipping
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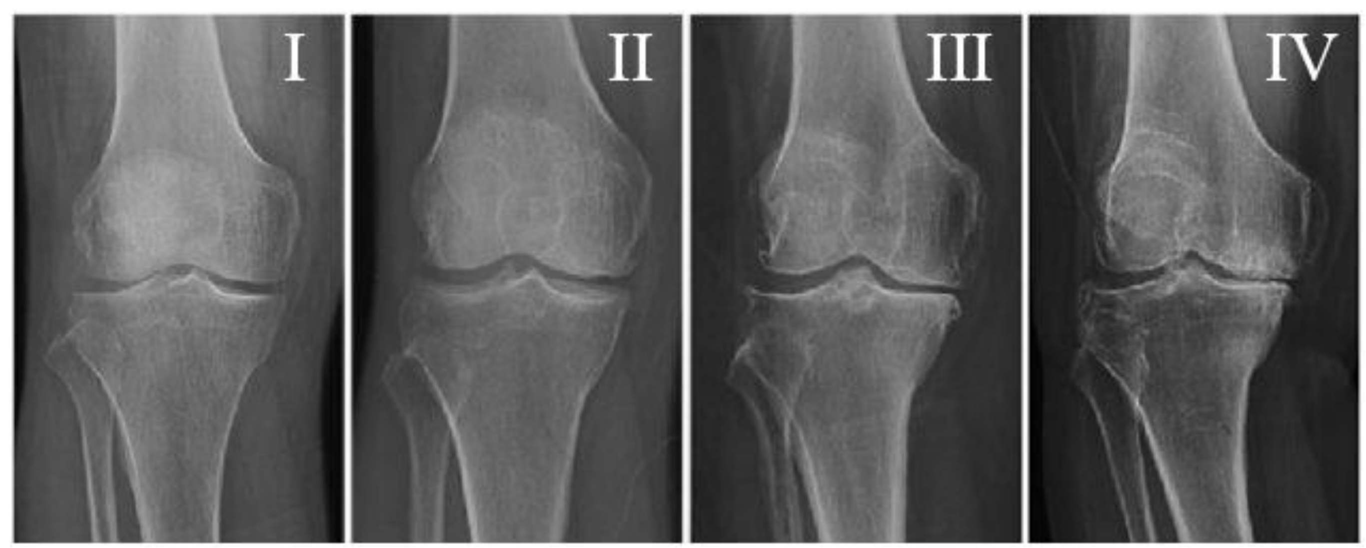
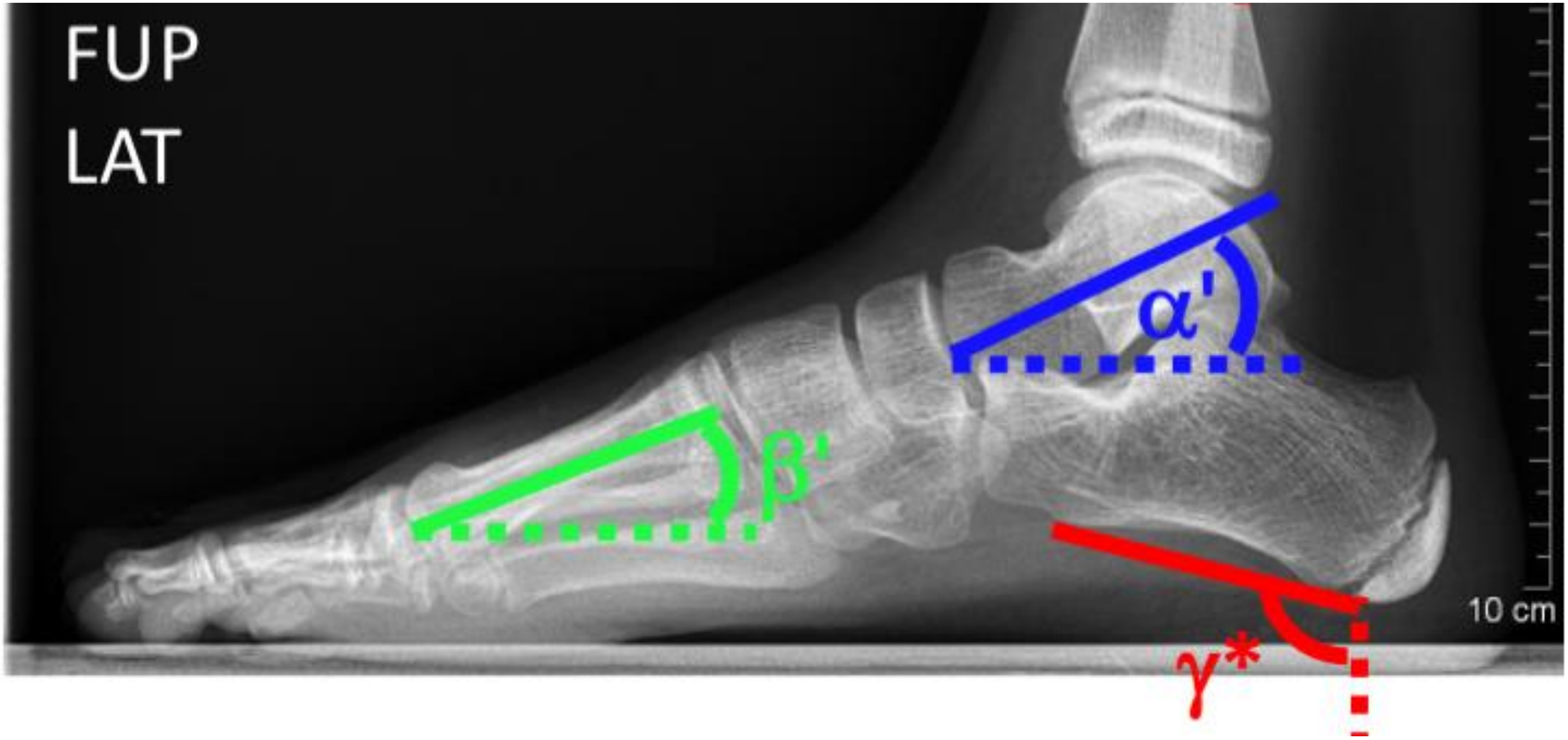


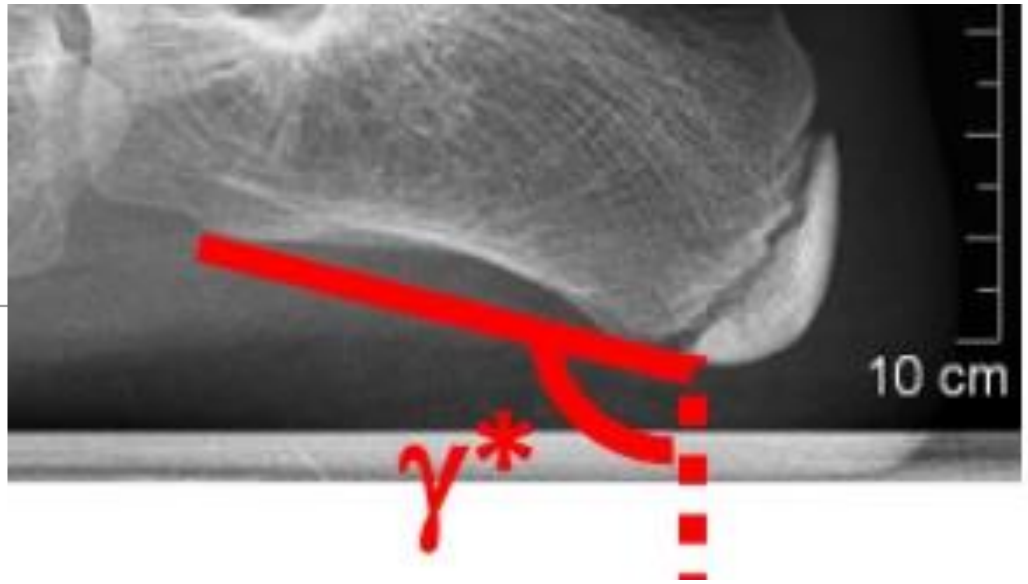
Kellgren, J. H. et al. Ann. Rheum. Dis. 16, 494–502 (1957)

Radiographic readouts: continuous variables

- Most DICOM / X-ray viewers have integrated tools for distance, angles, surface...
- The secret to a good measurement SOP lies in defining good landmarks.

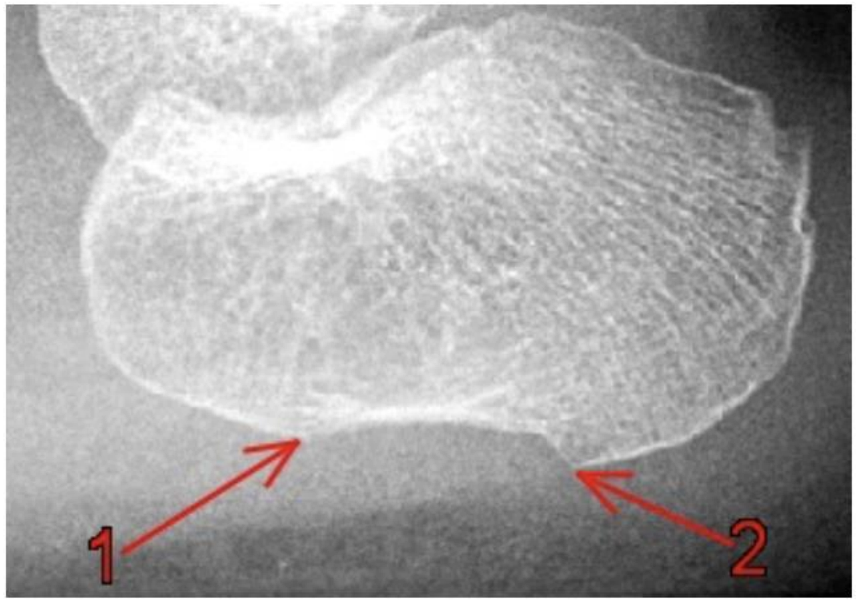


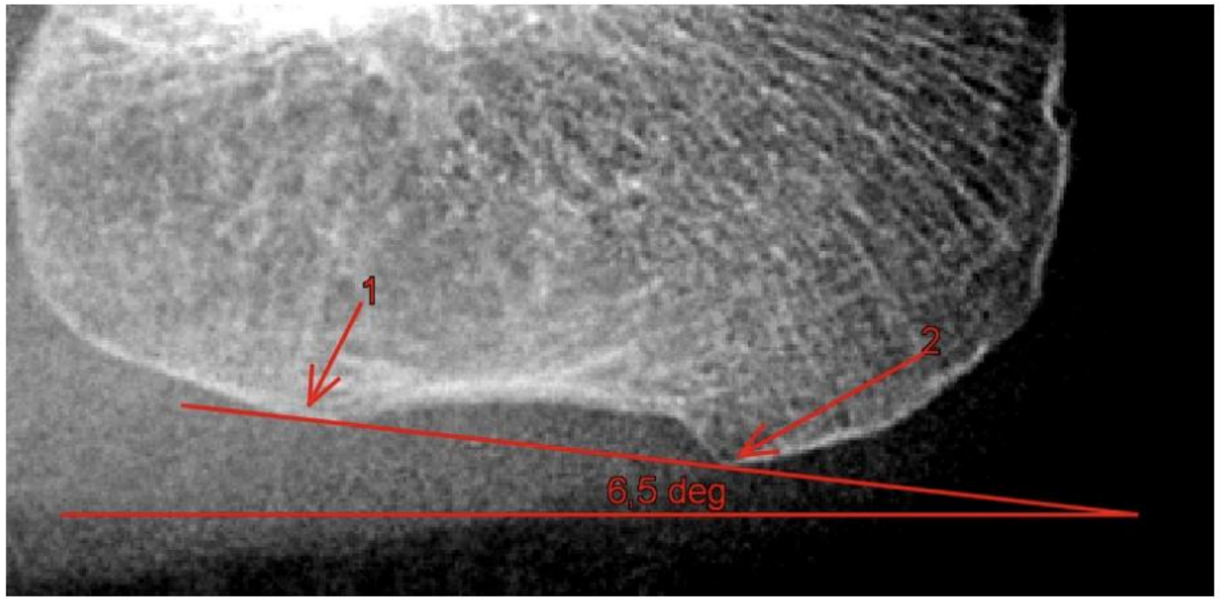
Example: Calcaneus pitch



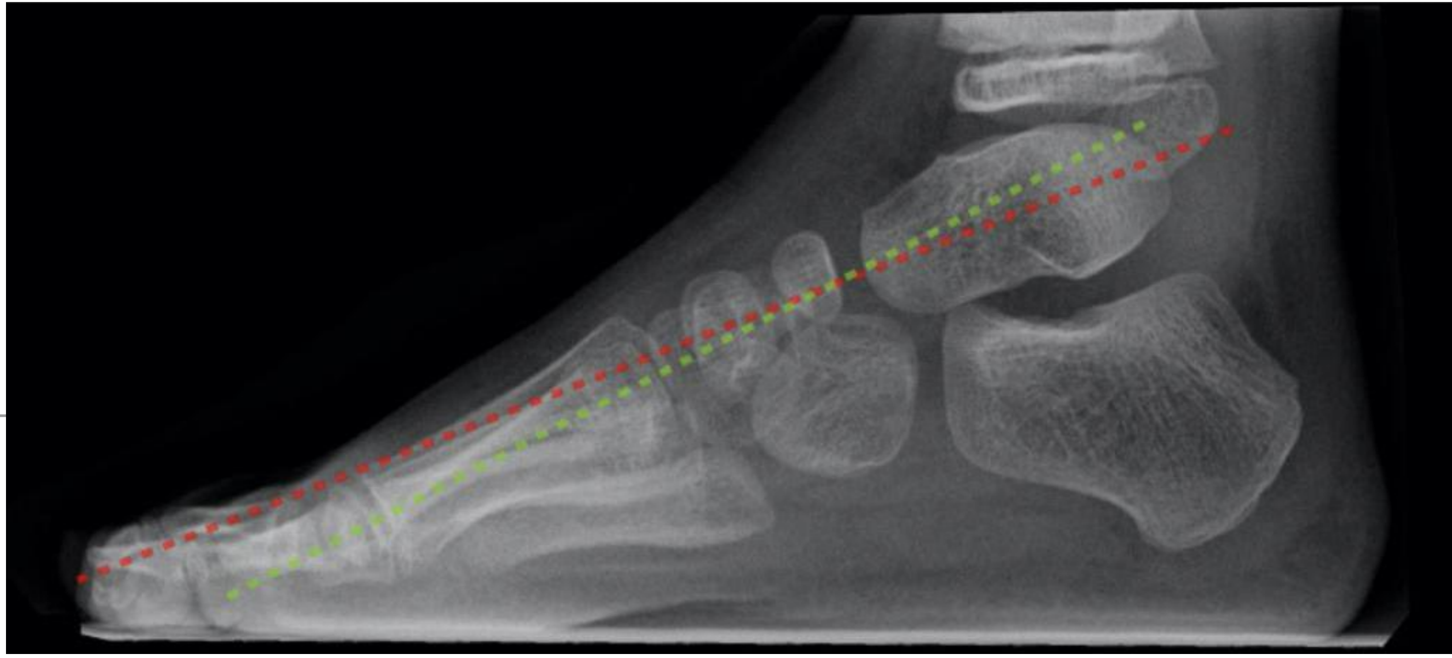
Protocol

- Identify the two edges of the calcaneum
- measure calcaneus pitch as angle against horizontal (press shift during second segment)





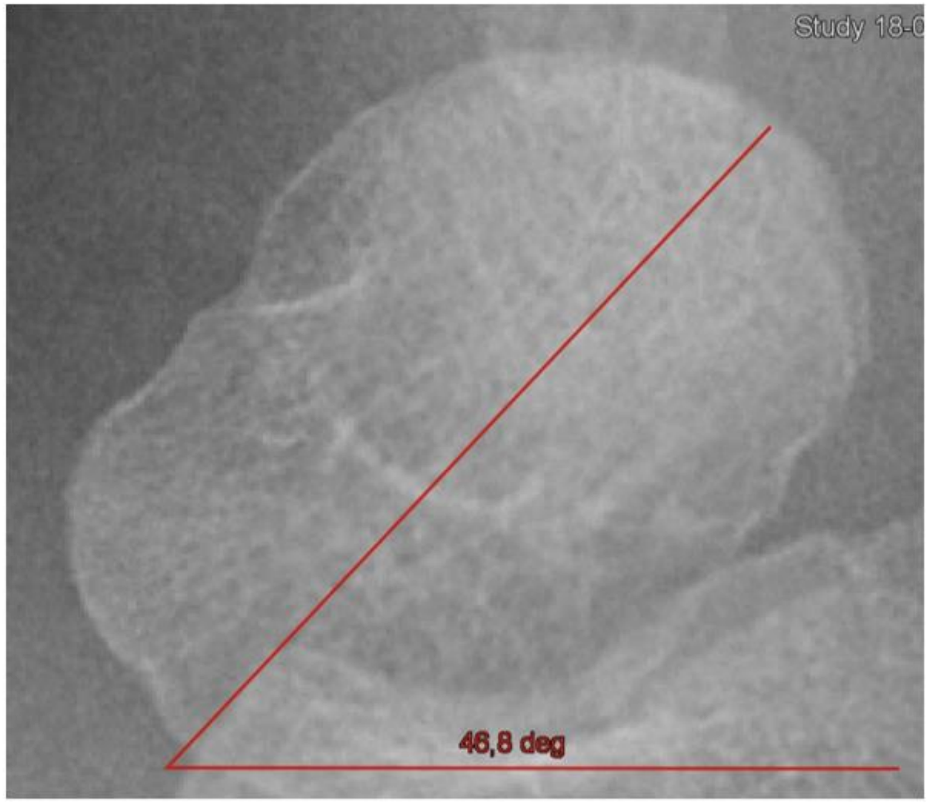
Example: Meary's angle

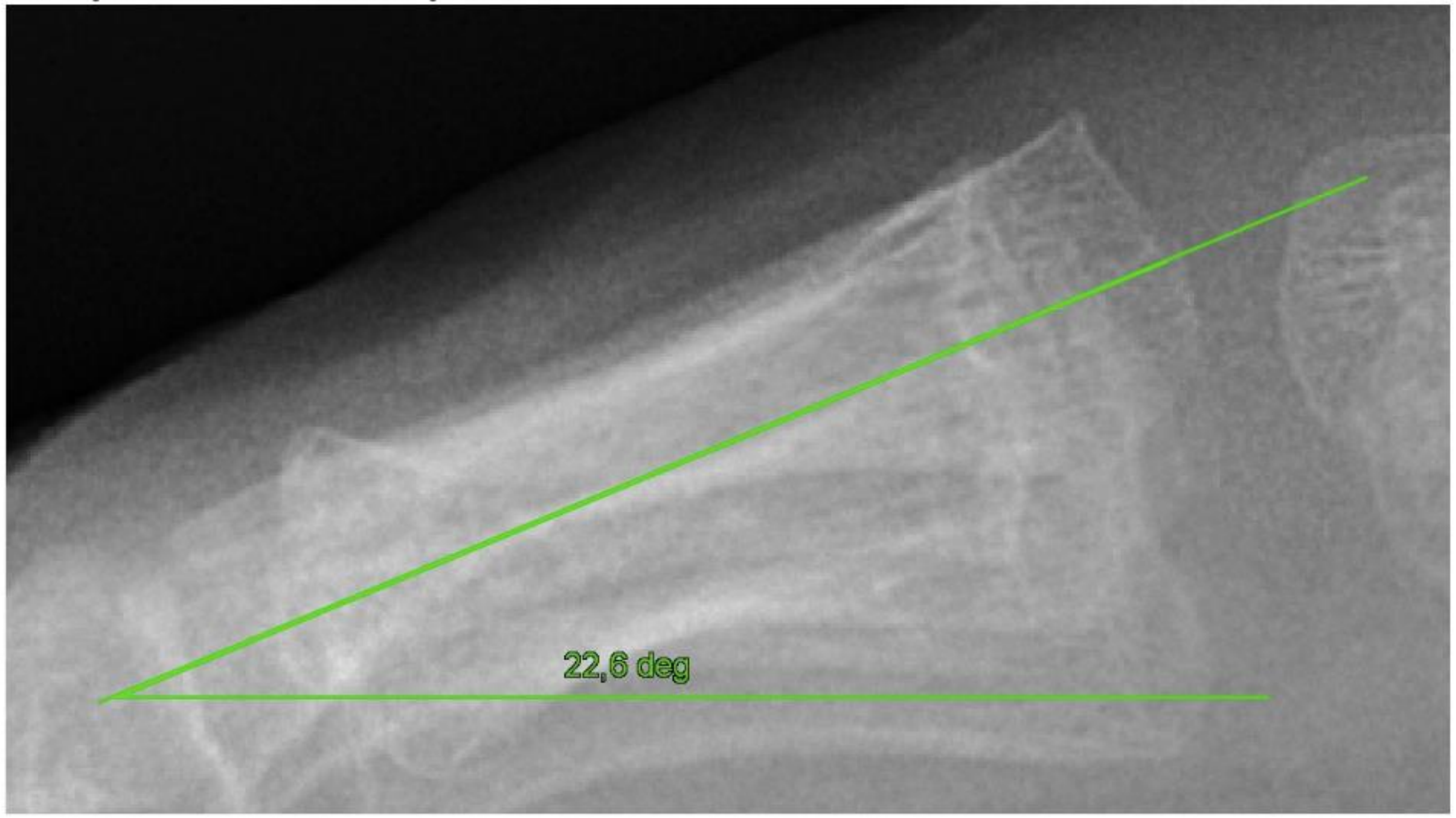


talo-first metatarsal angle

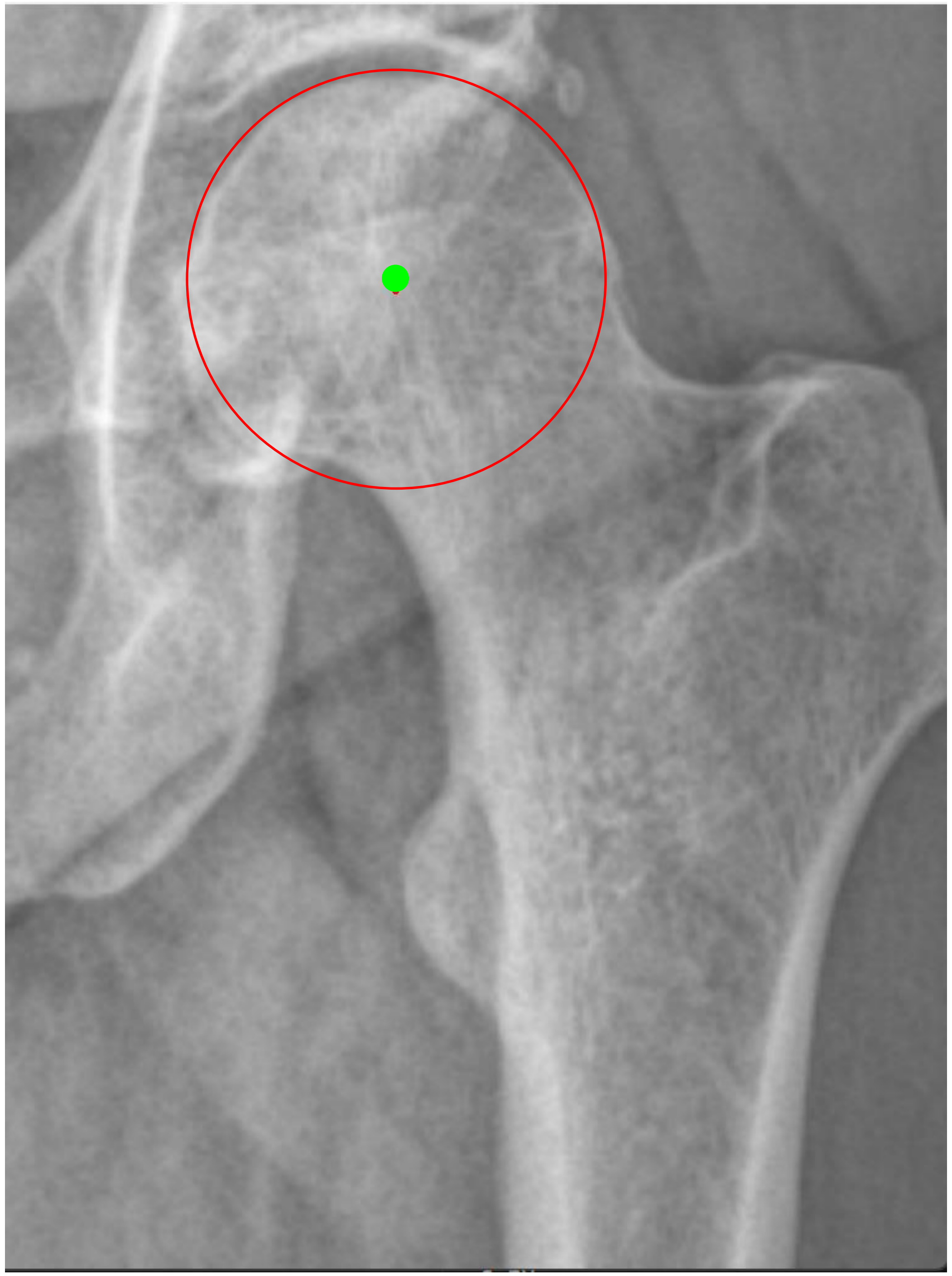
Protocol:

