Physical limits: Sensitivity, specificity and quantitation:

Computed Tomography

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µCT-Scanners

- µCT-scanners vary with respect to design and image processing software
  - Ex vivo bench top systems
    - High resolution imaging (5-50 µm)
    - Slow (scan times 10-60 minutes)
    - Usually not gantry based
    - High x-ray dose
  - In vivo µCT-scanners
    - Usually gantry based systems (180° or 360° rotation)
    - Often flat panel detectors
    - Scanners with dual energy function available
    - Moderate resolution (50-150 µm)
    - Fast (scan times: 1 sec. - 10 minutes)
    - Lower x-ray dose

Non Gantry Based µCT

Bartling et al., CMIR 2007

Spatial resolution depend on
- distance between object and detector
- pixel size at the detector
- image reconstruction

„In vivo“ µCT scanners

Spatial resolution depend on
- pixel size at the detector
- image reconstruction
- „Real“ spatial resolution should be determined with phantoms (e.g. line pairs in thungsten wire phantoms)

Quantification

- CT is a quantitative image modality
  - X-ray absorption correlates with measured signal
  - X-ray absorption depend on the photon energy
- **CT number:** quantitative but not calibrated
- **Hounsfield Unit:** CT number normalised for water being 0 and air being -1000
  - Clinically used unit

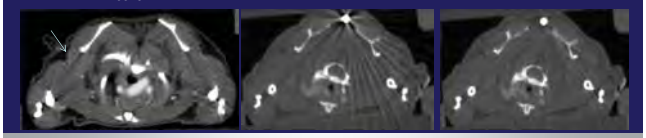
Pitfall

- Scanners are often not calibrated
  - CT numbers from different scans are not directly comparable
  - Different values for different energies (voltage)
  - Detector saturation (particularly for flat panels)
    - if object is too small
    - if power (mAs) is too high

Artefacts

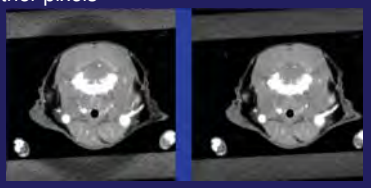
- Beam hardening artefacts
  - Most detectors do not acquire spectral information
  - Selective removal of soft X-rays from the X-ray beam
  - Linearity not given - loss of information - reconstruction errors
  - If not corrected reduction of the reconstructed attenuation coefficient toward the centre
  - Additional artifacts for bone, metal and CA within the object

bone metal corrected



Artefacts

- Ring artefacts
  - Calibration error for single pixels
    (change in pixel sensitivity during and between different scans due to heating)
  - Strong: defect detector pixels /detector line
  - Solution:
    - Interpolation from other pixels
    - Change of detector



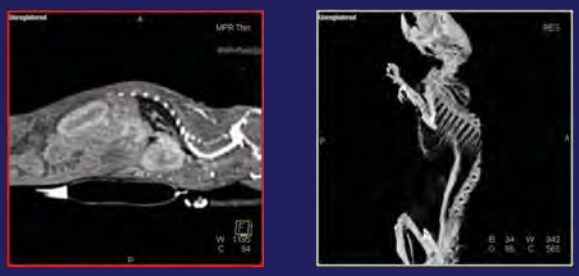
Potential problems

- Background noise
  - increases with increasing spatial resolution
  - decreases with increasing current
  - 10-30 HU for clinical scanners ((~200µm)^3)
  - up to 60 HU for µCT-scanners ((50-100µm)^3)

Tips:

- Decrease energy (voltage)
- Slow CA injection (careful with postprocessing model)
- Averaging
- Beam hardening correction (not provided by most manufacturers)

Clinical CA: 4D Perfusion Imaging



- Contrast agent: Imeron 400 (1:1 in NaCl)
- Scan parameters: 80kV, 50mA, 5s rotation time, 4 rotations
- 360° reconstruction 180° overlap

Bartling (DKFZ), Grasruck (Siemens), et al.

DCE µCT: Data postprocessing

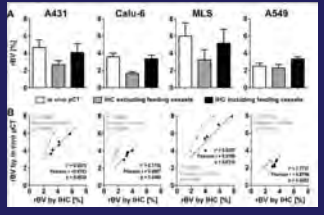
- RBV determination using blood pool CA
- First pass analysis (e.g. Miles model)
- Compartment models
  - Brix
  - Tofts

+ robustness -

Vessel Function: µCT for rBV-Analysis

$$rBV\ (\%) = 100 \times \frac{HU_{tumor}\ \text{after CA} - HU_{tumor}\ \text{before CA}}{HU_{blood}\ \text{after CA} - HU_{blood}\ \text{before CA}}$$

