UNIVERSITY OF KUOPIO

Microtomography imaging as a characterization tool for solid dosage forms

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HDR
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Content

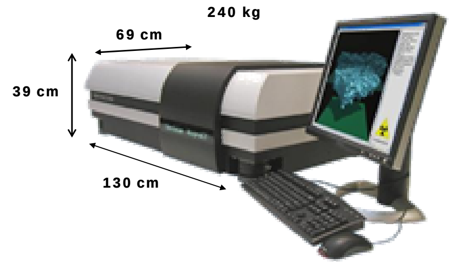
Microtomography imaging (microCT imaging)

WHY ?

Allows us to visualize and measure three-dimensional (3D) object structures non-destructively

MicroCTimaging

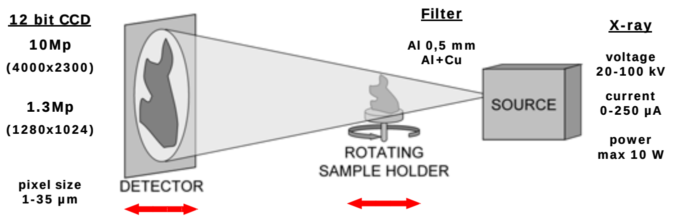
SkyScan 1172
High Resolution microCT



http://www.skyscan.be/home.htm

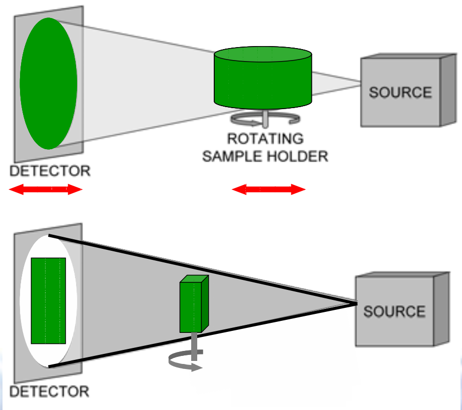
MicroCTimaging

Basic principles: 1. Scanning



System obtains multiple normal X-ray images of the object from different angular views as object rotates

Object (location, size)



MicroCTimaging

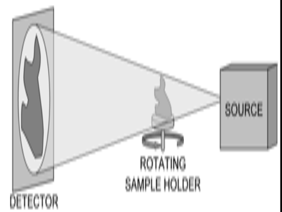
Basic principles: 2. Data acquisition

- At each angular position an x-ray image will be acquired
- Each point on the x-ray image contains information about the attenuation of x-rays inside the sample along the x-ray path
- X-ray attenuation depends on density variations
- Localisation of x-ray attenuation points inside the sample is based on the amount of x-ray images (rotation)

MicroCTimaging

Basic principles: Brightness and contrast

Measured brightness = an inverse indicator of x-ray attenuation in the analysed sample along the x-ray path



Contrast relates to the range of brightness levels in the image of a sample

NOTE! Good contrast in x-ray images is needed for it be possible to reconstruct well contrasted cross section images

MicroCTimaging

Basic principles: 3. Reconstruction

process, by which, taking the set of x-ray images, a dataset stack of virtual cross section images is created

- x-ray images are translated by the algorithm (filtered back-projection) into cross section images where pixel values indicate brightness
- computer synthesizes a stack of virtual cross section slices through the object

MicroCTimaging as a tool

Visualize:

- X-ray, cross section and 3D images
- allows cutting the reconstructed set of results in alternative directions
- possible to see three orthogonal sections with selection of the viewing point inside three dimensional reconstructed space (example)
- possible to do 3D visualizations (example)

Analyse:

- structural parameters by utilising cross section and 3D images

Example 1: Granule Ø < 1 mm

- Material: microcrystalline cellulose
- Method: wet granulation, extrusion and spheronization
- Granulation liquid: 1:1 mixture (w/w) of water and ethanol
- Size fraction: 800-900 μm was separated by sieving

Furthermore:

After the preparation some single granules were exposed to 10 % compression

two types of granules

Uncompressed Compressed

Example 1: Granule Ø < 1 mm

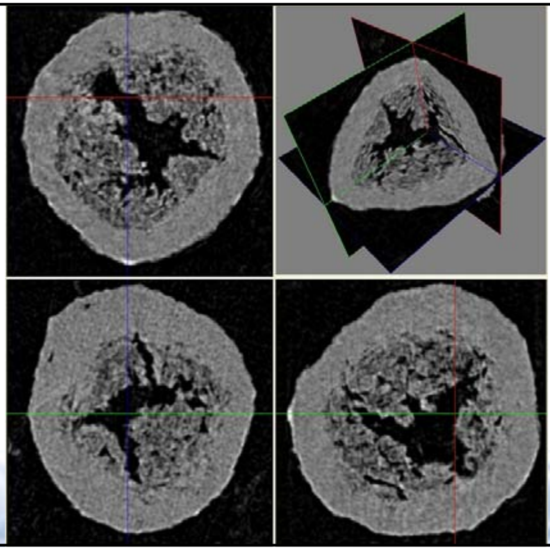
- Scanning
  - Voltage 59 kV
  - Current 167 μA
  - Detector camera 1,3 Mp
  - Rotation 180 deg
  - Rotation Step 0,7 deg
  - X-ray images 269
  - Frame averaging 20
  - Exposure time 158 ms

  ⟶ Scanning time 18 min
- Reconstruction
  - ring artefact correction
  - beam hardening correction
  - noise reduction
  - 330 cross sections

  ⟶ Reconstruction time 1 min

⟶ Image pixel size 3,13 μm

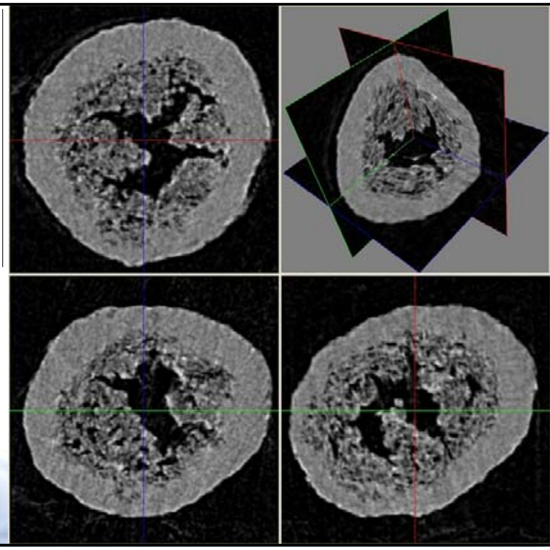
1 mm



Un-compressed granule

Cross-section images with different orthogonal sections

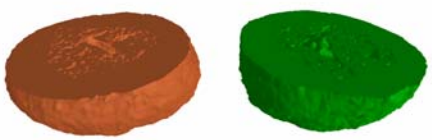
1 mm



Compressed granule

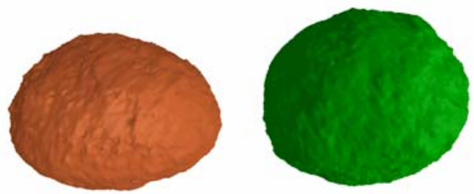
Cross-section images with different orthogonal sections

Example 1: 3D visualization



compressed uncompressed

Example 1: 3D visualization



compressed uncompressed

Example 1: Granule

- Examples of structural parameters:

	Compressed pellet	Uncompressed pellet
Total granule volume	0,354 mm³	0,384 mm³
Total granule surface	10,382 mm²	10,183 mm²
Resolution! Volume of pores	0,033 mm³	0,037 mm³
Resolution! Surface of pores	5,912 mm²	5,561 mm²

Example 1: Observations

- large continous hole inside the granule
- outer layer of the granule is denser than the inner parts
- need for better resolution
- with the image pixel size of 3.13 µm structural dissimilarities are minor

Example 1: 3D visualization

Scanning
- Detector camera 10 Mp
- Rotation 180 deg
- Rotation Step 0,3 deg
- X-ray images 626
- Frame averaging 10
- Exposure time 2356 ms
- **Scanning time 5 h**

Reconstruction and analyses
- Ring artefact correction
- Beam hardening correction
- Noise reduction
- 870 cross sections
- Reconstruction time 59 min