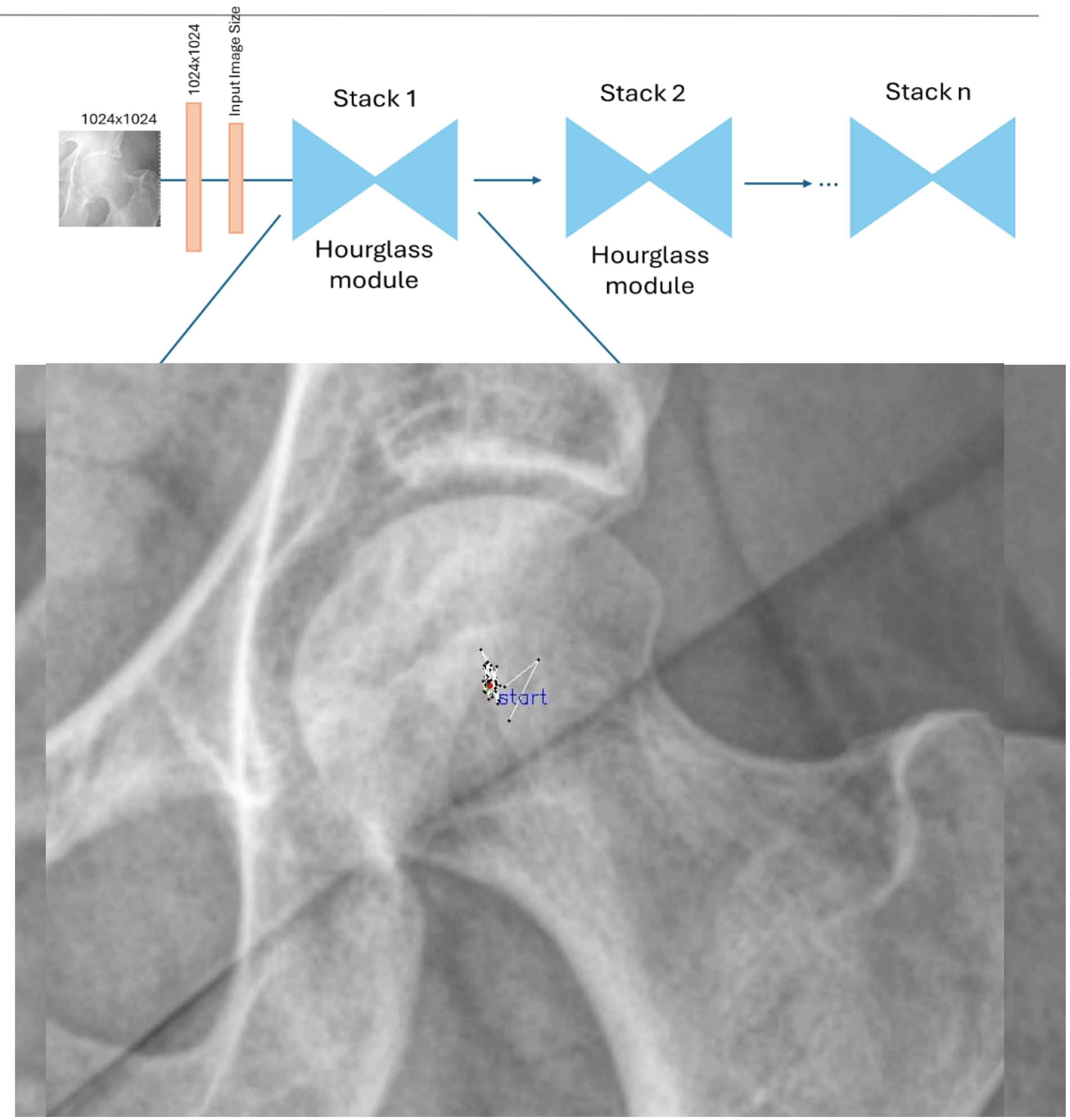
- Measure talus pitch (against horizontal)
- Measure MT1 pitch
- Talo-MT-I is computed as MT1 pitch – talus pitch





Machine learning in x-ray evaluations





Radiographic readouts: reliability?

- Can you get the same measurement twice?
- Can two readers get the same measurement?

Intrarater reliability

Interrater reliability

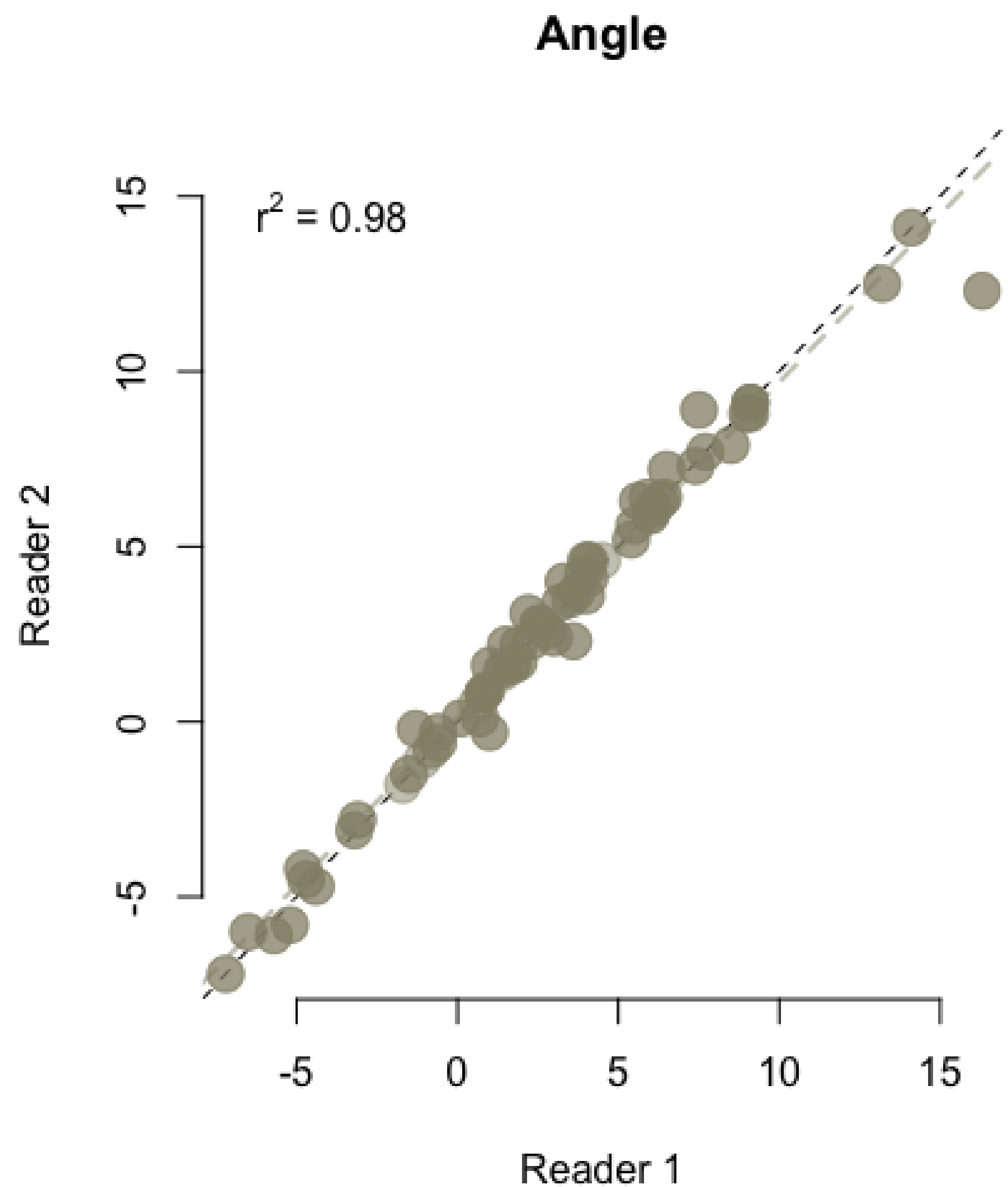
- Various methods:
  - Pearson's correlation (r^2)
  - Bland-Altmann plot
  - Intra- class correlation coefficient (ICC)

$$\text{Reliability index} = \frac{\text{true variance}}{\text{true variance} + \text{error variance}}$$

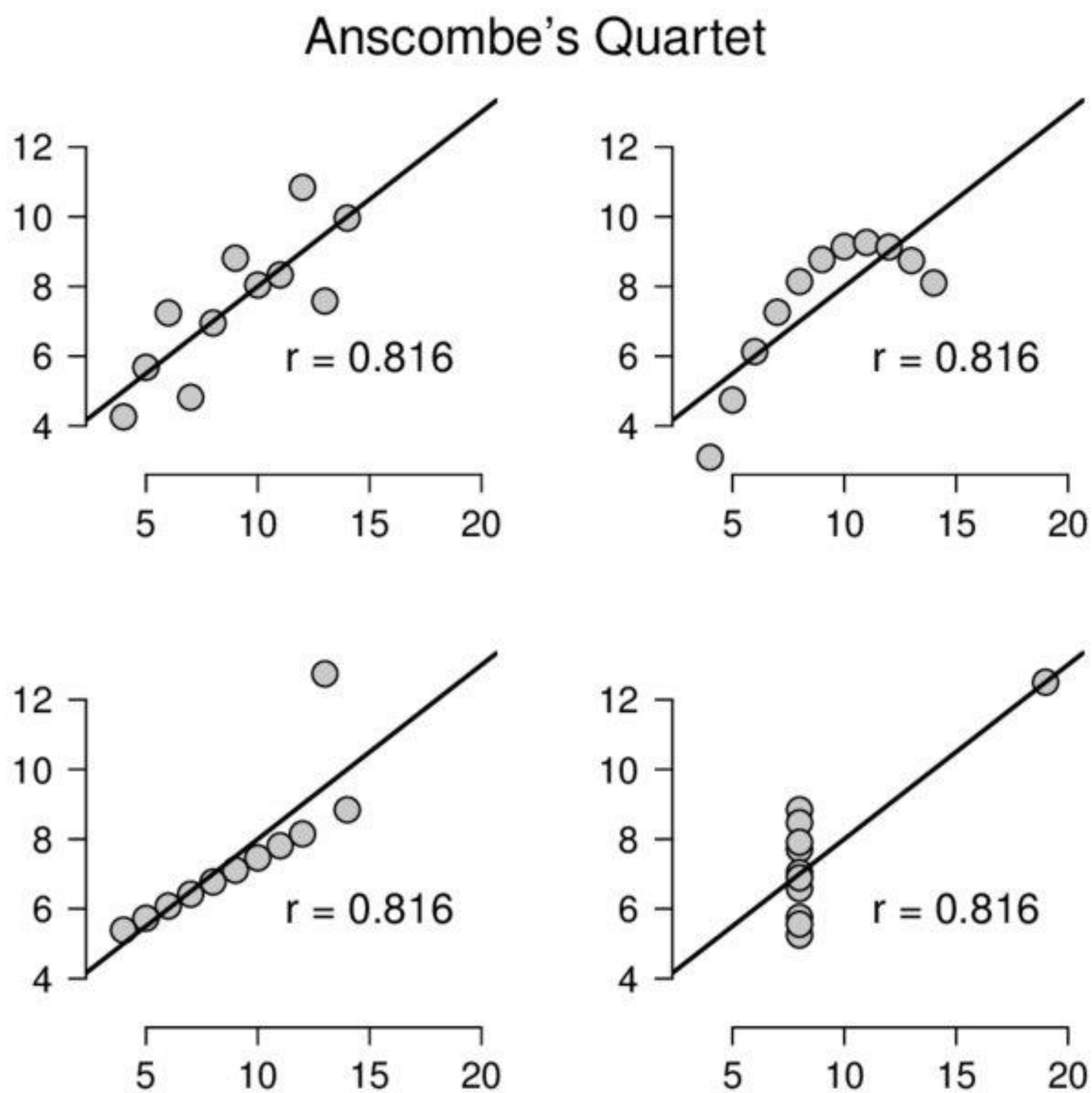
Angle_reader1	Angle_reader2
4.5	4.6
1.4	1.4
6	5.9
2.6	2.8
2.6	2.8
1.9	2.2
1.9	2.2
2.5	2.8
2.5	2.8
9	8.8
9	8.8
3.9	4.2
3.9	4.2
6.1	6.1
2.3	2.3
2.3	2.3
-3.2	-3.1
-3.2	-3.1

Radiographic readouts: reliability?

Angle_reader1	Angle_reader2
4.5	4.6
1.4	1.4
6	5.9
2.6	2.8
2.6	2.8
1.9	2.2
1.9	2.2
2.5	2.8
2.5	2.8
9	8.8
9	8.8
3.9	4.2
3.9	4.2
6.1	6.1
2.3	2.3
2.3	2.3
-3.2	-3.1
-3.2	-3.1

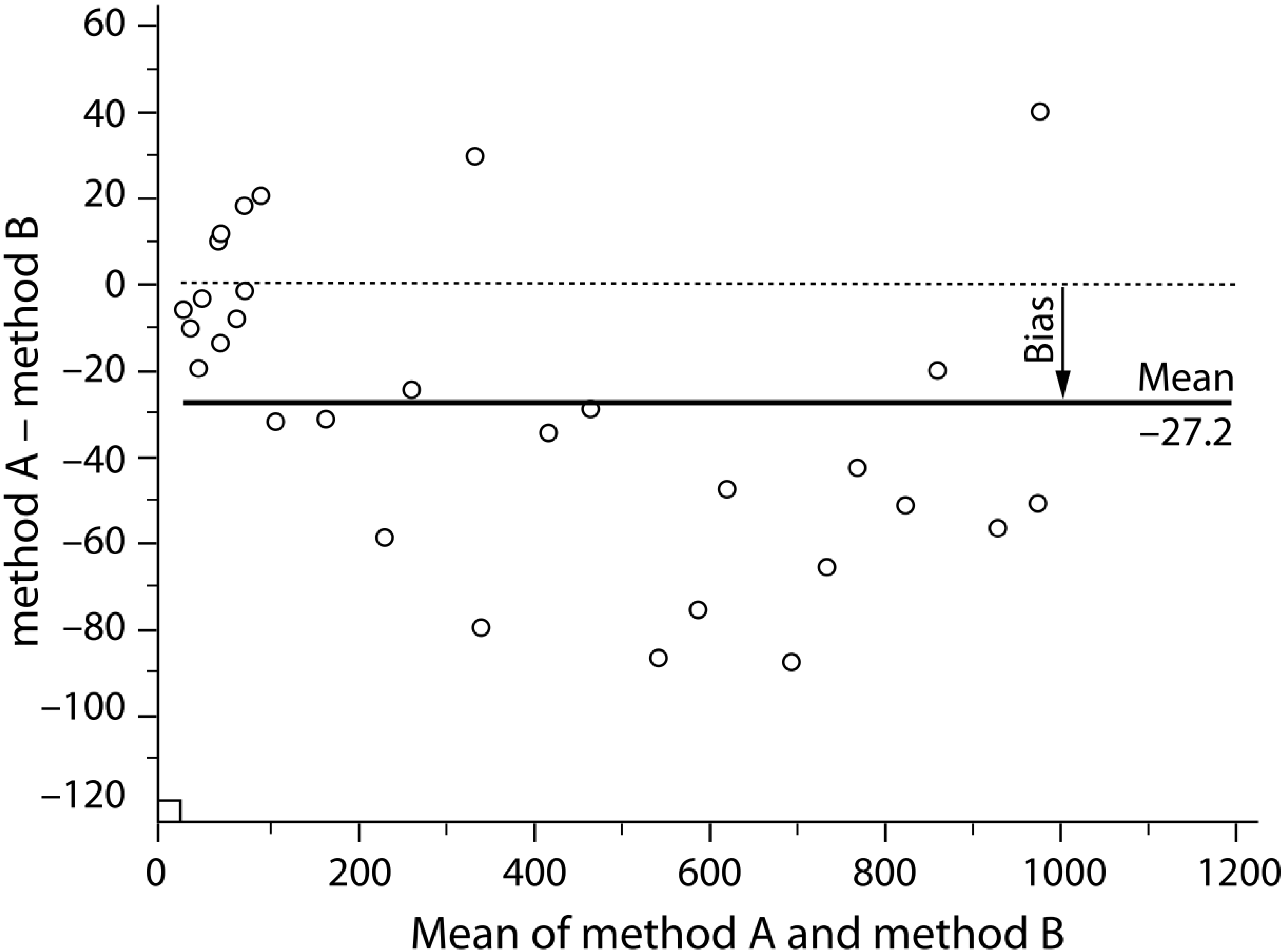


Correlation coefficient is not enough…



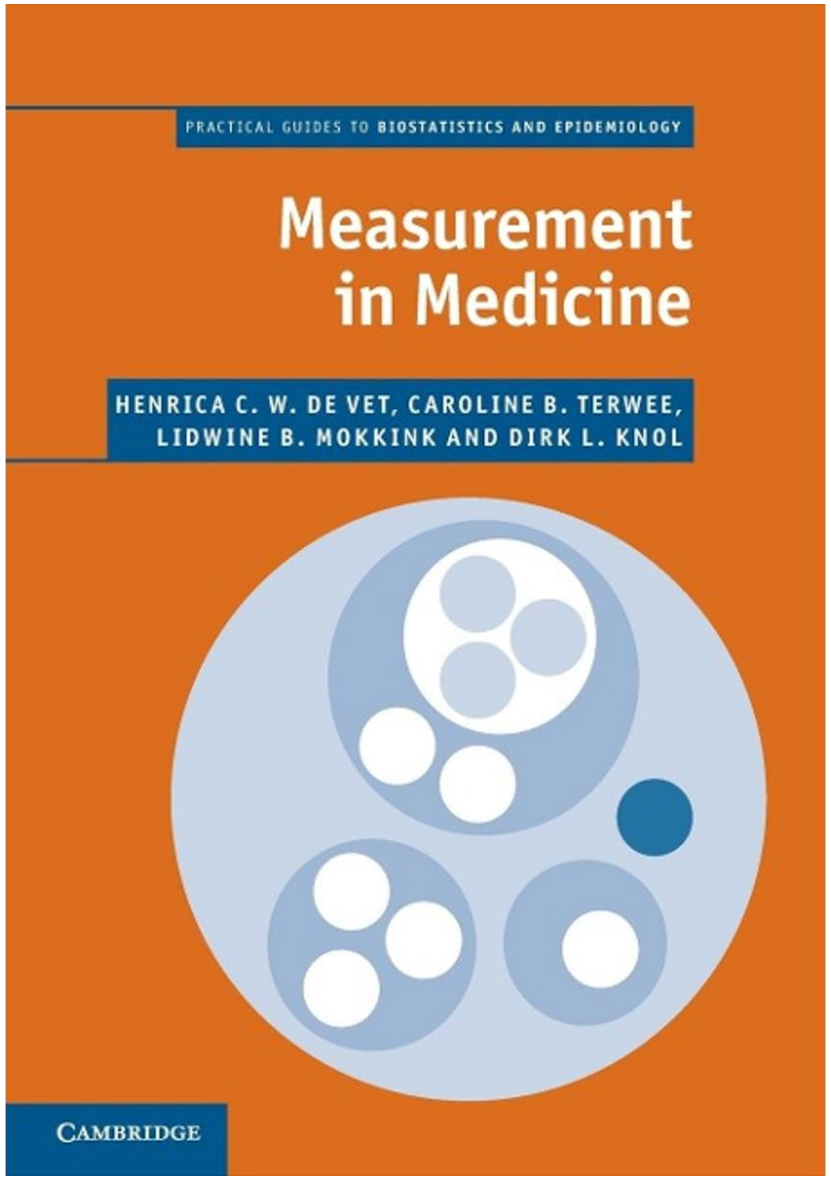
Heathcote *et al*. An Introduction to Good Practices in Cognitive Modeling. doi:10.1007/978-1-4939-2236-9_2.