A431:	SCC
Calu-6:	Lung cancer
MLS:	Ovarian cancer
A549:	Lung cancer

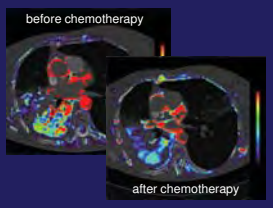


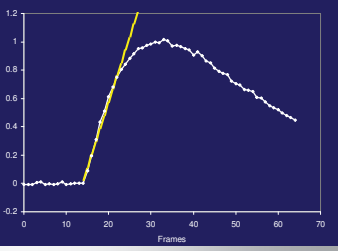
Ehling, Gremse, Lammers et al. (ExMI)

First pass analysis (Miles model)

Assumption: no CA extravasation during first pass

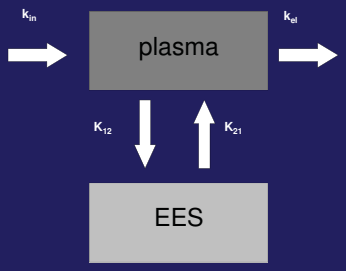
$$\text{Perfusion} = \frac{\text{max. slope tissue fct}}{\text{maximum AIF}}$$





Miles et al. Radiology 1993 188: 405

Two compartment models

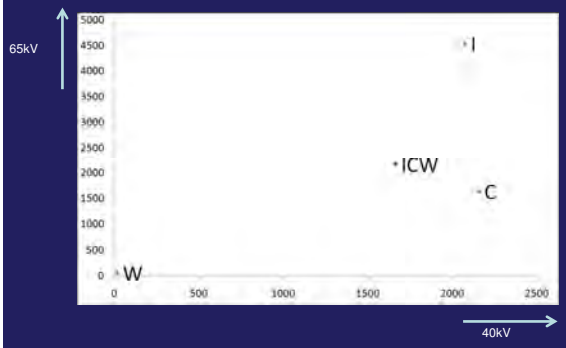


Brix 1991:
- Assumes CA infusion

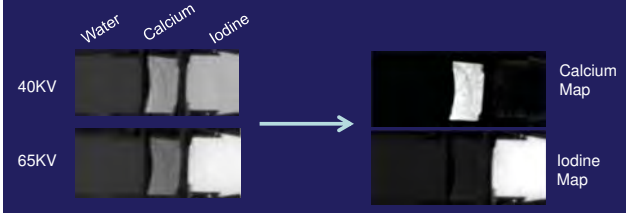
Tofts 1991:
- Assumes bolus injection
- AIF curve pre-defined

Newer models:
- Measured AIF

Dual Energy Triangle



Dual Energy CT

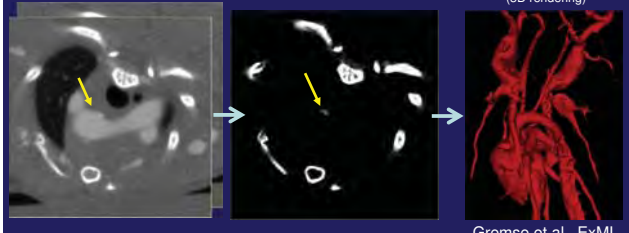


- Decomposition in three components
- Water, calcium and iodine

Gremse et al., ExMI

Calcium / Iodine Maps

Dual Energy Scan | Calcium Map | Iodine Map (3D rendering)

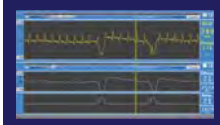


Gremse et al., ExMI

- Atherosclerotic mouse under western diet
- No need for native scan / calcium quantification

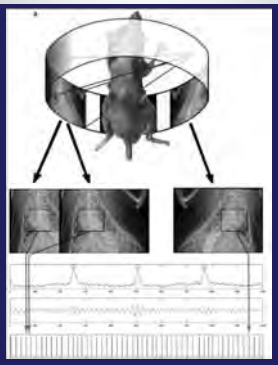
Cardiac Gating and Breath Triggering

- 1025L Monitoring and Gating System (I4SA); BNC cabel (1/0 trigger signal)
  - Pneumatic pillow
  - ECG-electrode



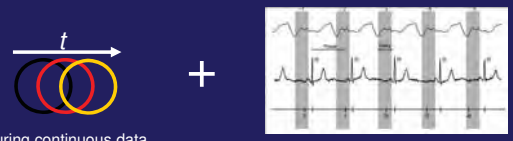
Bartling (DKFZ), Grasruck (Siemens), et al.

Intrinsic Gating



Dinkel, et al. Circulation Cardiovasc. Imaging 2008

Retrospective Gating



During continuous data acquistion, several complete rotations are acquired….

….together with physiological data such as ECG or respiratory motion. Gating intervals of acceptable projections are defined (grey bars) and…

…projections are sorted according to the gating signals.