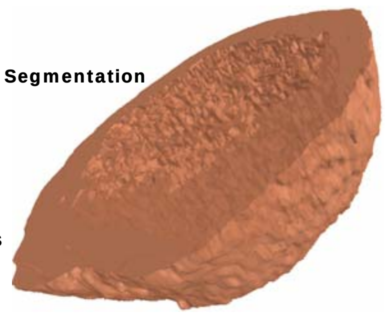


Image pixel size 1,09 µm

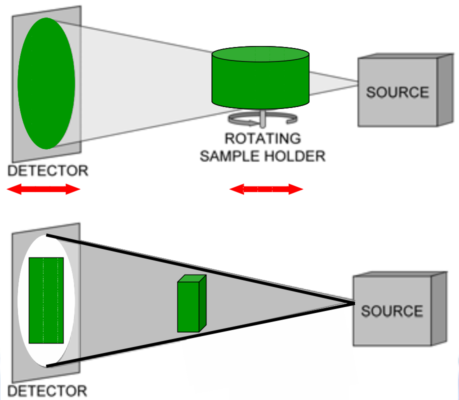
Example 2: Tablet Ø 10 mm

- Materials:
  - potato starch acetate (SA)
  - propranolol HCl or atenolol
- Binary mixture tablets 50/50 % (v/v)
  - tablet compaction simulator
  - cylindrical tablets ø 10 mm
  - porosity 13 %

→ two types of tablets

SA + atenolol SA + propranolol HCl

Object size

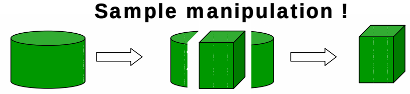


Example 2: Tablet

- Scanning
  - Voltage 59 kV
  - Current 167 µA
  - Detector camera 10 Mp
  - Rotation 180 deg Step 0,3 deg
  - X-ray images 626
  - Frame averaging 20
  - Exposure time 2356 ms
  - Scanning time 9 h
- Reconstruction and analyses
  - ring artefact correction
  - beam hardening correction
  - noise reduction
  - 1955 cross sections
  - Reconstruction time 9h48min

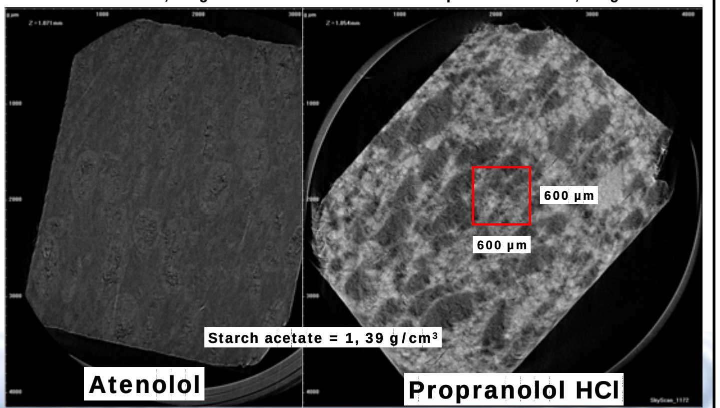
⟶ Image pixel size 1,04 µm

Sample manipulation !

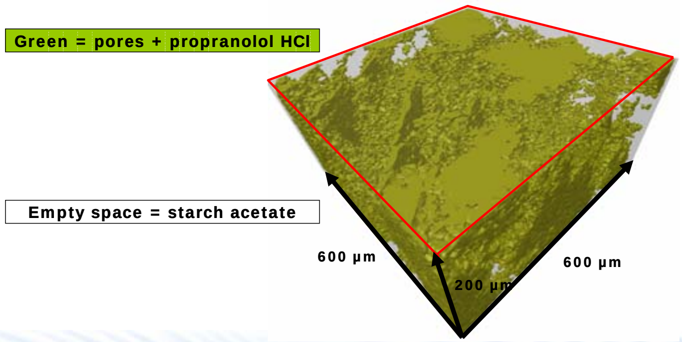


Example 2: Cross section examples

Atenolol = 1, 36 g/cm³ Propranolol HCl = 1, 24 g/cm³



Example 2: Region of Interest



Summary

	Granule		Tablet	
Object size Ø	< 1 mm		10 mm	→ 3 mm
Detector camera	524x1000	2096x4000		2096x4000
Rotation step	0,7	0,3		0,3
Frame averaging	20	10		20
Exposure time	158	2356		2356
Scanning time	18 min	5 h		9 h
cross sections	330	870		1955
Reconstruction time	1 min	59 min		9h48min
Image pixel size	3,16	1,09		1,04

Conclusions

- time-consuming method
- design your research carefully
- pharmaceutical materials and dosage forms are challenging

Future plans

- other dosage forms
- powders and powder particles
- density maps

Acknowledgments

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QUESTIONS ?

COMMENTS !

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