Bland Altmann plot



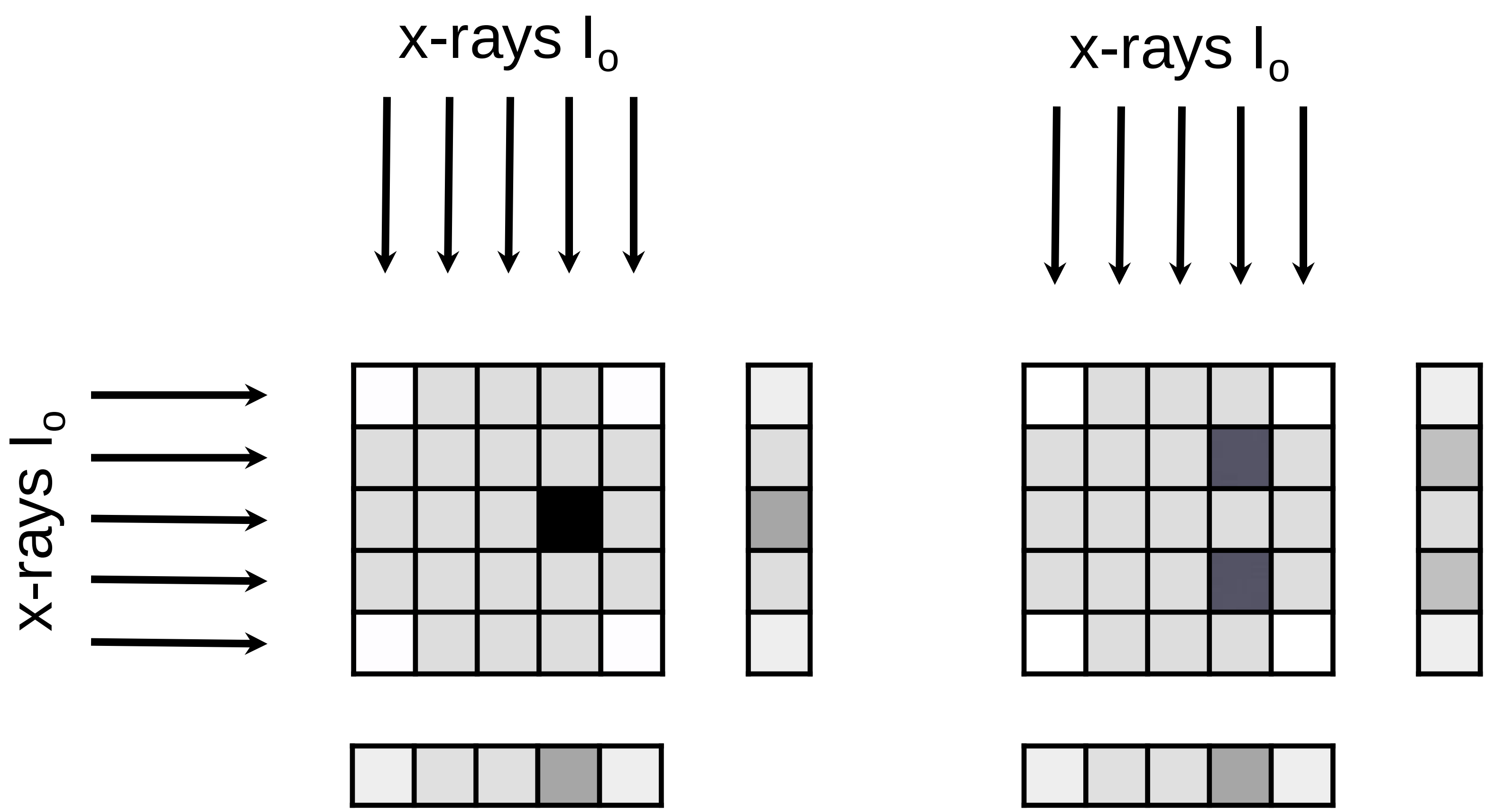
Further reading

- Reliabilty
  - Intraclass correlation coefficient (inter-raters) for continuous variables
  - Kappa for categorical variable (eg scores)



Limitations?

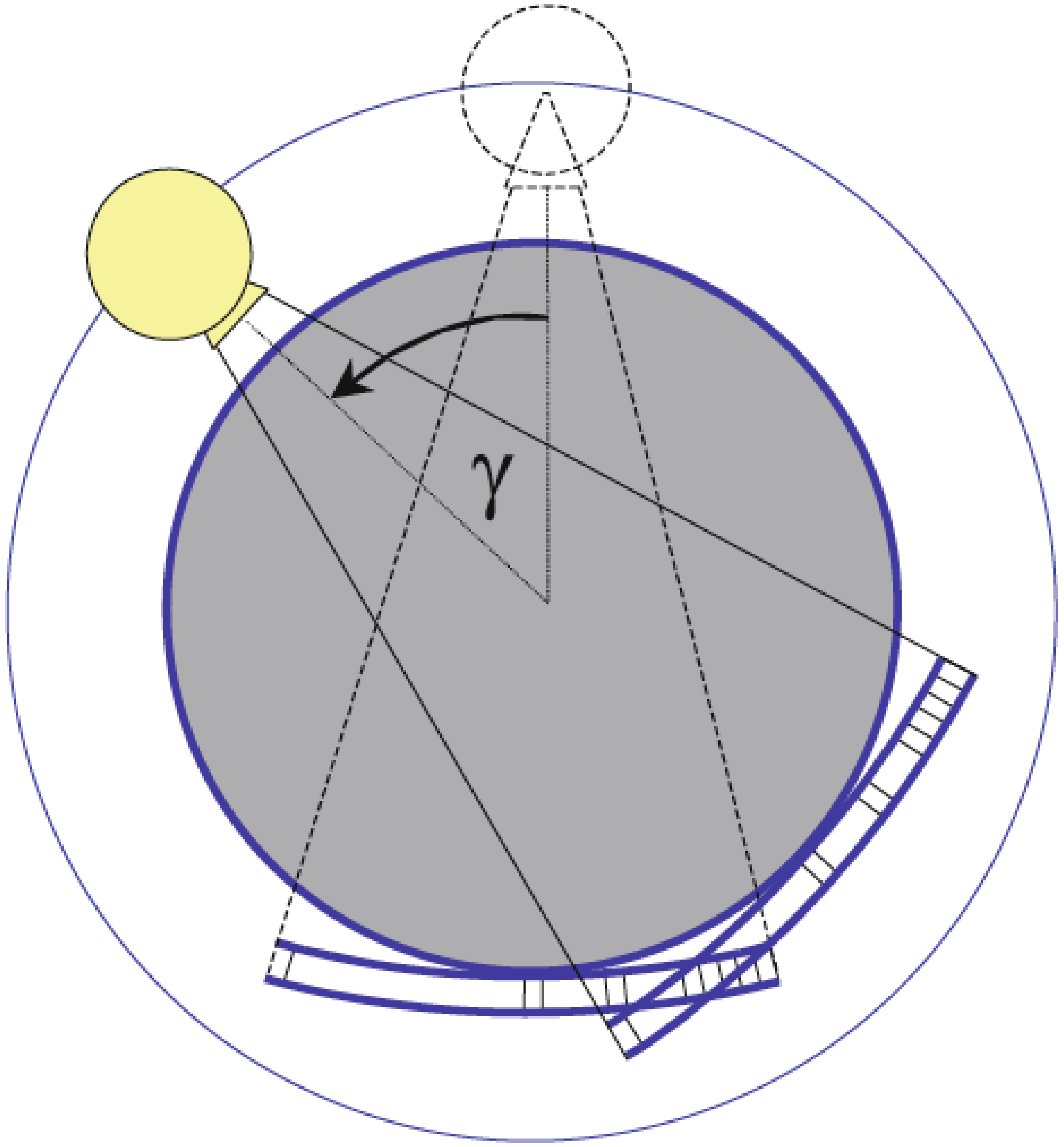
The projection limitation

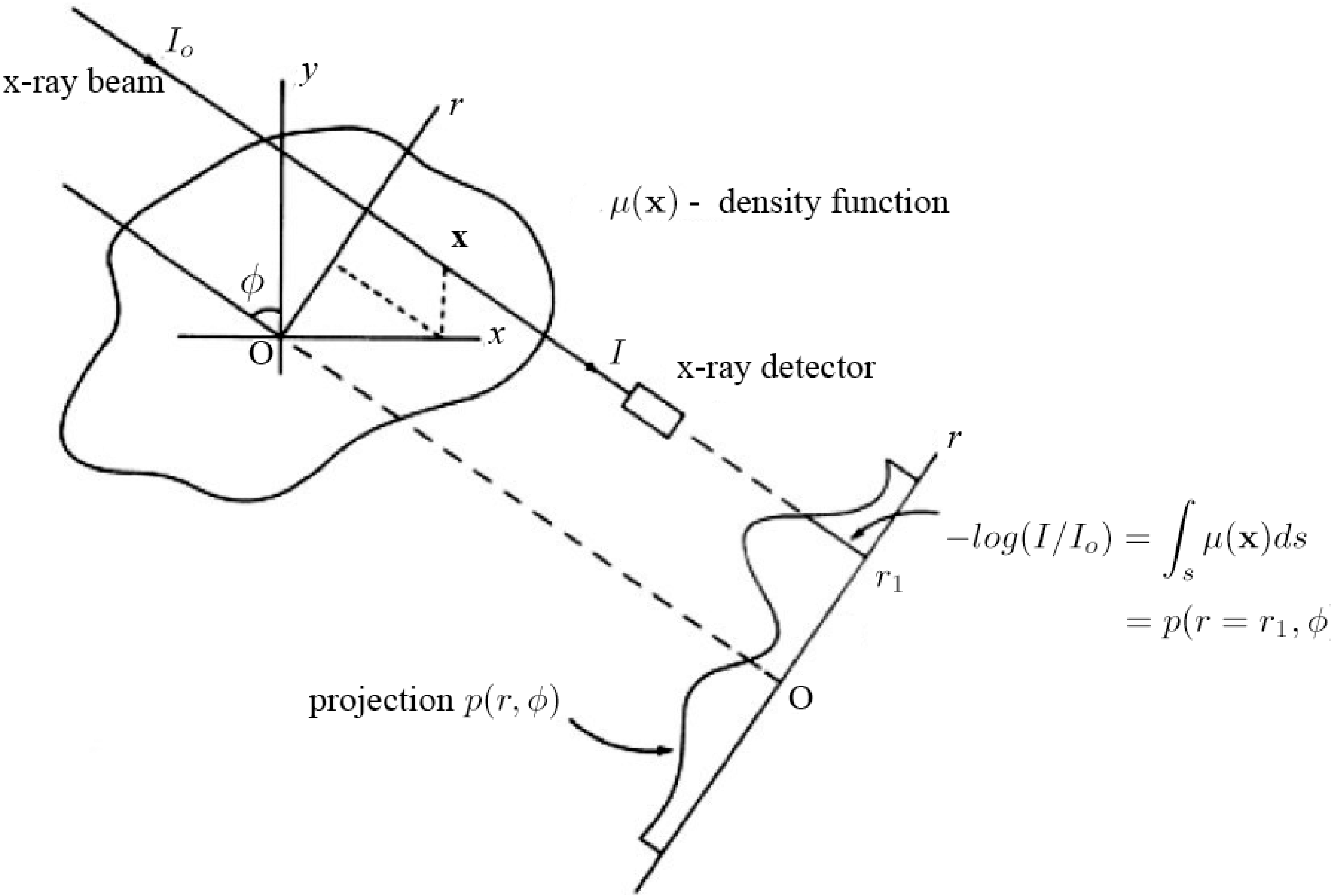


Computed tomography

Computed tomography: method of acquisition

- Rotation of the x-ray tube and detector around the object
- Projection is recorded at each angular step



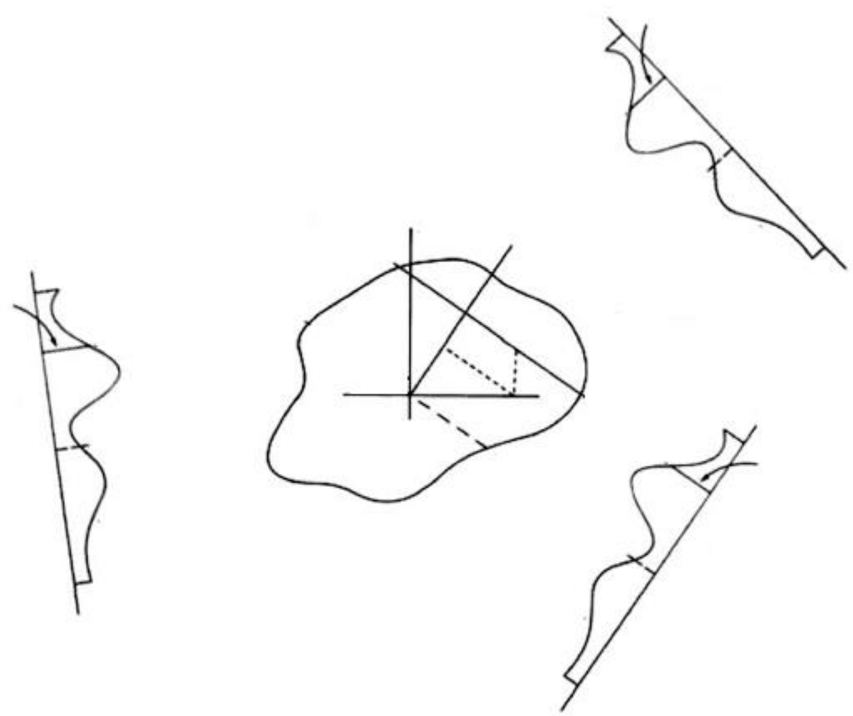


I_o
x-ray beam
y
r
$\mu(\mathbf{x})$ - density function
$\mathbf{x}$
ϕ
x
O
I
x-ray detector
r
$-log(I/I_o) = \int_s \mu(\mathbf{x})ds$
r_1
$= p(r = r_1, \phi)$
projection $p(r, \phi)$
O

The central problem of computed tomography

The projections *p* can be determined experimentally as functions of (r,ϕ) by measuring I/I_o with a x-ray detector.

<u>But how to compute $\mu(x,y)$ from collections of $p(r,\phi)$?</u>



Set of projections = **sinogram** in the radon space

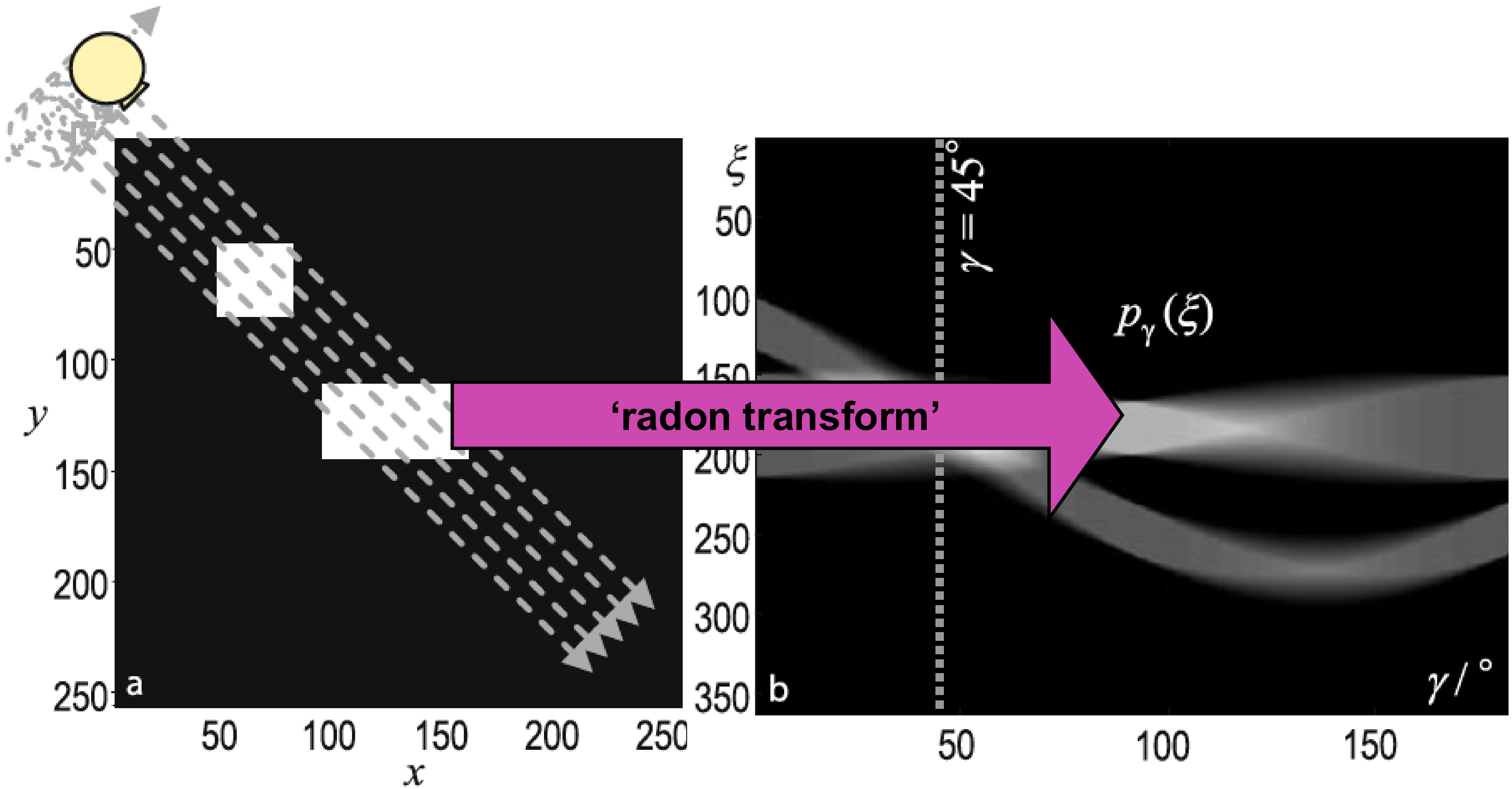


Image reconstruction

analytical solutions to the inverse problem

Inverse radon transform or Fourier transforms

Limitations:

- needs lot of projections
- CPU-consuming

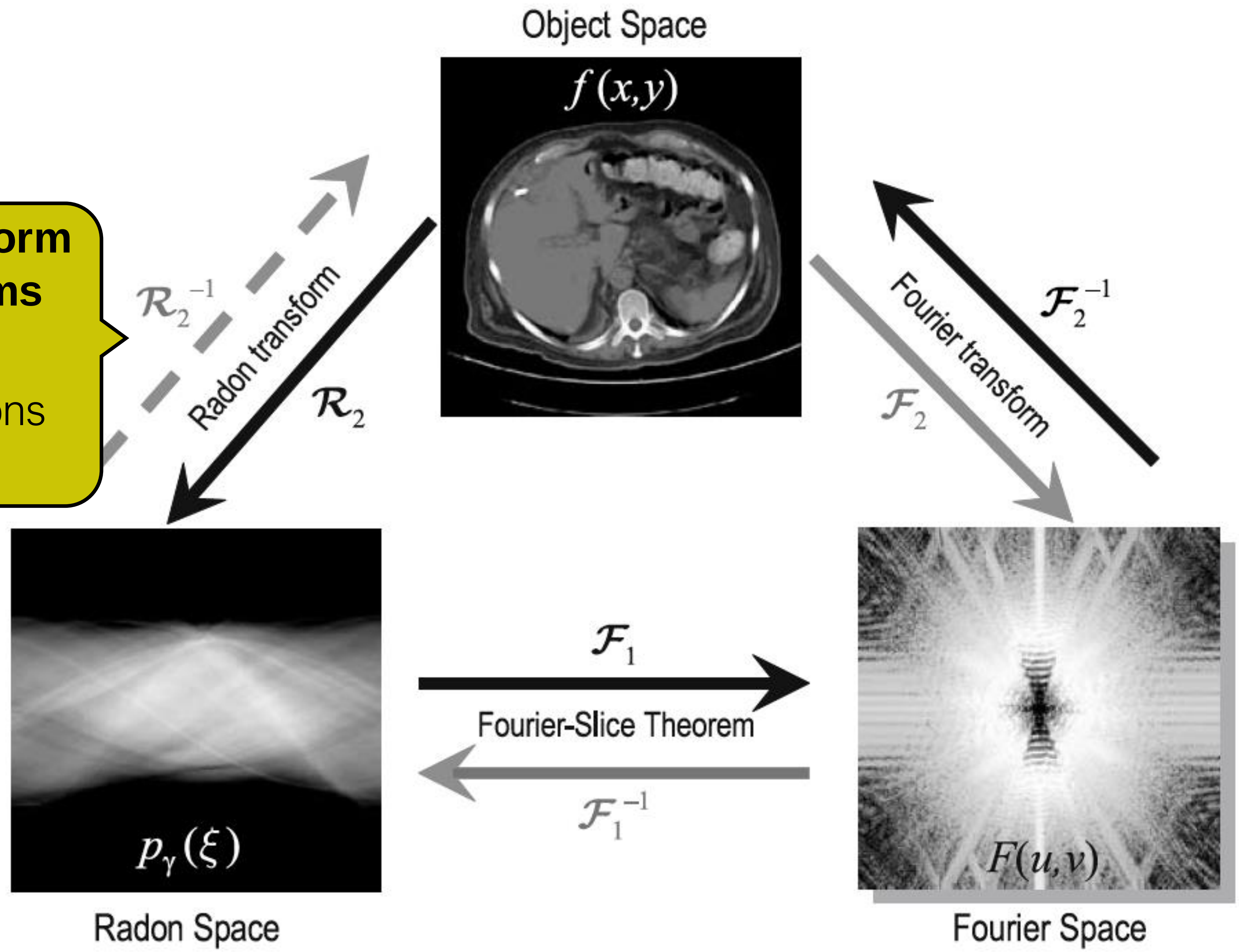
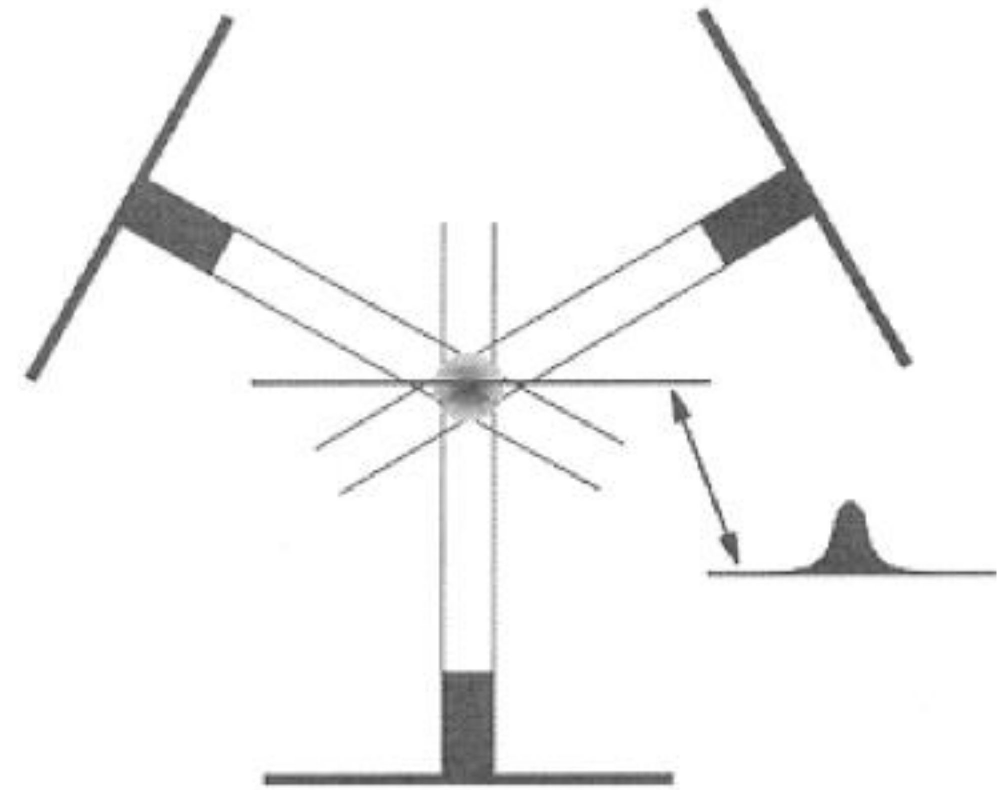