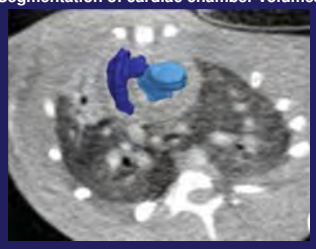
Resulting in one new, gated dataset that can be used for volume reconstruction.

fpVCT Breath Triggering (Rat)

- Contrast agent: Fenestra (2.5 ml) Bartling (DKFZ), Grasruck (Siemens), et al.
- Scan parameters: 80kV, 50mA, 5s rotation time, 16 rotations

Blood Pool CA: Cardiac Function

Segmentation of cardiac chamber volumes

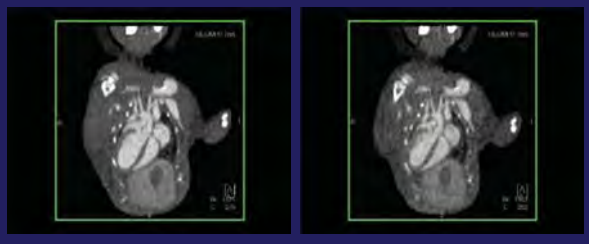


- Scan parameters: 80kV, 50mA, 5s rotation time, 16 rotations
- Breath gating: 20-80% between 2 respirations
- Cardiac gating: 5 equisized phases through cardiac cycle
- Contrast agent: Fenestra (2.5 ml) Bartling (DKFZ), Grasruck (Siemens), et al.

Cardiac Imaging

Dobutamin stress test (mouse)

before after Dobutamin inj.



Dinkel et al., Circulation: Cardiovasc. Imag. (2008)

Summary

- CT is a versatile quantitative imaging modality
- CT numbers depend on voltage and detector calibration
- Artefacts (beam hardening, rings)
- Background noise
- Perfusion CT
- Dual energy applications
- Motion correction

Related Publications "Basic considerations about probes and suitable imaging modalities"

1. Kalender W., Deak P., Engelke K., Karolczak M. X-Ray and X-Ray-CT. Book title: Kiessling F., Pichler B. Small animal imaging - Basics and practical guide (ISBN 978-3-642-12944-5), Springer, New York: 125-141

2. Bartling SH, Stiller W, Semmler W, Kiessling F. Small animal computed tomography imaging. Curr Med Imaging Rev 3, 45-49 (2007).

3. Torchilin VP, Frank-Kamenetsky MD, Wolf GL. CT visualization of blood pool in rats by using long-circulating, iodine-containing micelles. Acad Radiol 6(1), 61-65 (1999).

4. Weichert JP, Lee FT Jr, Chosy SG, Longino MA, Kuhlman JE, Heisey DM, Leverson GE. Combined hepatocyte-selective and blood-pool contrast agents for the CT detection of experimental liver tumors in rabbits. Radiology 216(3), 865-71 (2000).

5. Bakan DA, Doerr-Stevens JK, Weichert JP, Longino MA, Lee FT Jr, Counsell RE. Imaging efficacy of a hepatocyte-selective polyiodinated triglyceride for contrast-enhanced computed tomography. Am J Ther 8(5), 359-65 (2001).

6. Kiessling F, Greschus S, Lichy M, Bock M, Fink C, Vosseler S, Moll J, Mueller MM, Fusenig NE, Traupe H, Semmler W. Volumetric computed tomography (VCT): a new technology for noninvasive, high-resolution monitoring of tumor angiogenesis. Nat. Med. 10(10), 1133-1138 (2004).

7. Eisa F, Brauweiler R, Hupfer M, Nowak T, Lotz L, Hoffmann I, Wachter D, Dittrich R, Beckmann MW, Jost G, Pietsch H, Kalender WA. Dynamic contrast-enhanced micro-CT on mice with mammary carcinoma for the assessment of antiangiogenic therapy response. Eur. Radiol. 22(4), 900-907 (2012).

8. Gremse F, Grouls C, Palmowski M, de Vries A, Gruell H, Das M, Mühlenbruch G, Akhtar S, Schober A, Kiessling F. Virtual Elastic Sphere Processing Enables Reproducible Quantification of Vessel Stenosis in CT and MR Angiographies. Radiology, 260:709-717 (2011).

9. Dinkel J, Bartling SH, Kuntz J, Grasruck M, Kopp-Schneider A, Iwasaki M, Dimmeler S, Gupta R, Semmler W, Kauczor HU, Kiessling F. Intrinsic gating for small-animal CT: A Robust, ECG-less paradigm for deriving cardiac phase Information and Functional Imaging. Circ. Cardiovasc. Imaging, 1:235-243 (2008).

10. Mondy WL, Cameron D, Timmermans JP, De Clerck N, Sasov A, Casteleyn C, Piegl LA. Micro-CT of corrosion casts for use in the computer-aided design of microvasculature. Tissue Eng Part C Methods, 15:729-38 (2009).