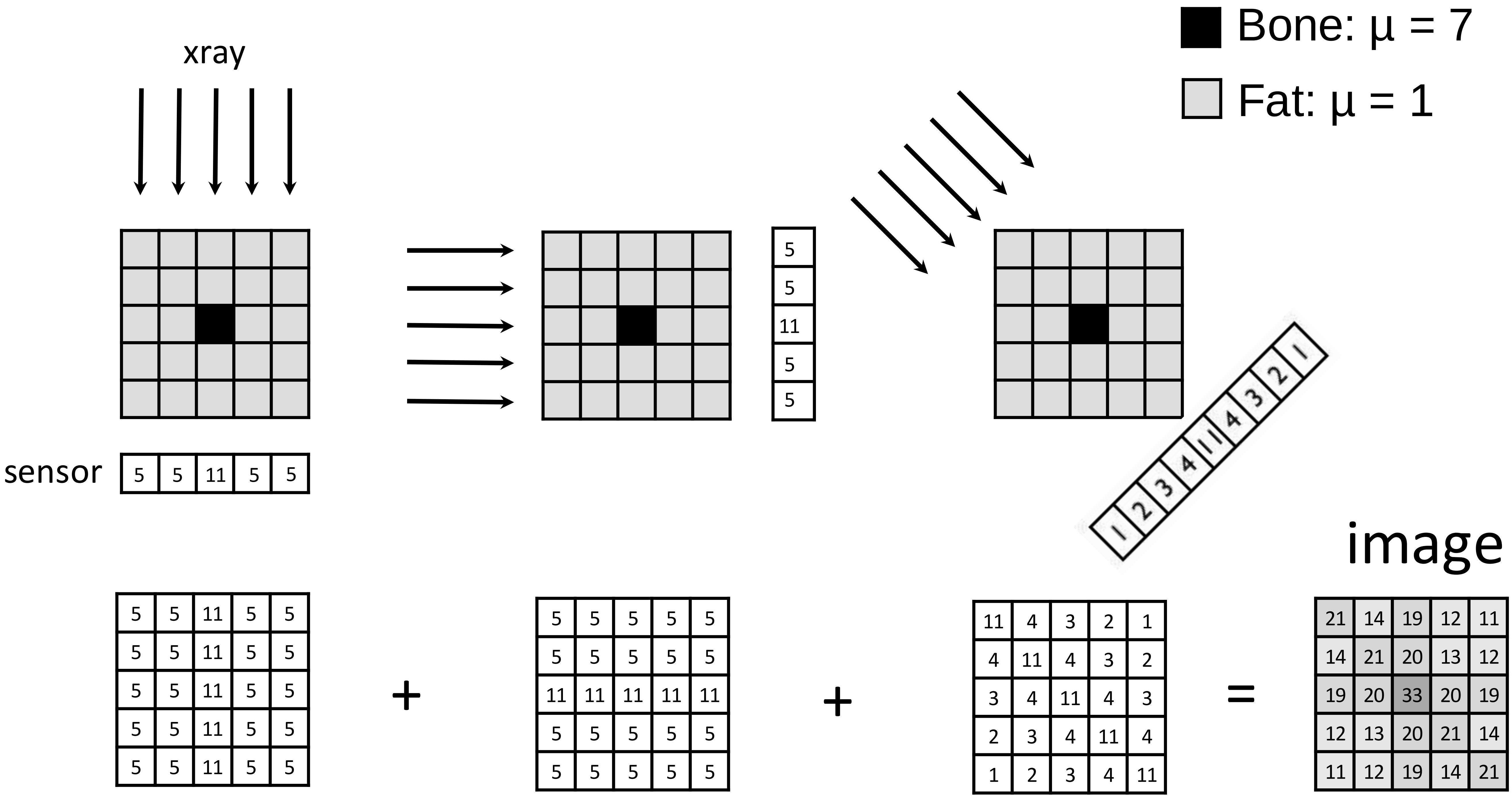
Image reconstruction
Simple back-projection

- Starts with an empty image matrix, and the μ value from each ray in all views is added to each pixel in a line through the image corresponding to the ray's path
- A characteristic 1/r blurring is a byproduct



simple backprojection

Simple back-projection



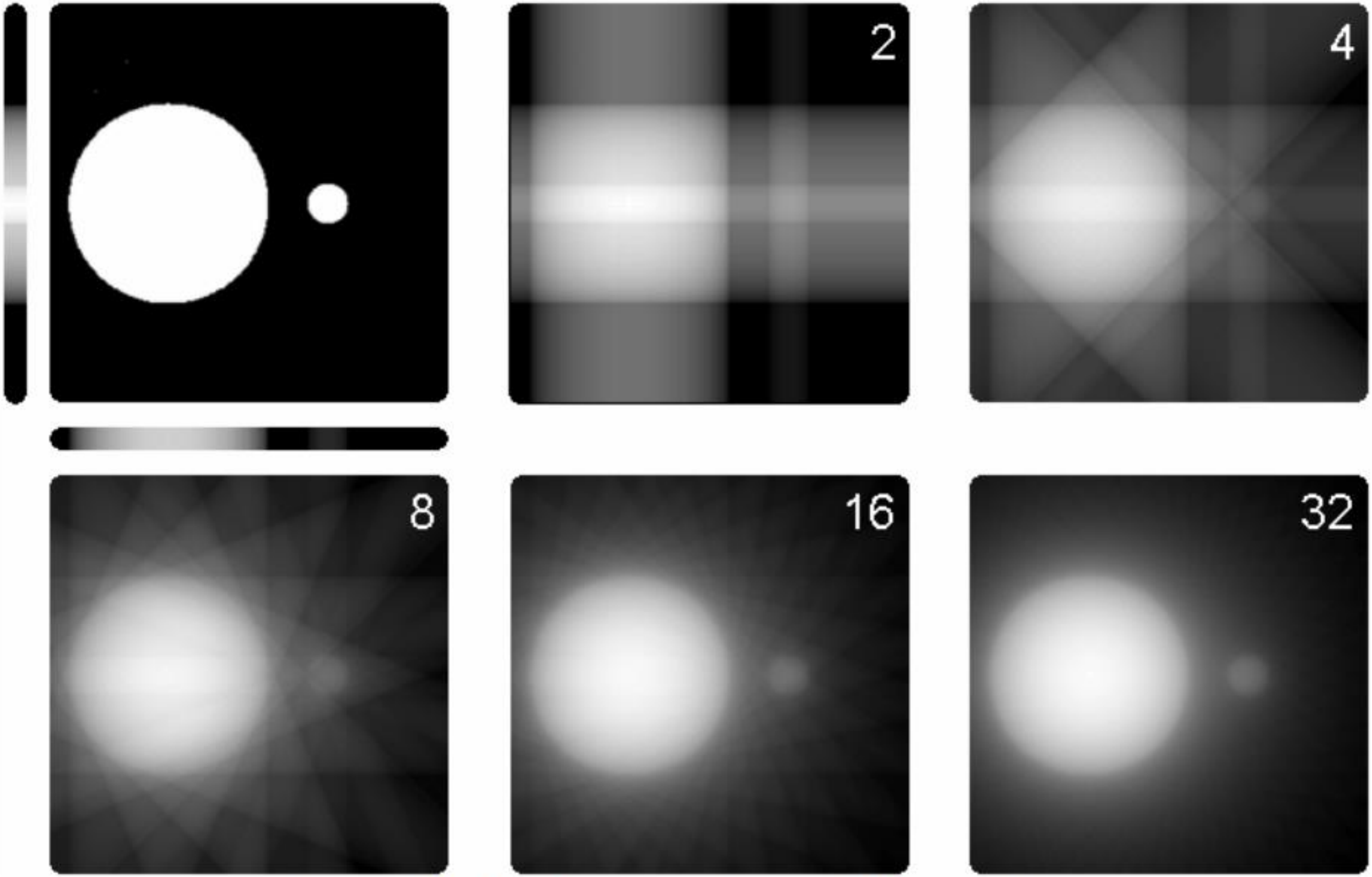
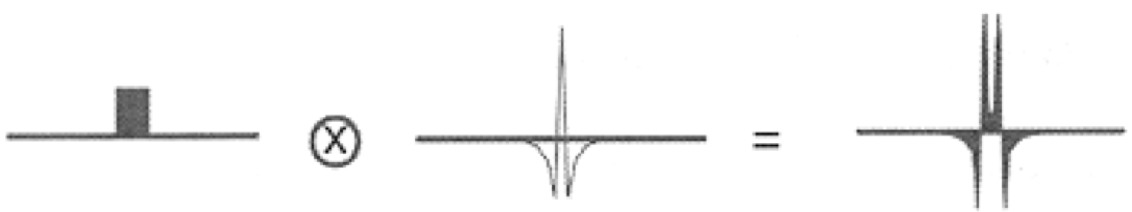
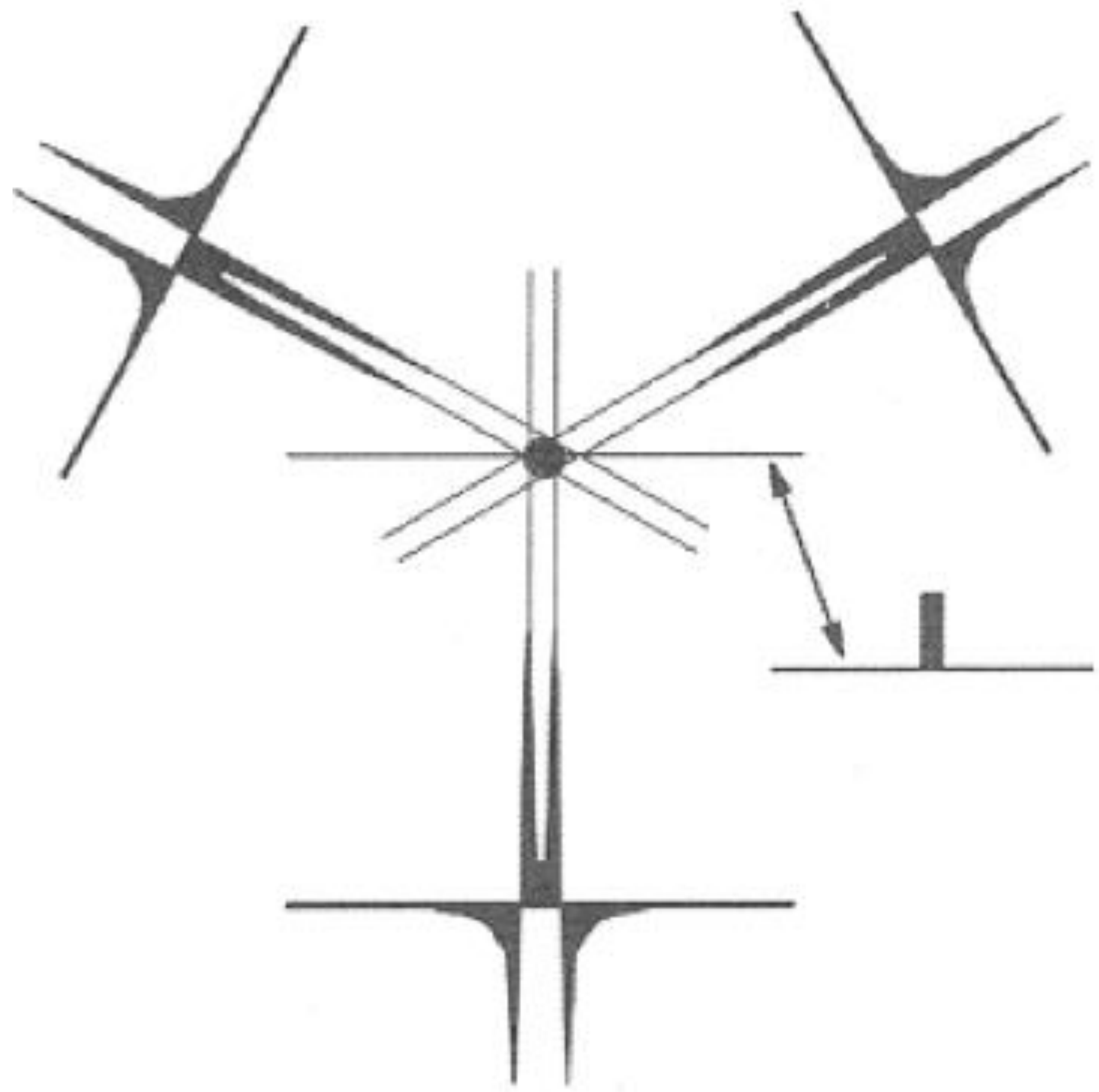


Fig 6.78: Back-projection without filter

Image reconstruction
Filtered back-projection

- The raw view data are mathematically filtered before being backprojected onto the image matrix
- Involves convolving the projection data with a convolution kernel





filtered backprojection

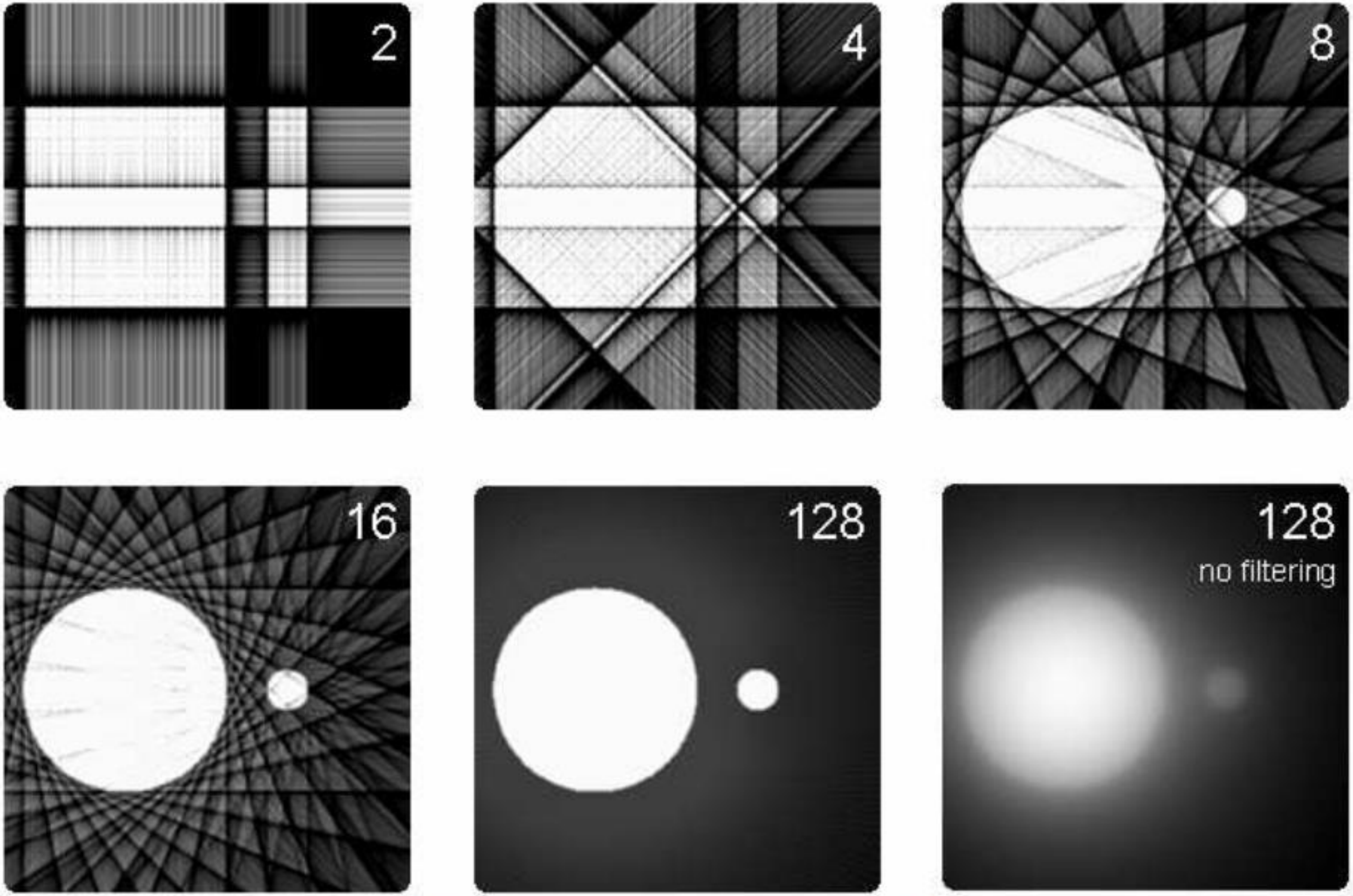


Fig 6.79: Back-projection with filter

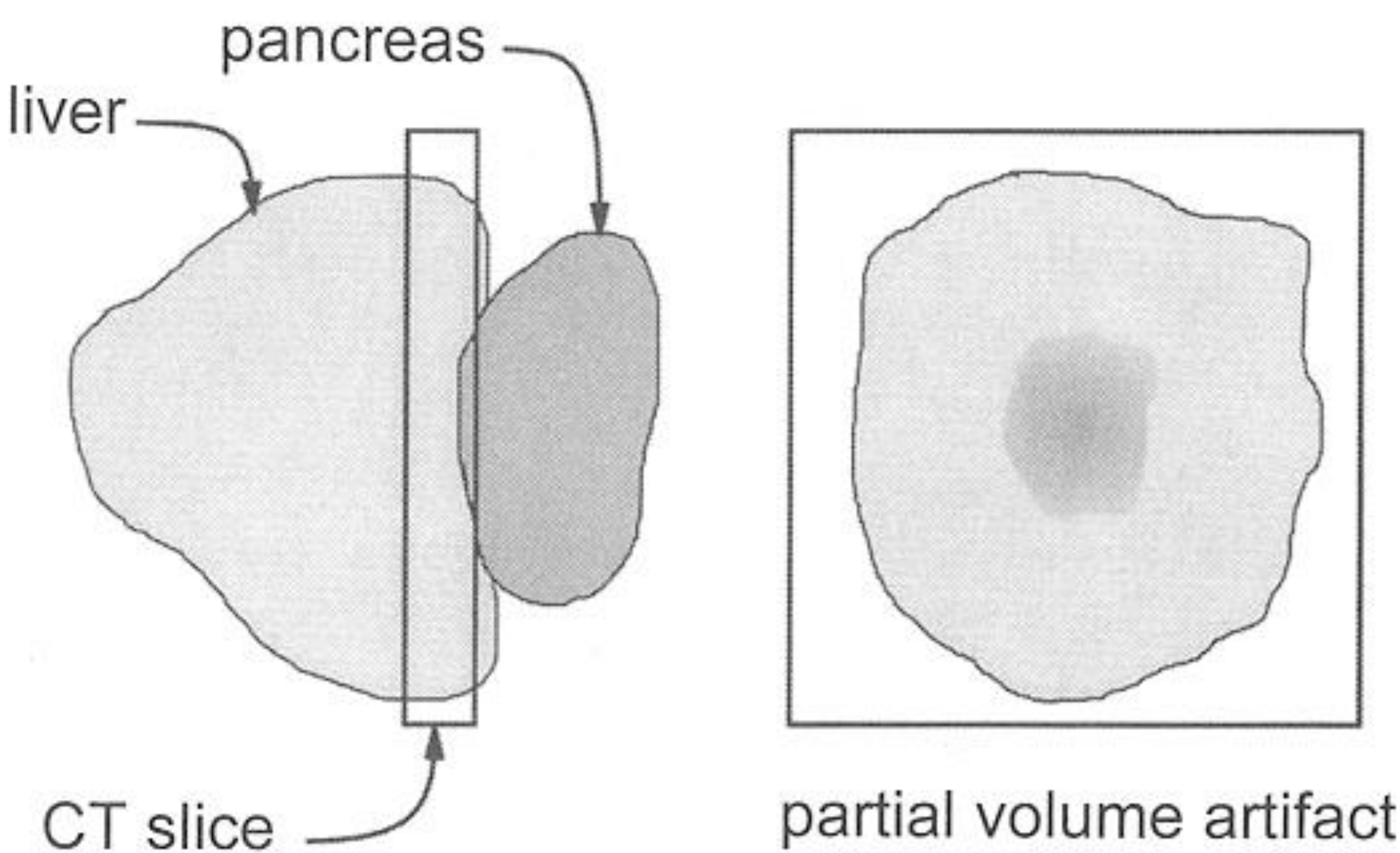
Exercise 4

Image artefacts in computed tomography

Motion artifacts

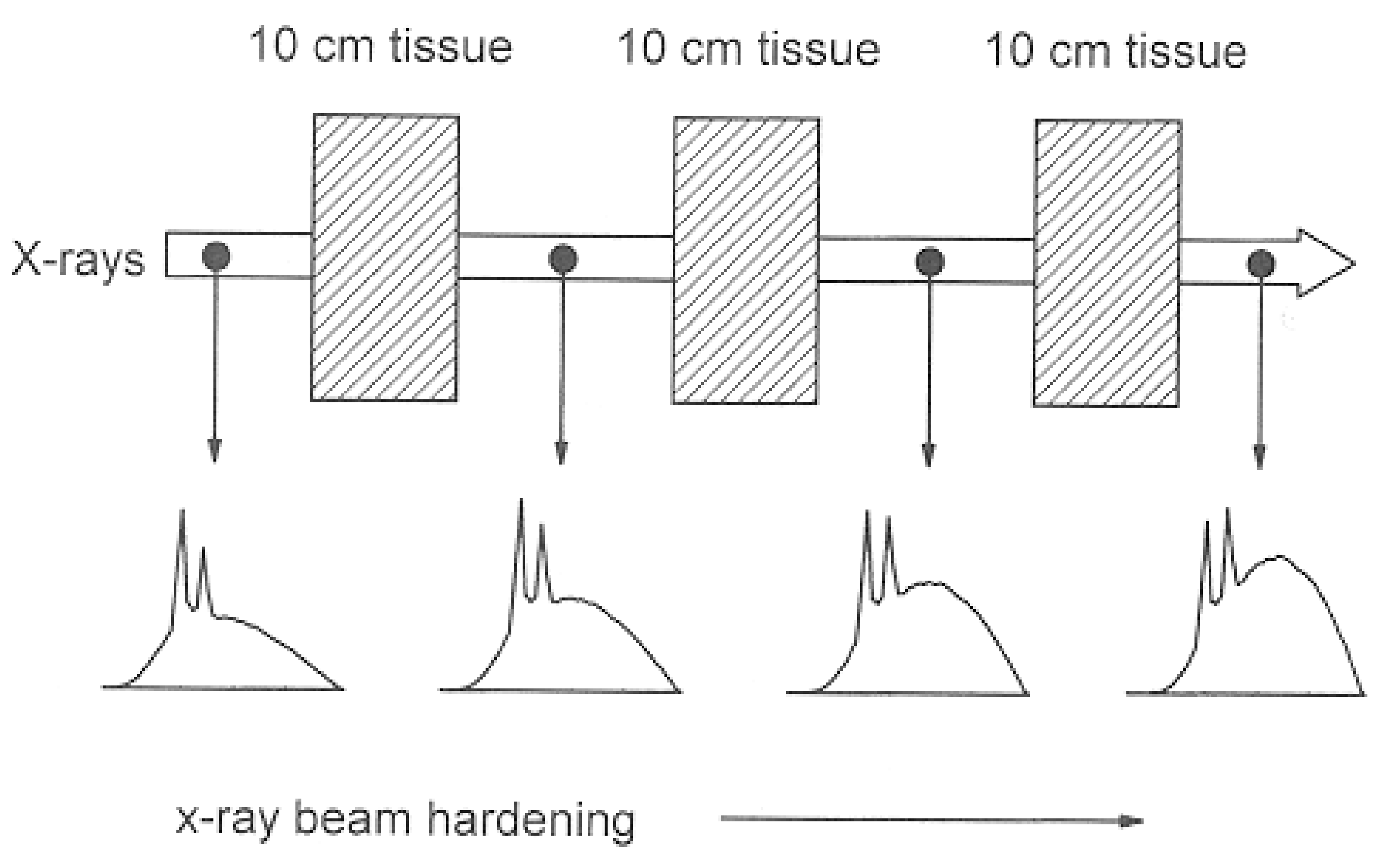
- Motion artifacts arise when the patient moves during the acquisition
- Small motions cause image blurring
- Larger physical displacements produce artifacts that appear as double images or image ghosting

Partial volume averaging



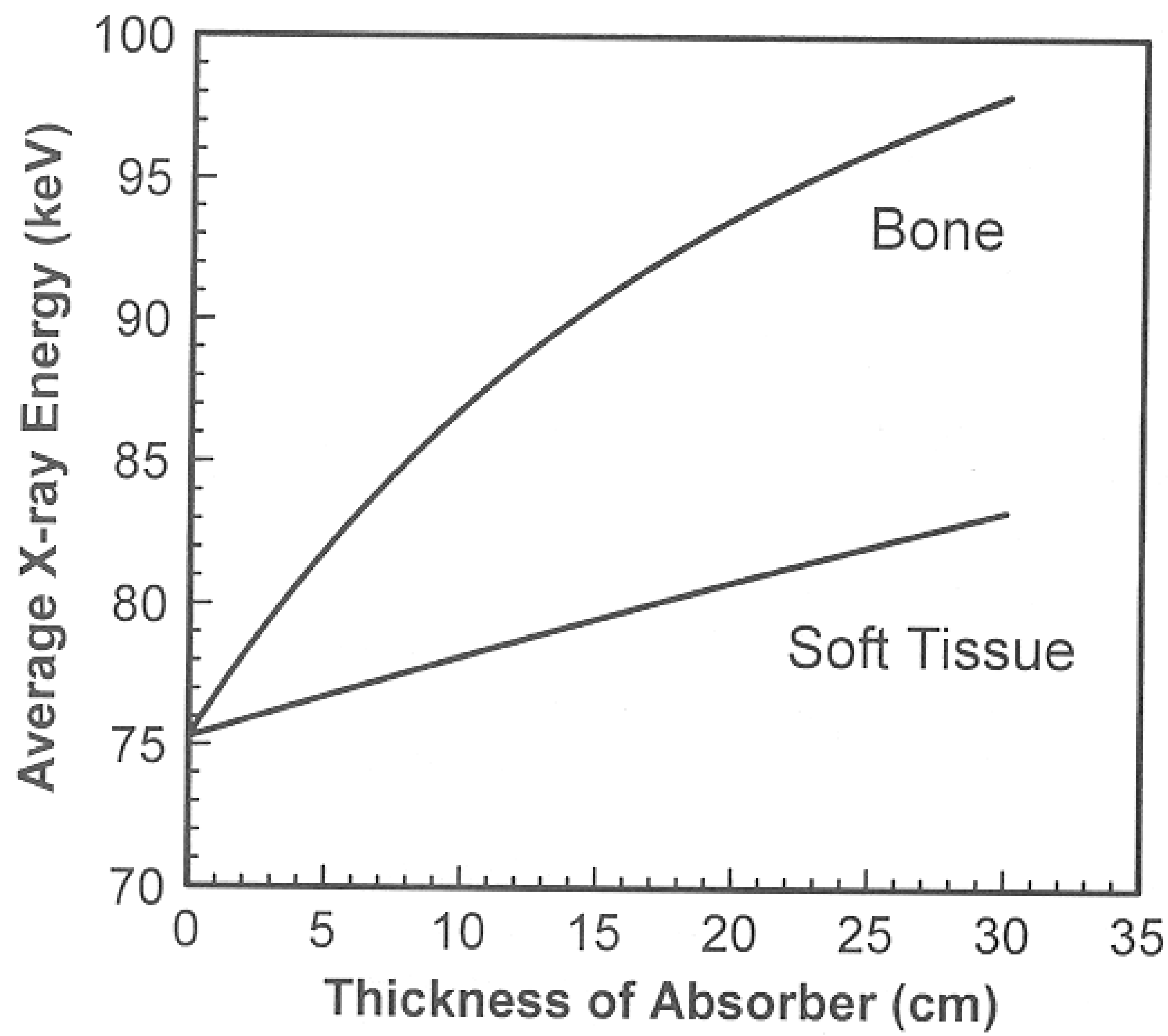
Beam hardening

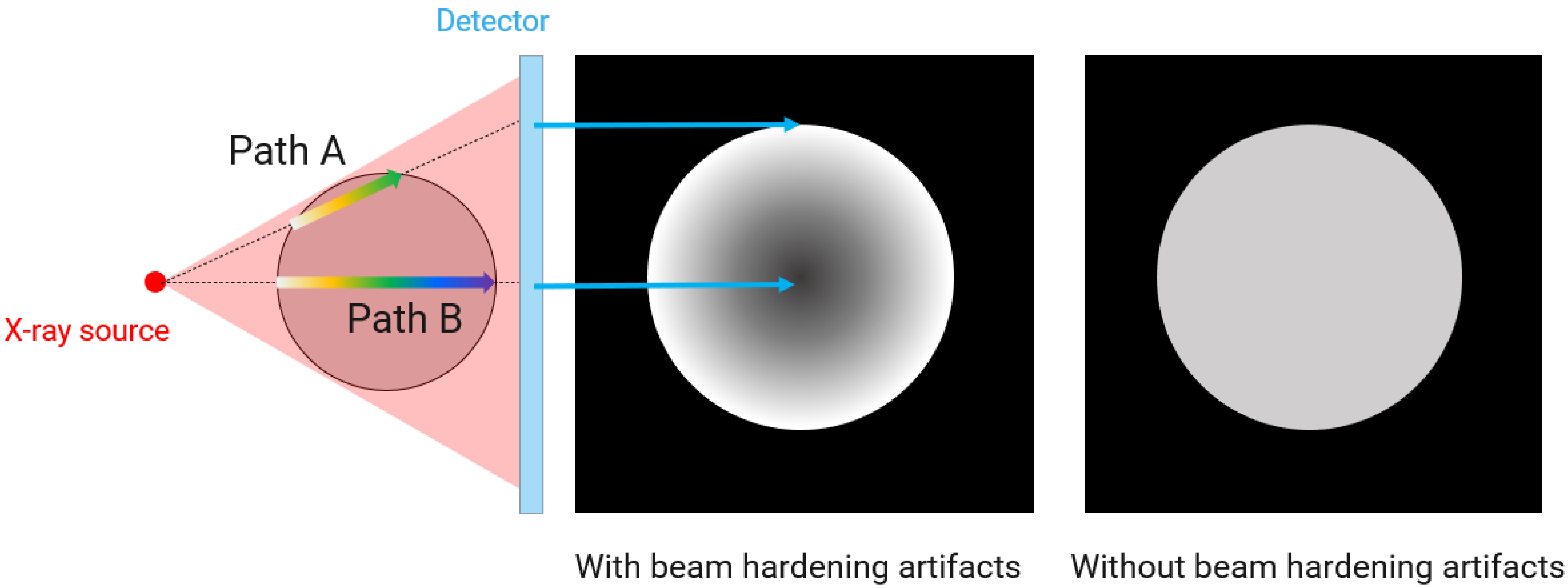
- Like all medical x-ray beams, CT uses a polyenergetic x-ray spectrum
- X-ray attenuation coefficients are energy dependent
- Lower-energy x-rays are attenuated to a greater extent than higher-energy
- The shape of the spectrum becomes skewed toward higher energies as it passes through the object
- Therefore it is less attenuated deeper in the tissue



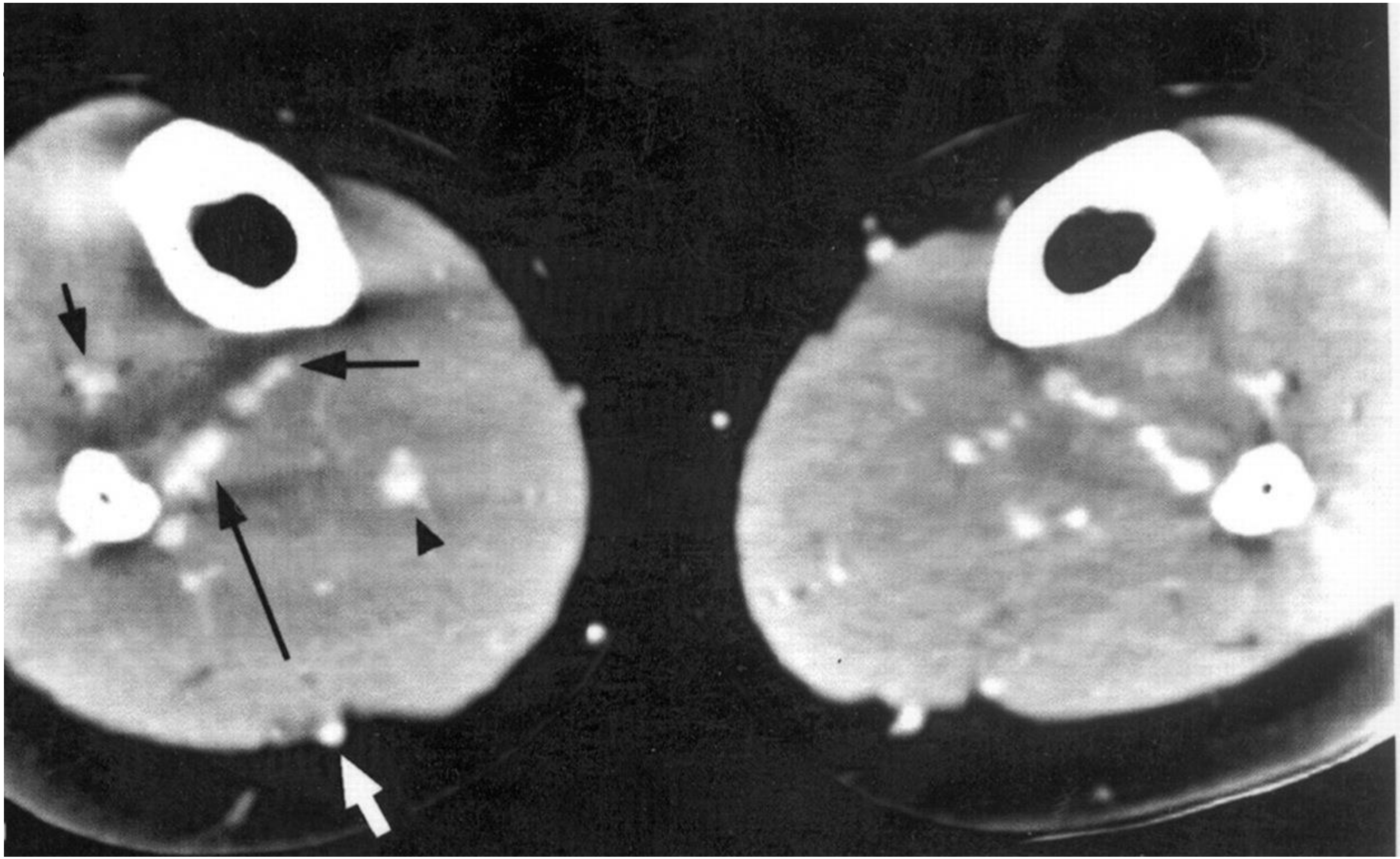
Beam hardening

- The average energy of the x-ray beam becomes greater ("harder") as it passes through tissue
- Because the attenuation of bone is greater than that of soft tissue, bone causes more beam hardening than an equivalent thickness of soft tissue

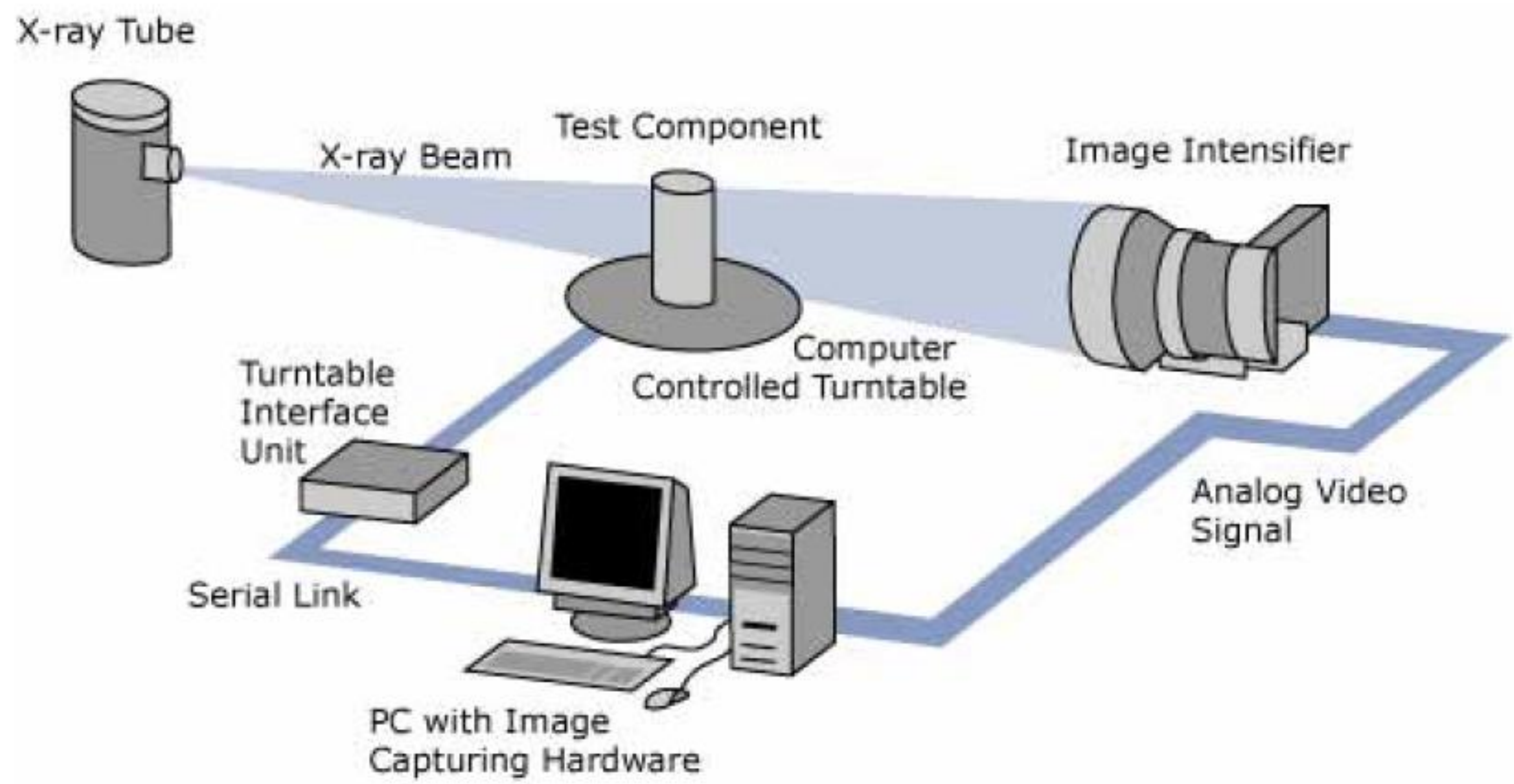



Detector
Path A
Path B
X-ray source
With beam hardening artifacts
Without beam hardening artifacts

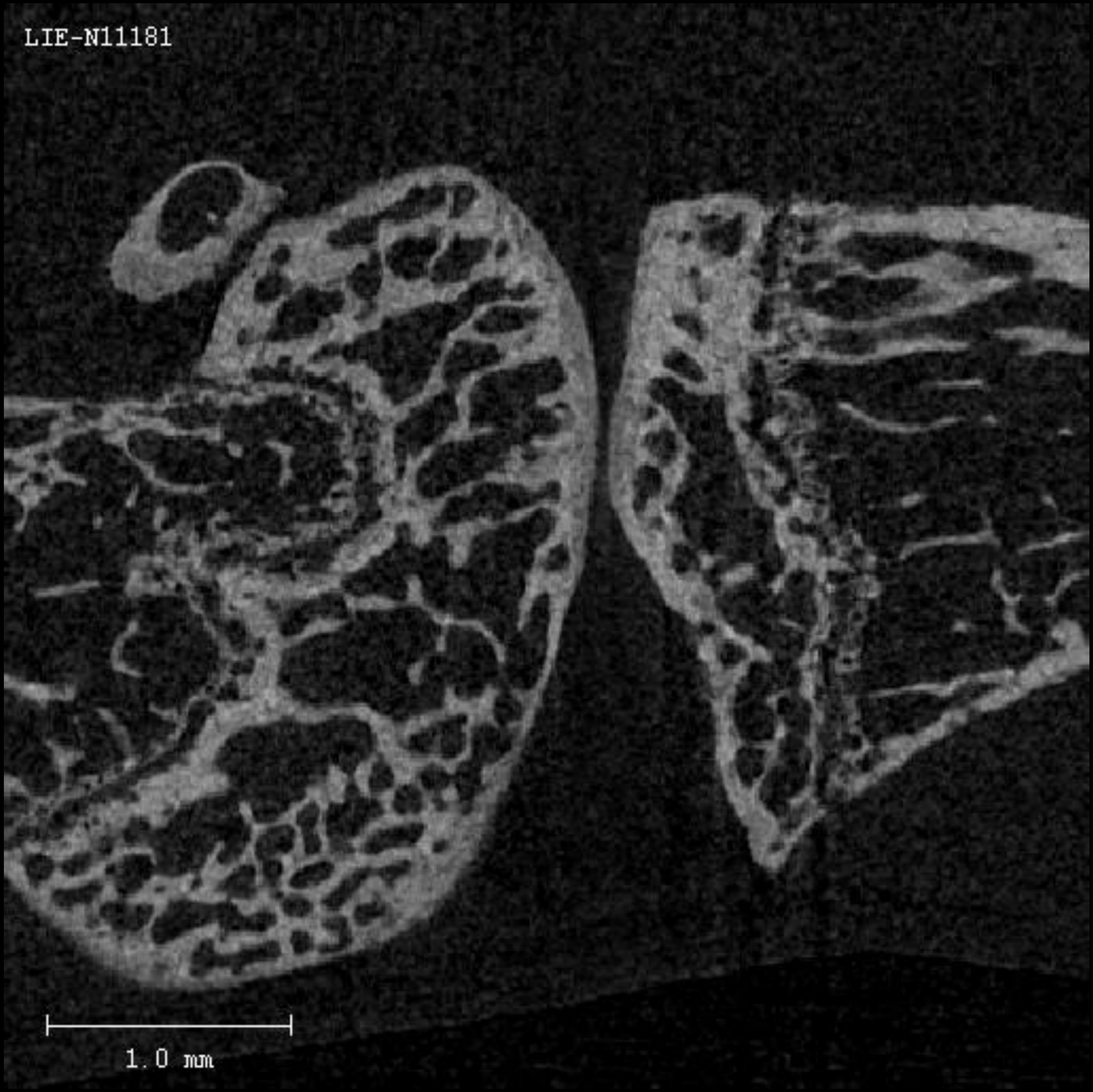
Beam hardening can cause false diagnostics



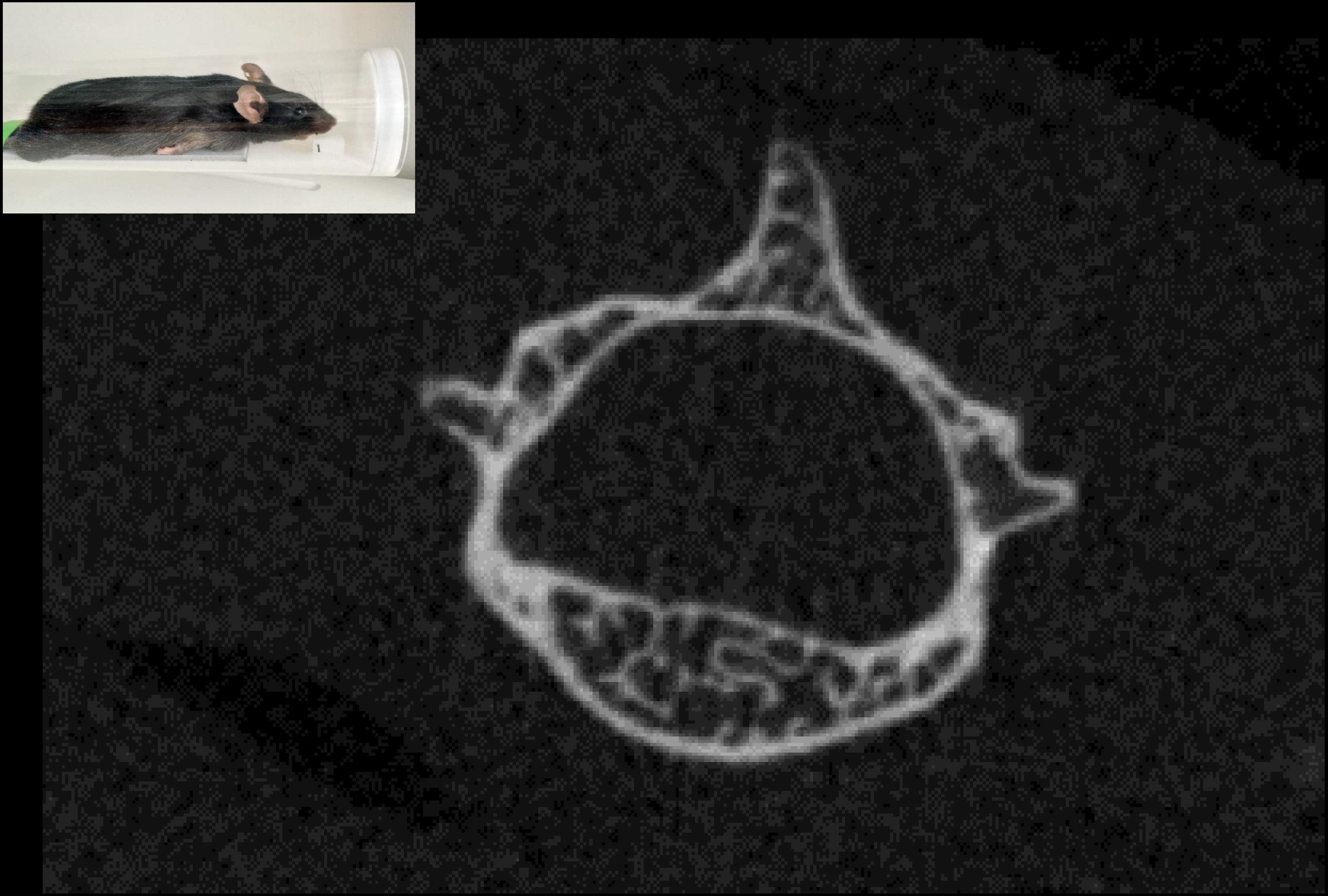
micro computed tomography



resolution > ~1μm



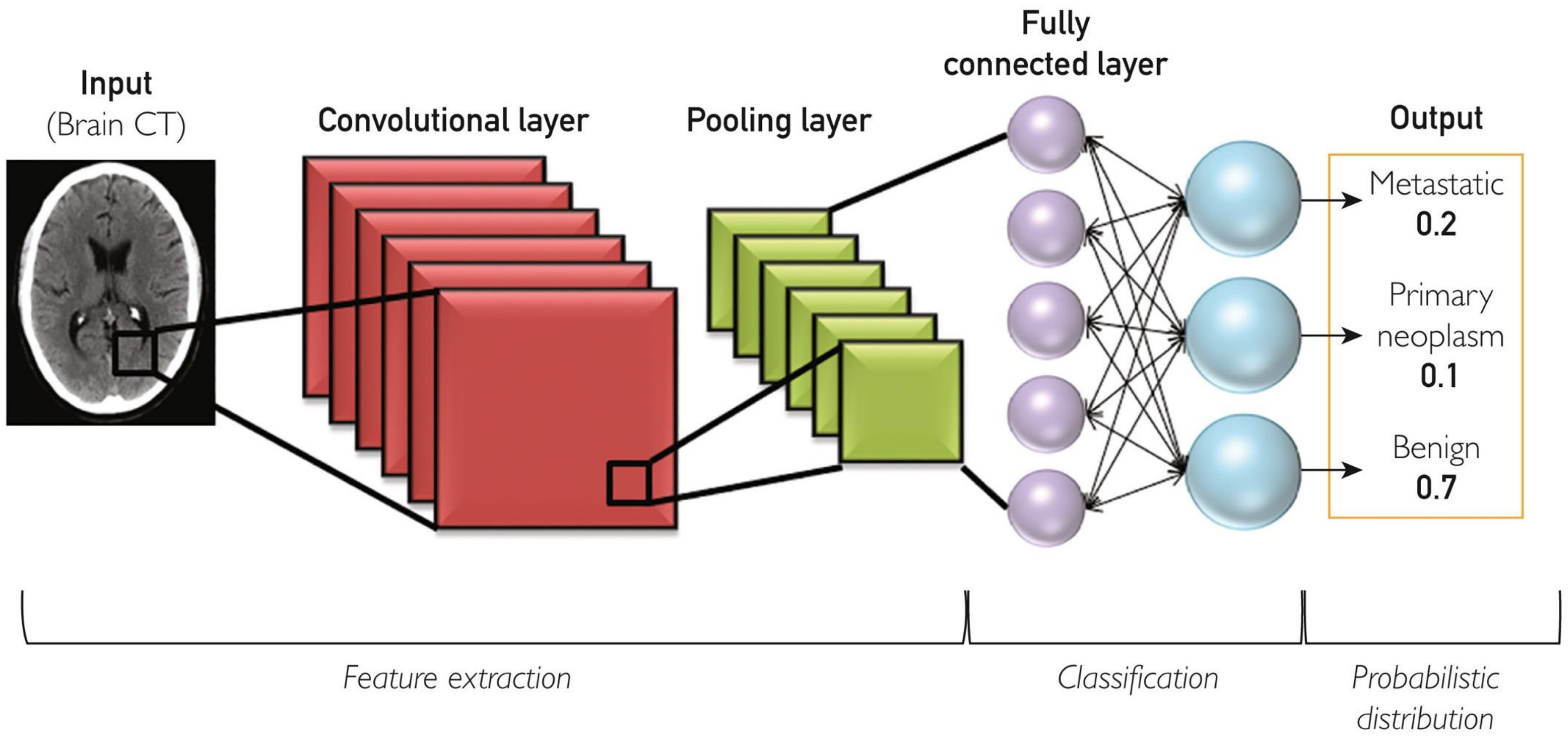
Mouse knee joint *in vivo*



Mouse vertebrae *in vivo*

3D image analysis

A note on deep learning for image analysis



- Such schemes can be extremely powerful for image segmentation and image classification
- Training is based on looping forward pass / backward learning for minimization of error
- Requires large datasets of **annotated images** to train the **millions of parameters**
- Research projects often don’t collect enough data for such models.

https://doi.org/10.1016/j.mcpdig.2023.08.006

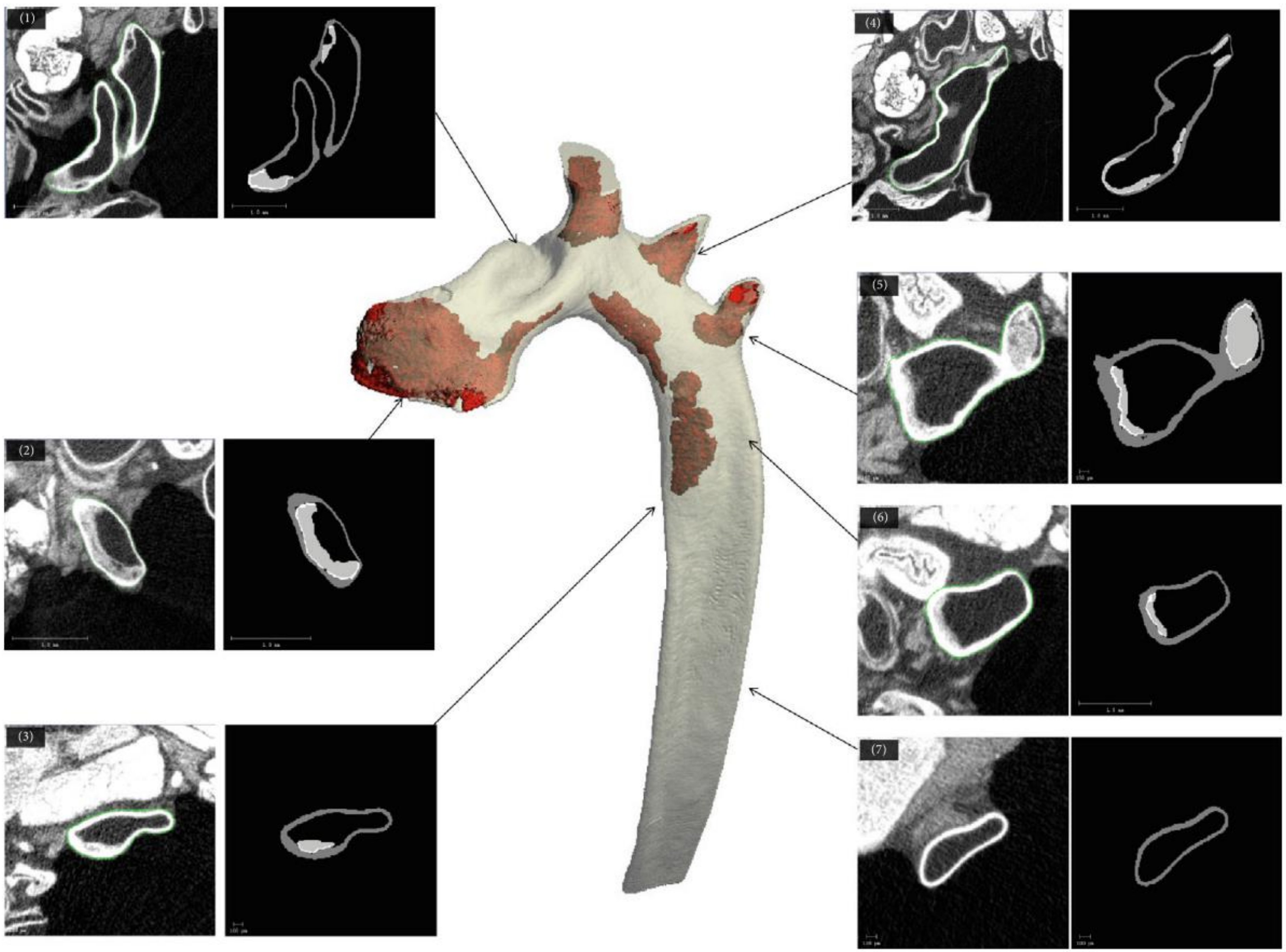
Heuristic image analysis

- Algorithmic. Uses step-by-step algorithmic logic or hand-crafted heuristics.
- Deterministic: Output is predictable and based on fixed input-output mapping (no training involved).
- Analytical / Model-driven: Uses mathematical models, often physics-based or geometric.

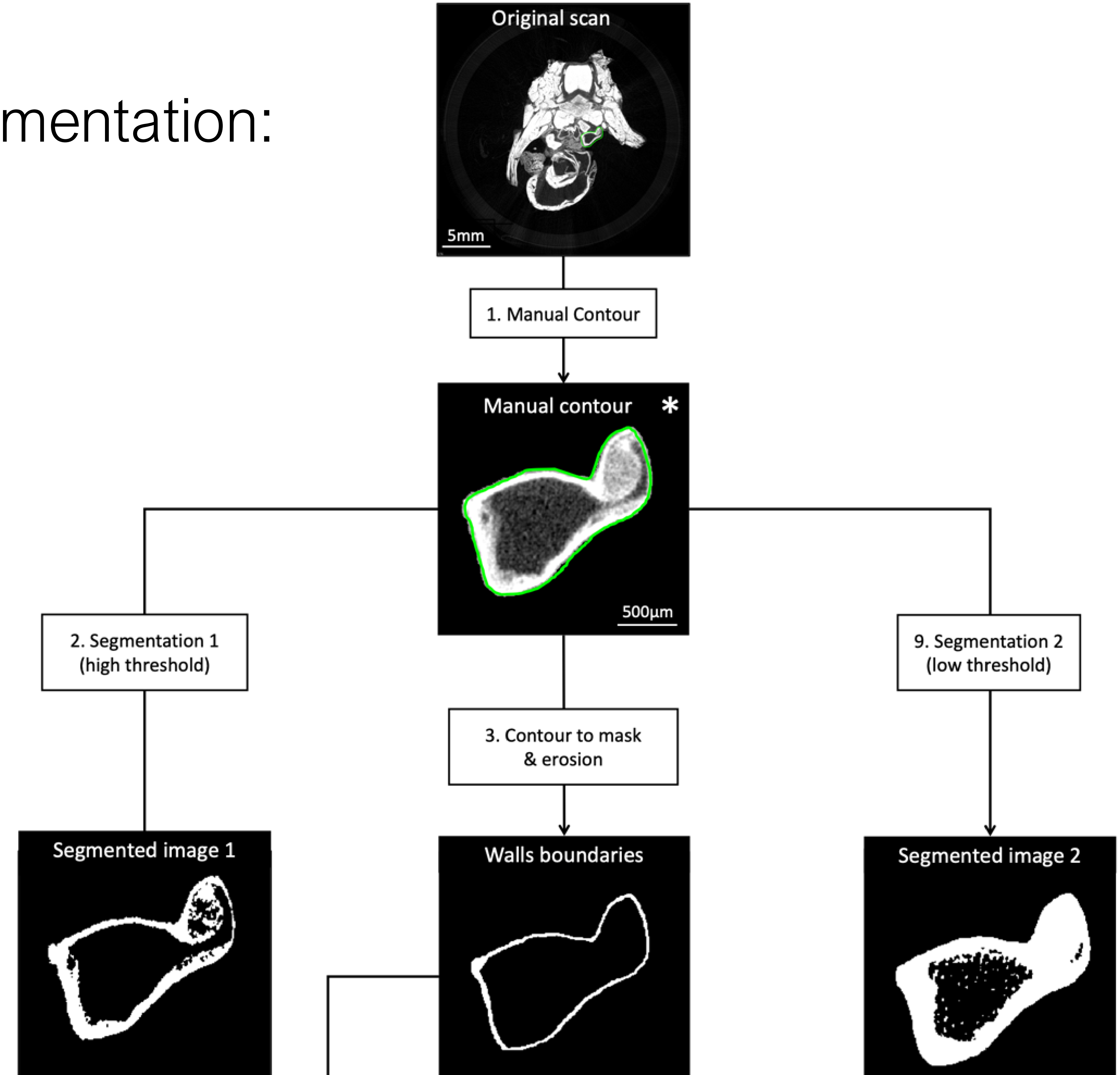
Common Techniques:

- Thresholding (global, adaptive)
- Edge detection (Sobel, Canny)
- Morphological operations (dilation, erosion)
- Watershed segmentation
- Region growing / region merging
- Level sets
- Active contours (snakes)

Example: compute atherosclerotic plaque thickness



Segmentation:



Example: bone evolution around an implant

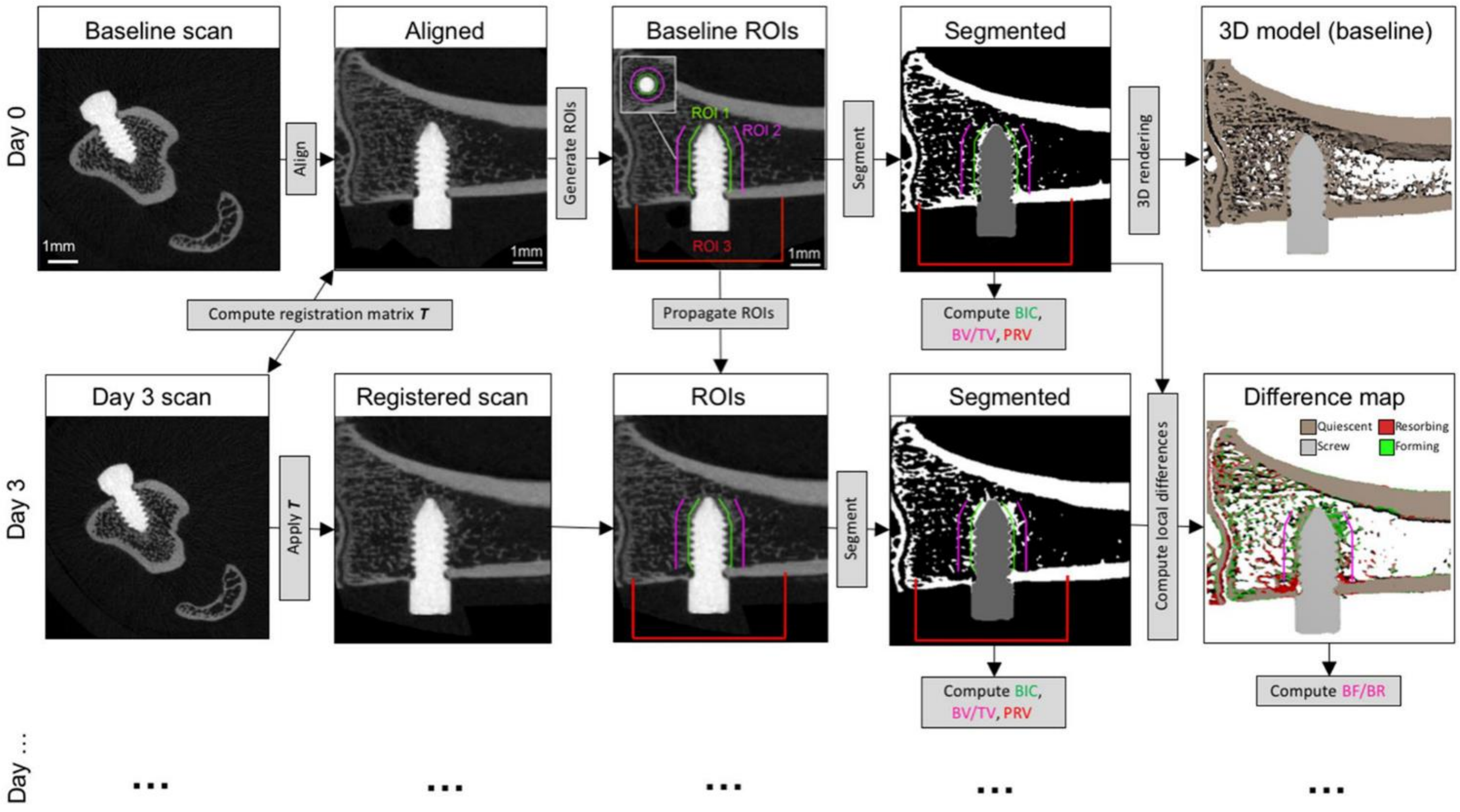
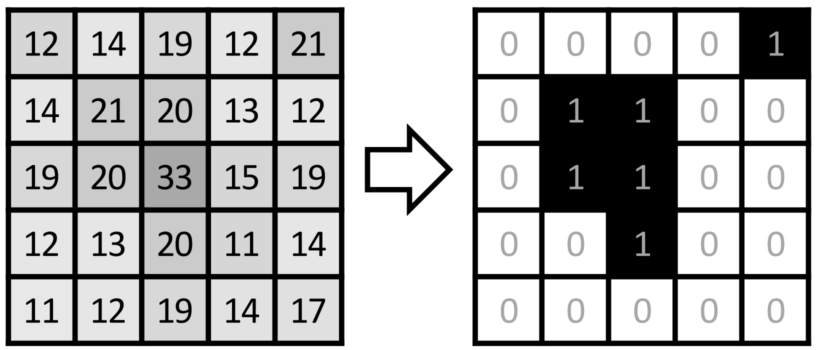


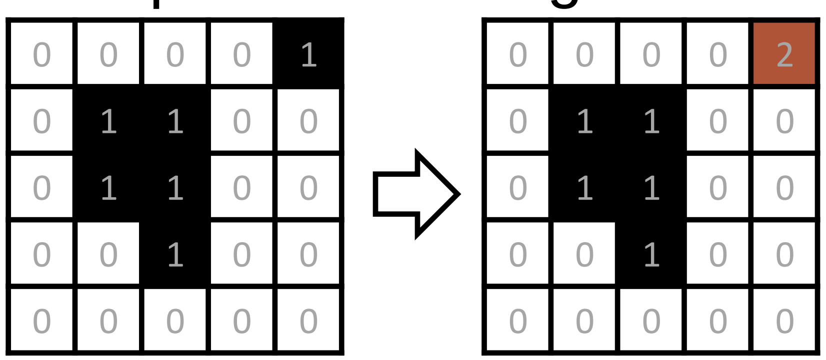
Image transformations for segmentation

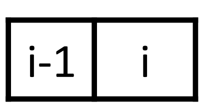
Thresholding:



$$if(v_i > t, 1, 0)$$

Component labeling:

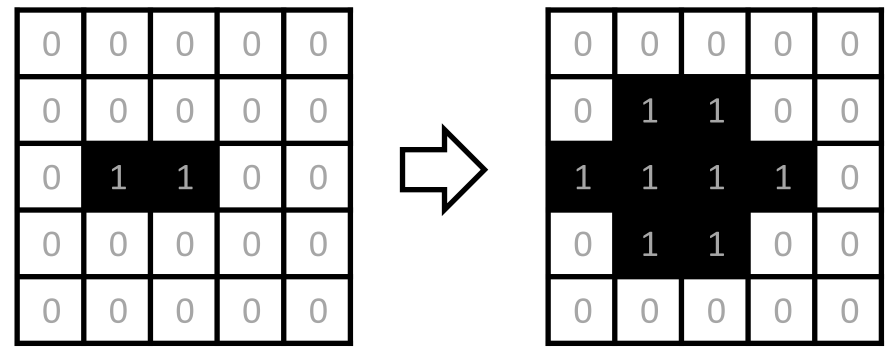


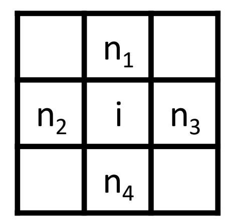


$$1)\begin{cases} v_i = 0 \rightarrow L_i = 0 \\ v_i \neq 0 \;\&\; L_{i-1} = 0 \rightarrow L_i = 1 \\ v_i \neq 0 \;\&\; L_{i-1} \neq 0 \rightarrow L_i = L_{i-1} \end{cases}$$

$$2)\begin{cases} L_i = 0 \rightarrow L_i = 0 \\ L_i \neq 0 \;\&\; L_{i-1} = 0 \rightarrow L_i = L_i \\ L_i \neq 0 \;\&\; L_{i-1} \neq 0 \rightarrow L_i = \min(L_{i-1}, L_i) \end{cases}$$

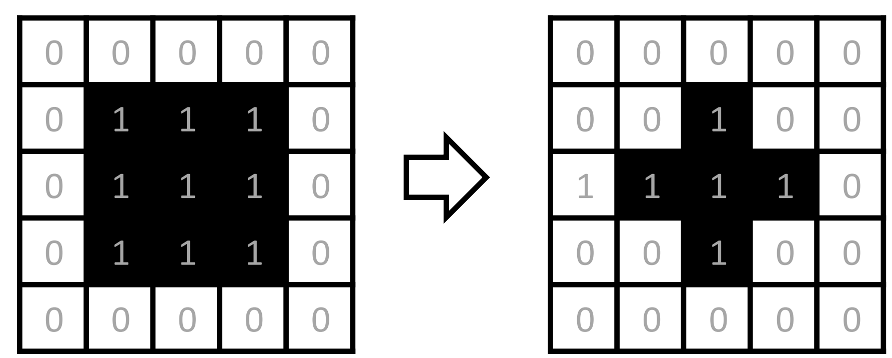
Dilation

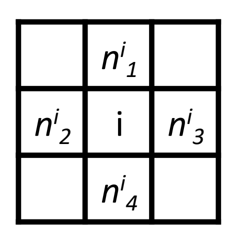




$$if\left(\sum_k n_k^i > 0, 1, 0\right)$$

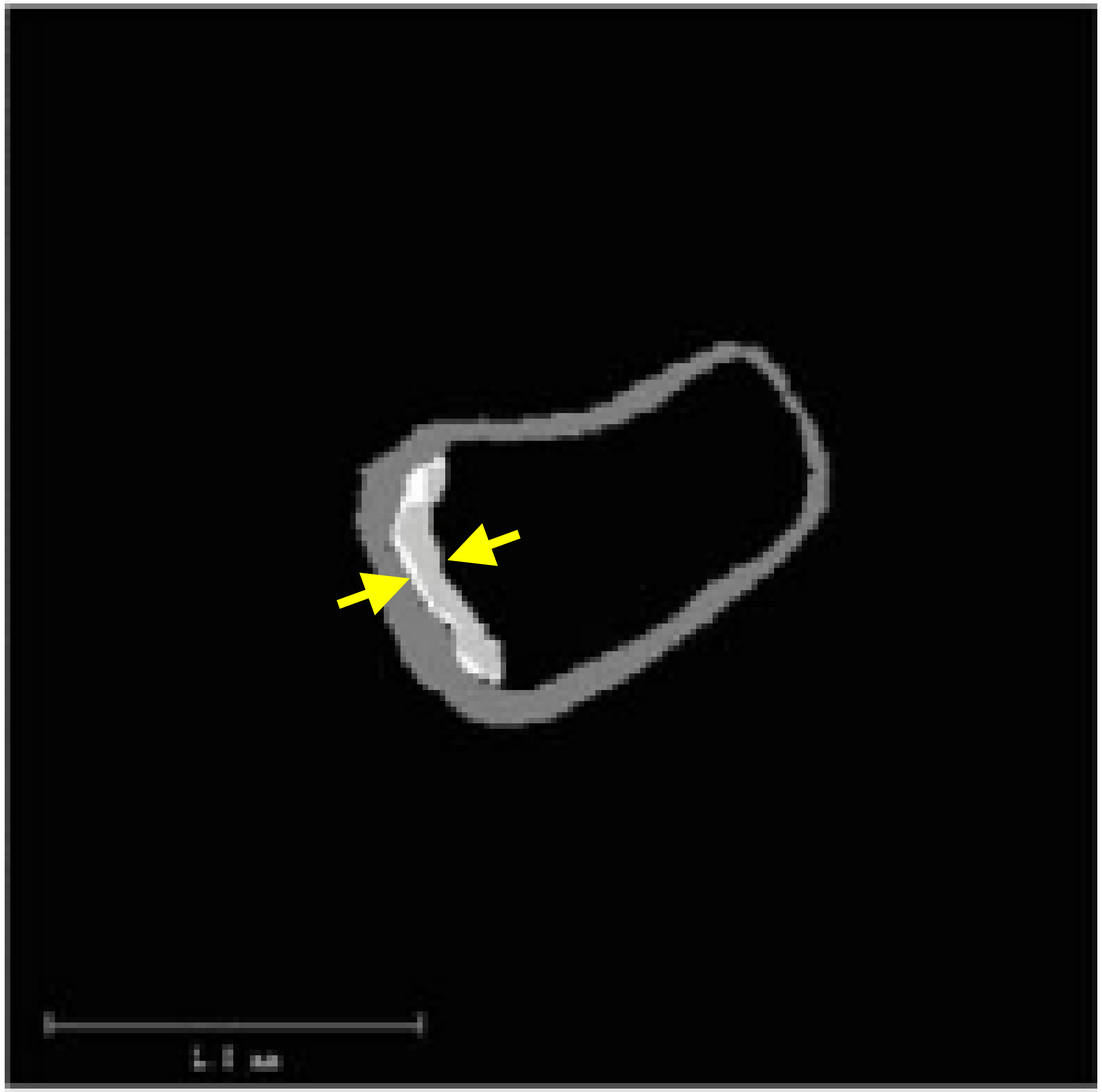
Erosion





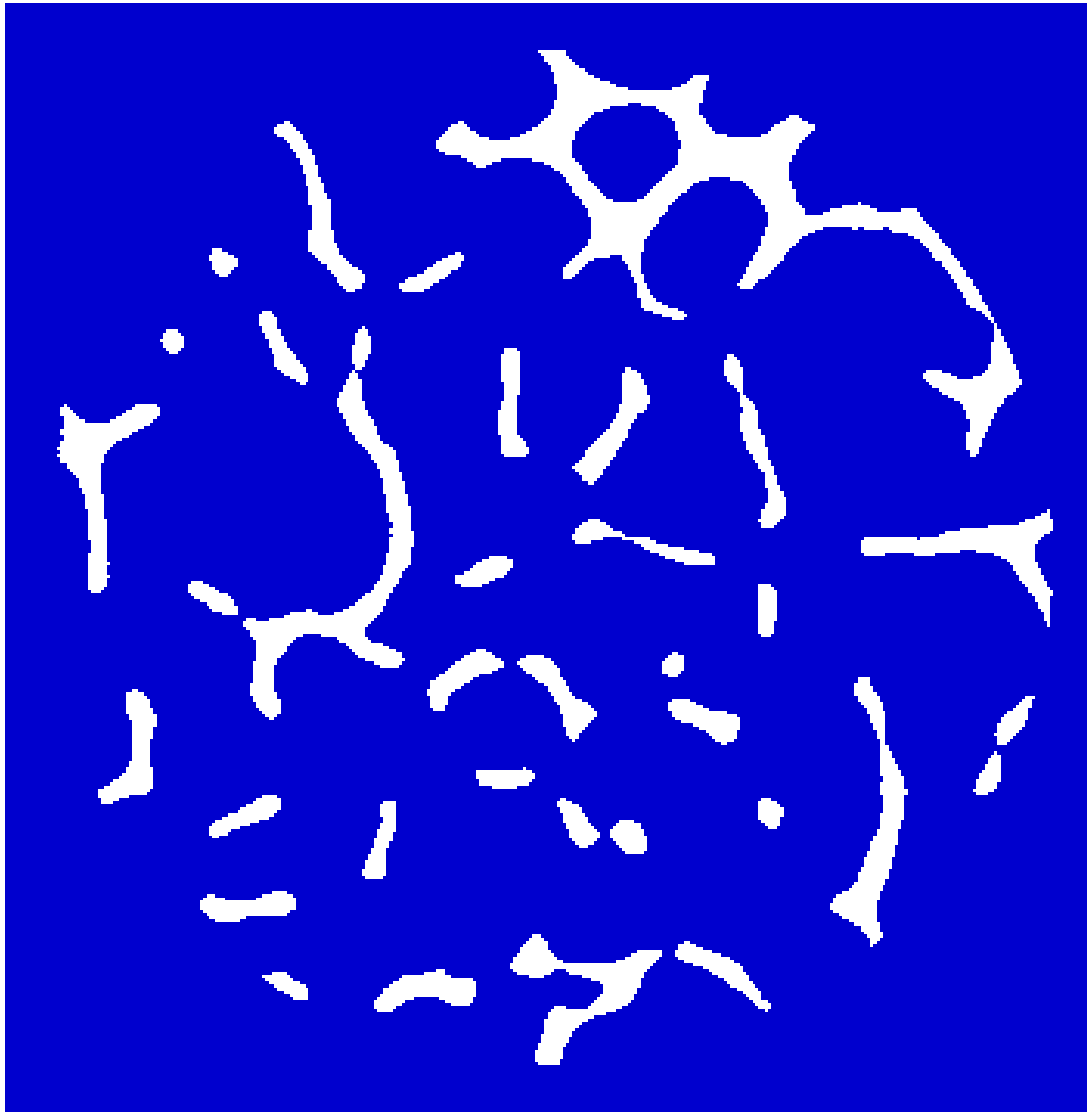
$$if\left(\sum_k n_k^i < 3, 0, 1\right)$$

Compute thickness of an object?

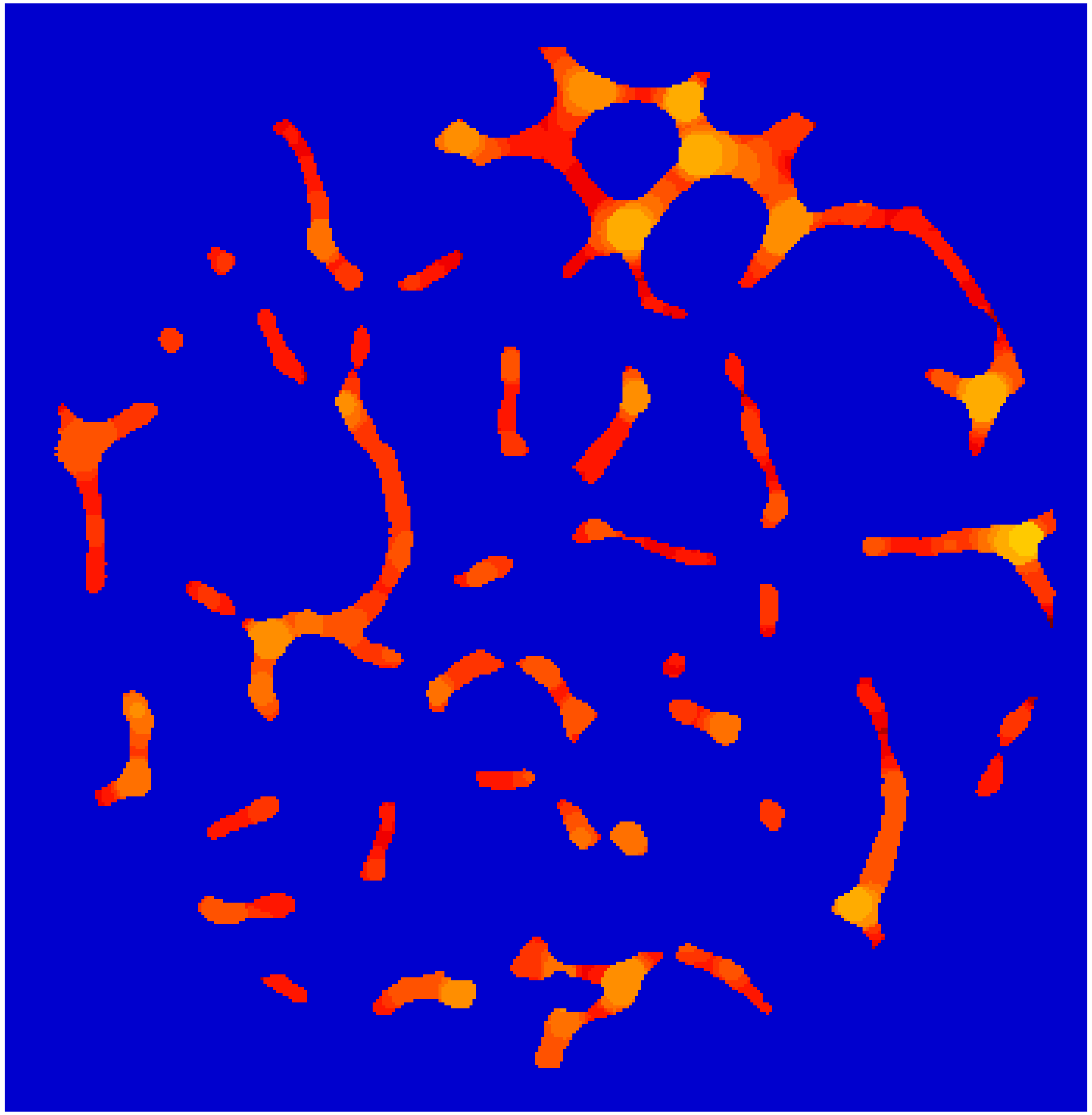


Distance maps (thickness, spacing)

Segmented object

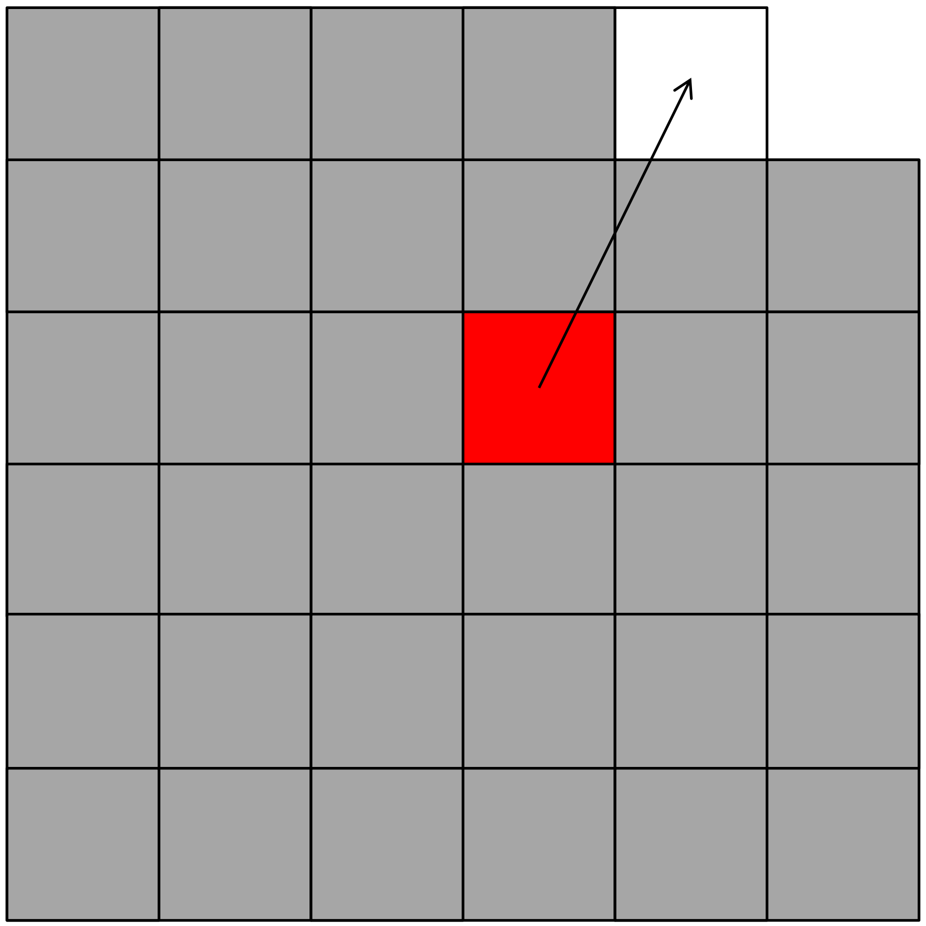


Distance map



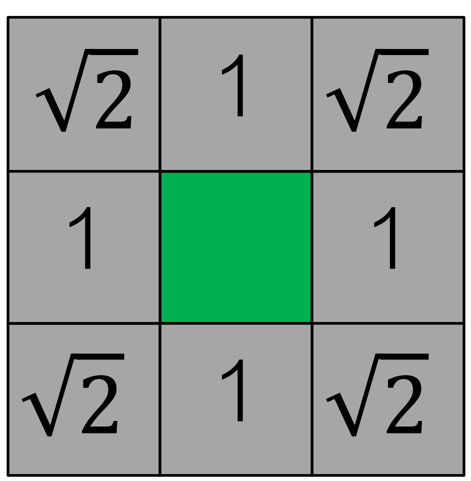
Distance map calculation

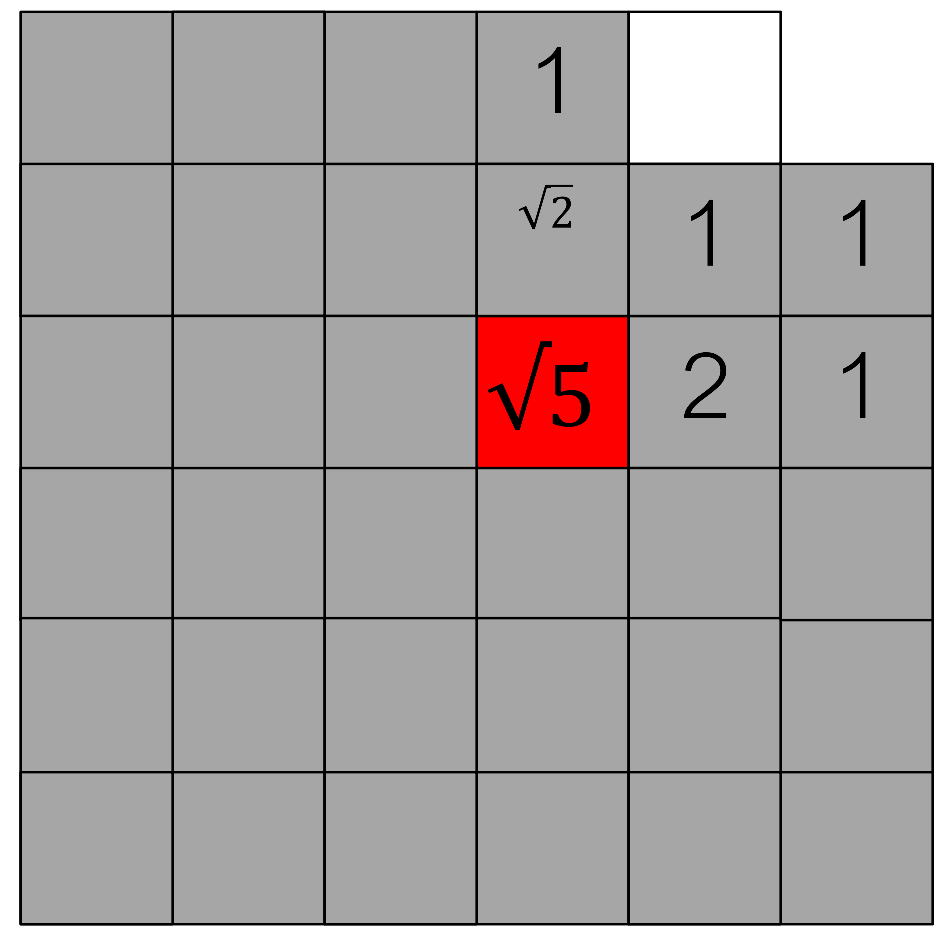
- How far is the red voxel away from the background?



Distance map calculation

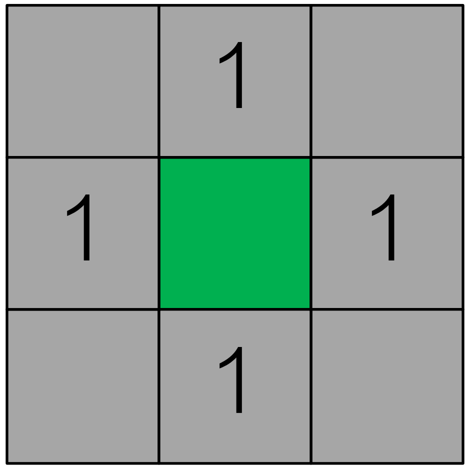
- How far is the red voxel away from the background?
- Euclidean Metric

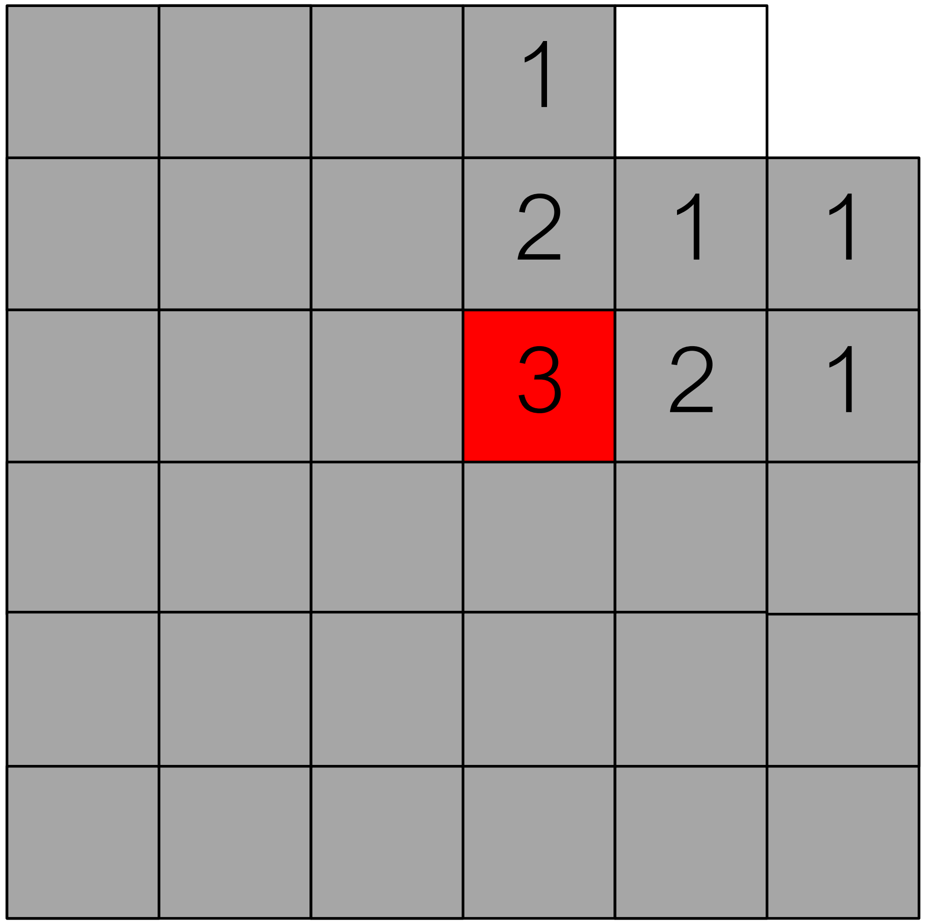




Distance map calculation

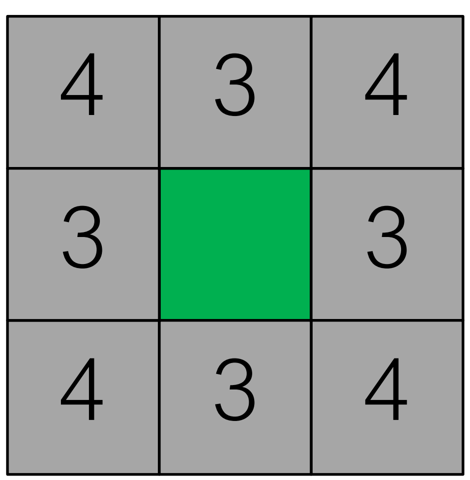
- How far is the red voxel away from the background?
- Manhattan Metric

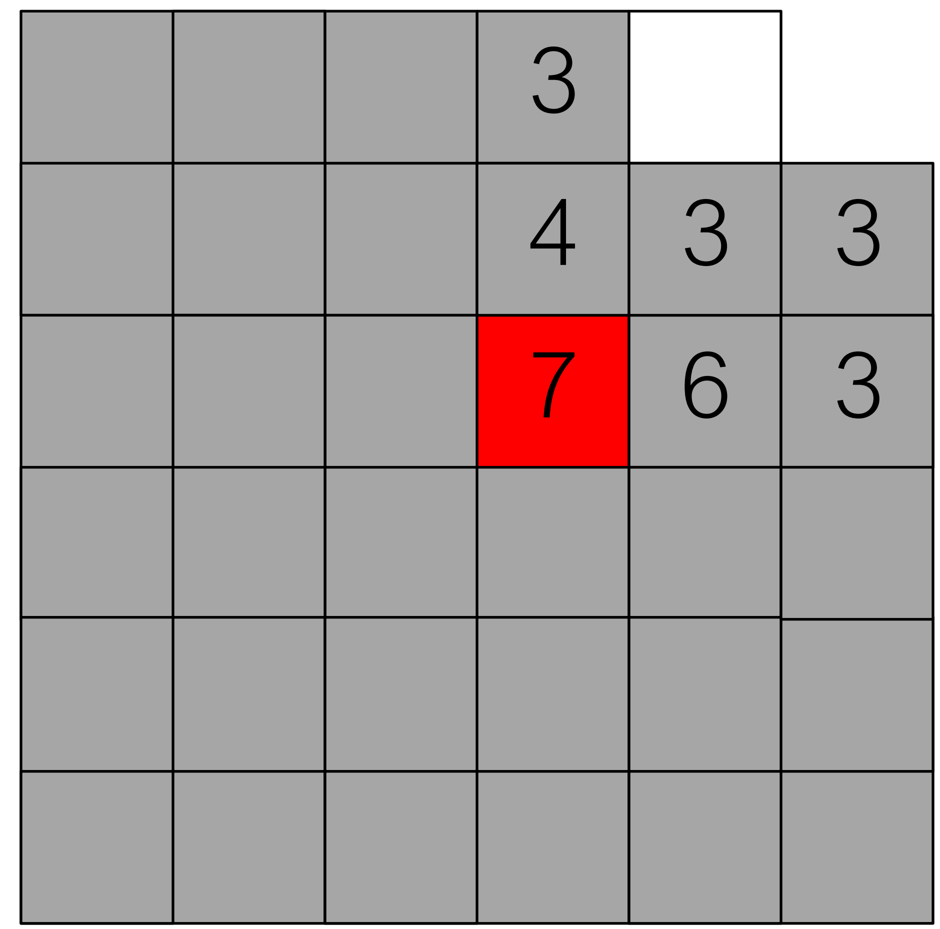




Distance map calculation

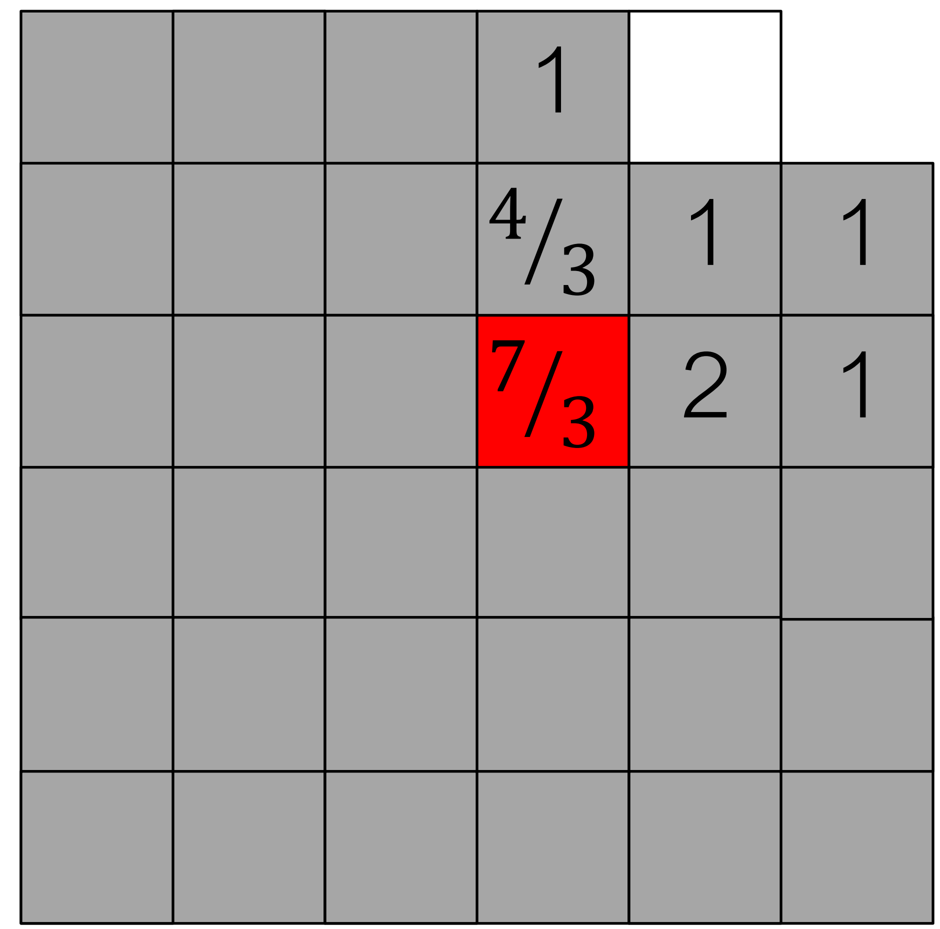
- How far is the red voxel away from the background?
- 3-4-5 Metric

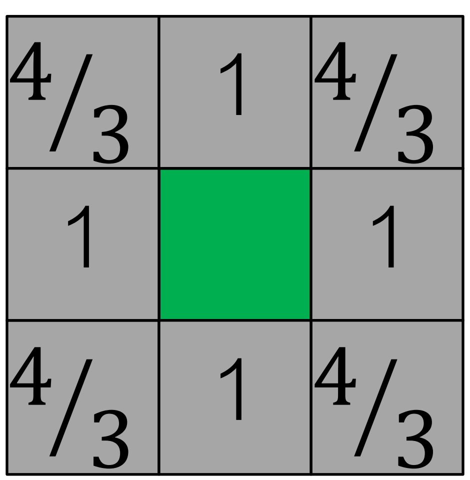




Distance map calculation

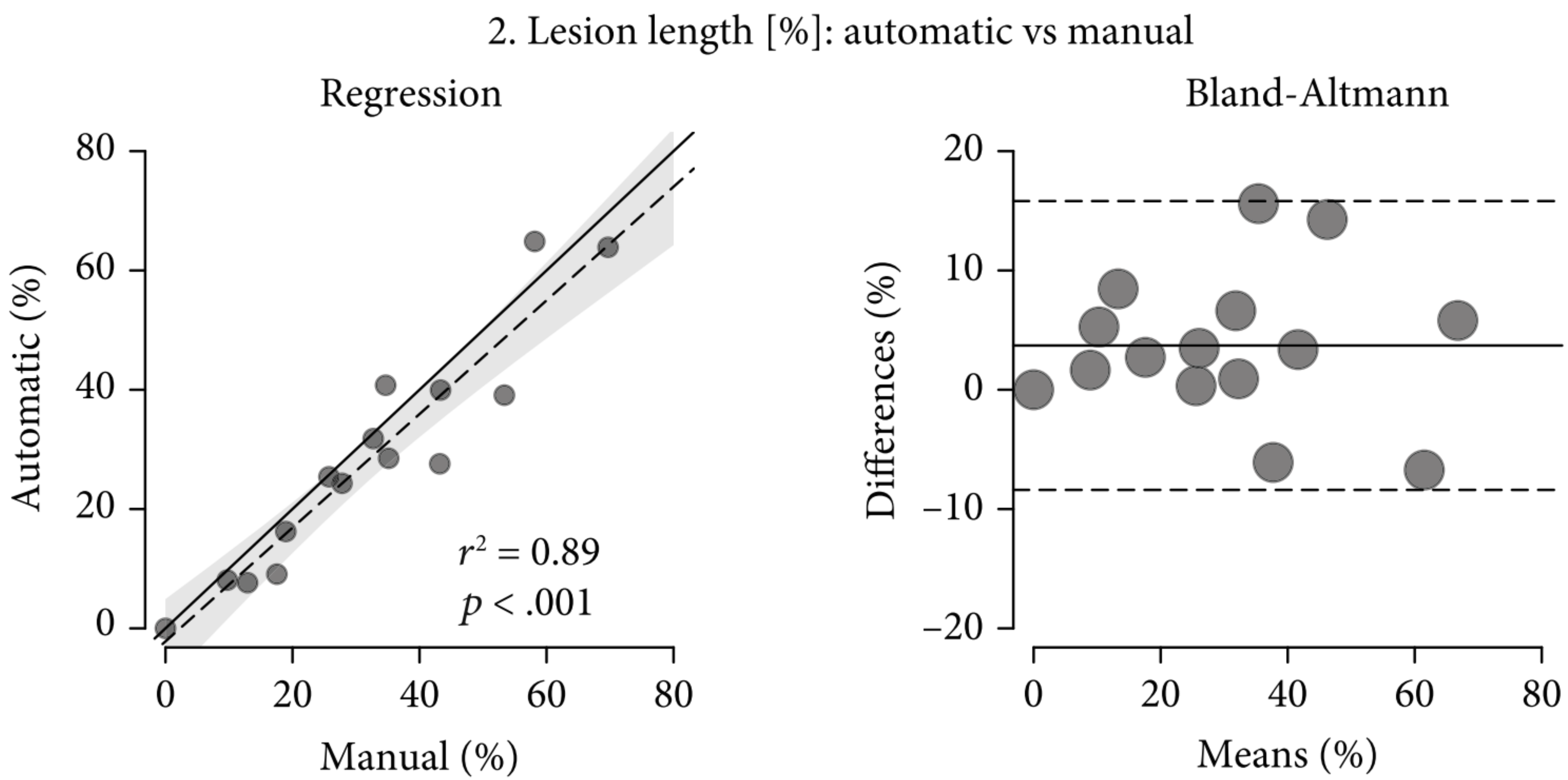
- How far is the red voxel away from the background?
- 3-4-5 Metric → Divided by 3





Compute thickness of an object?

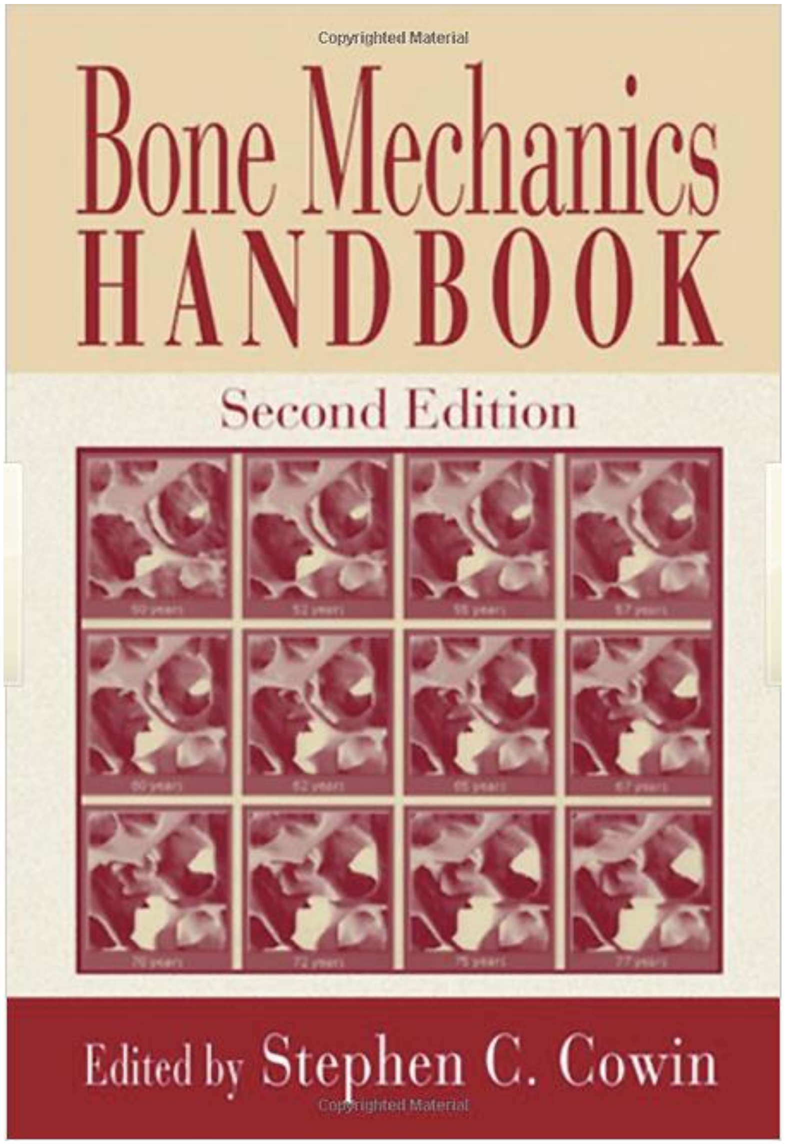
Plaque imaging: Validation

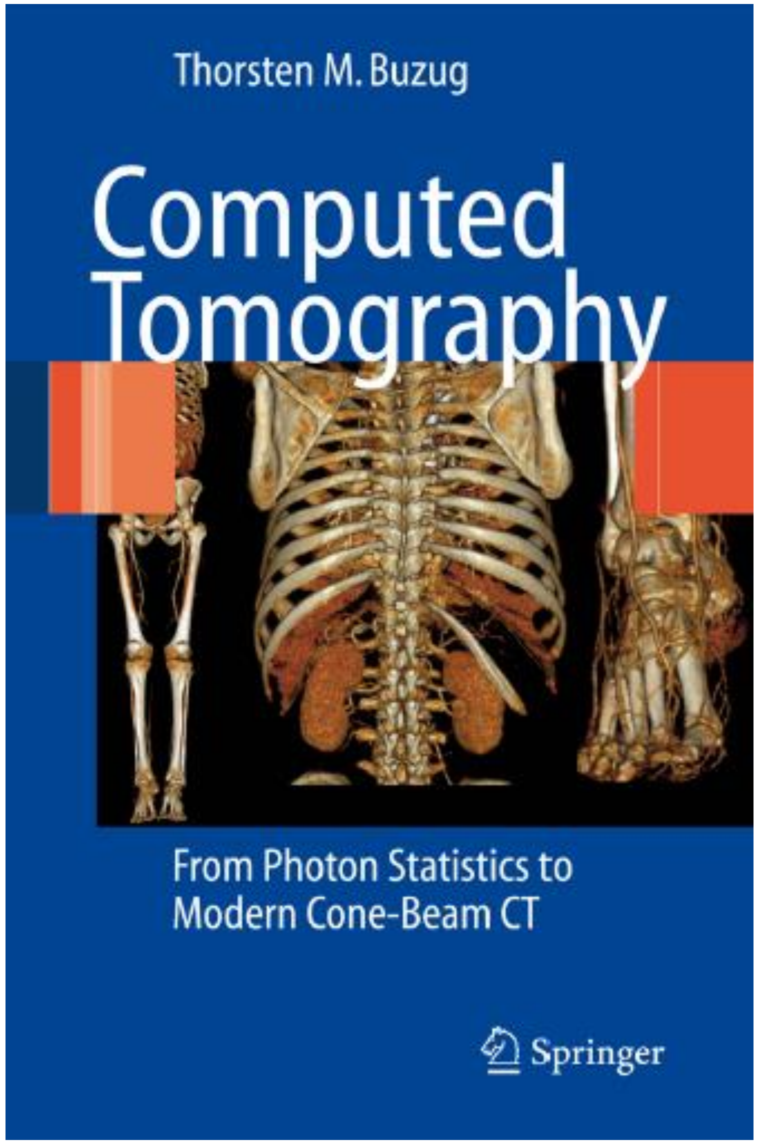


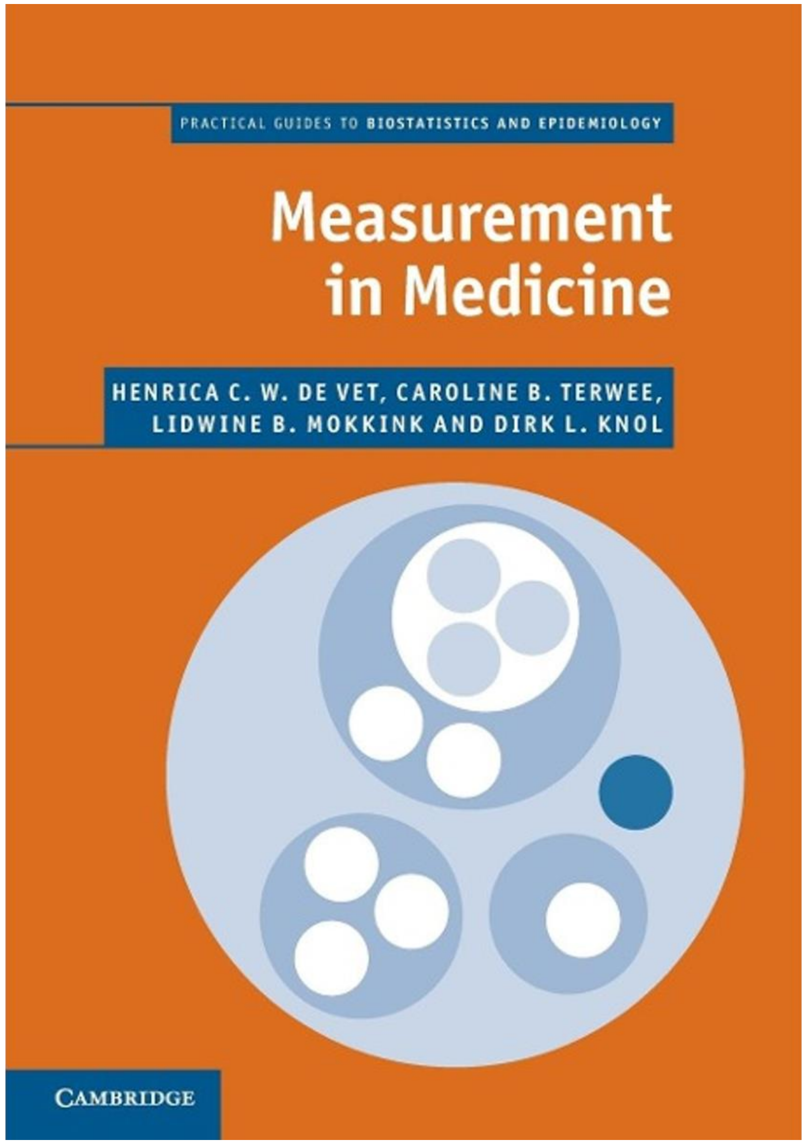
Stadelmann, V. A. *et al.* Automatic Quantification of Atherosclerosis in Contrast-Enhanced MicroCT Scans of Mouse Aortas Ex Vivo. *Int. J. Biomed. Imaging* **2021**, 1–9 (2021).

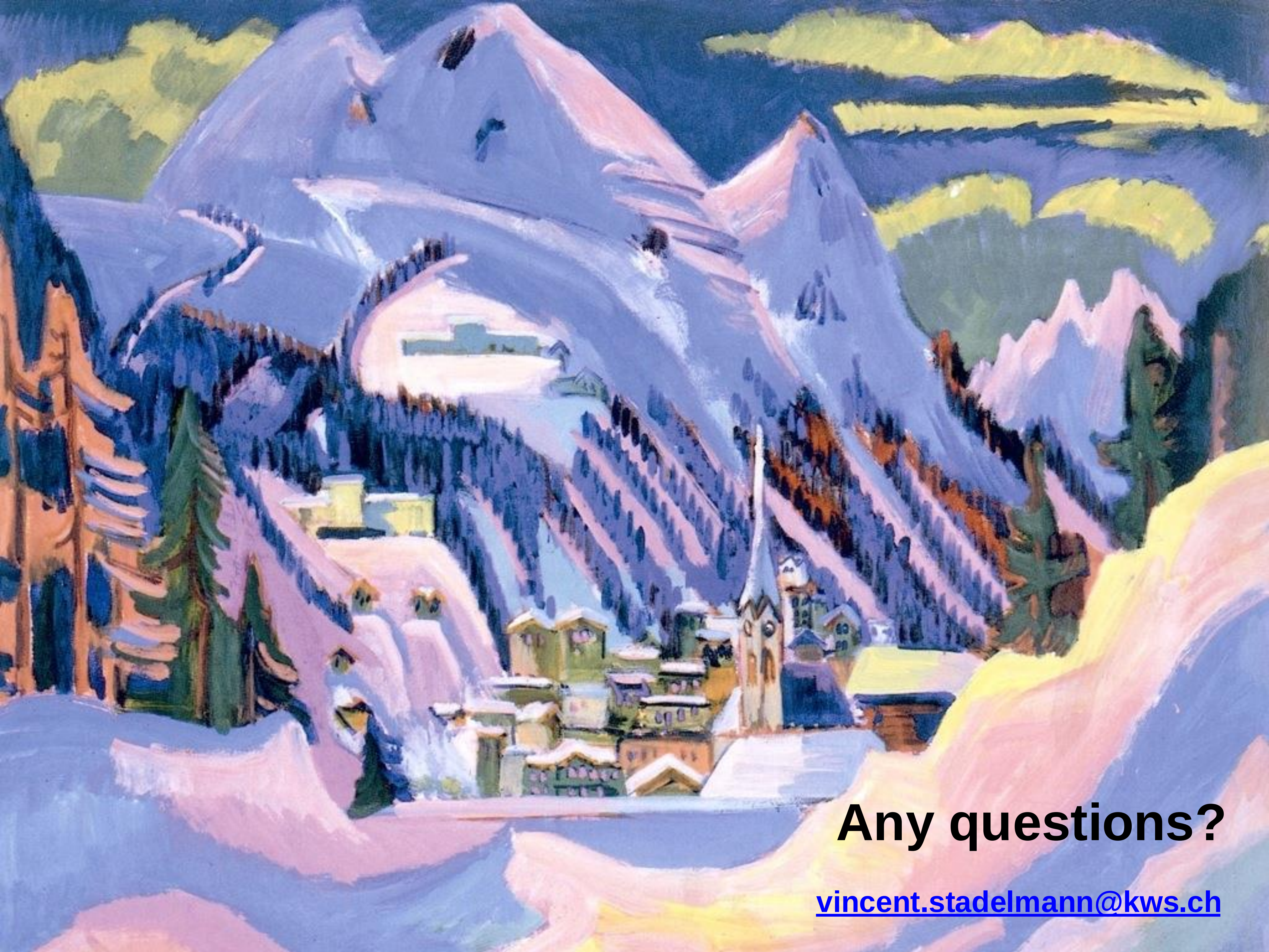
Exercise 4

Recommended readings









Any questions?

vincent.stadelmann@kws.ch