The Munich Compact Light Source – a laboratory-scale synchrotron facility for biomedical research

Martin Dierolf

Technical University of Munich (TUM)

Department of Physics & Munich School of BioEngineering

Chair of Biomedical Physics

painted by Simone Ferstl

LAL Seminar,

Orsay, March 26th 2019

Chair of Biomedical Physics

www.e17.ph.tum.de

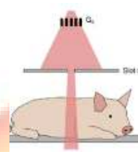
Research portfolio at Chair of Biomedical Physics

Biomedical Applications:
cancer detection, mammography, osteoporosis, atherosclerosis, lung imaging (emphysema), virtual histology, ...

Applications

Spectral CT

Dark-field Tomography



Dark-field Radiography

Small-animal research

TensorCT

X-ray Physics:
Imaging Technology & Algorithms

Staining-based nanoCT & microCT

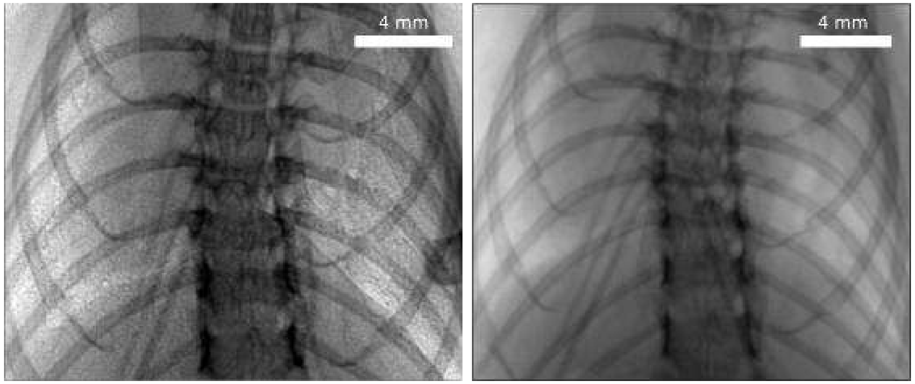
Munich Compact Light Source (MuCLS)

Basic Research

www.e17.ph.tum.de

Outline

The MuCLS:
- What is the MuCLS?
- How does it perform?
- How do we operate?



Biomedical research at the MuCLS:
- experimental setups
- selected applications

What is the MuCLS?

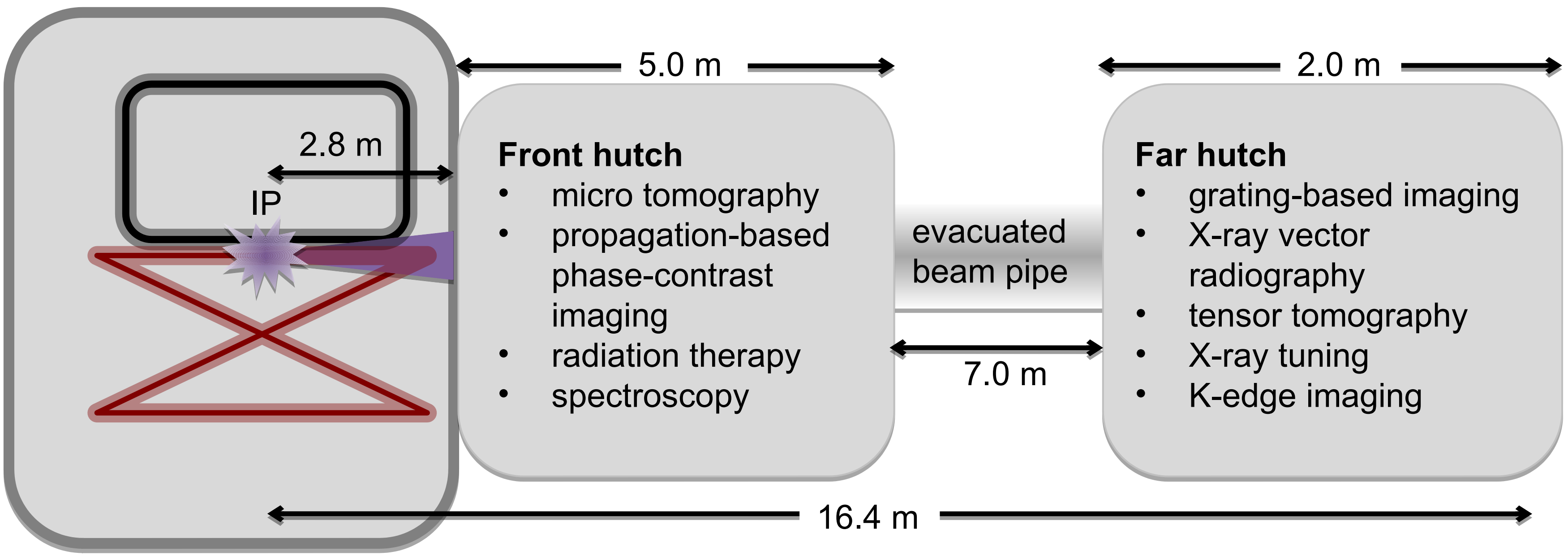


Figure adapted from Eggl, Ph.D. thesis, TUM (2017)

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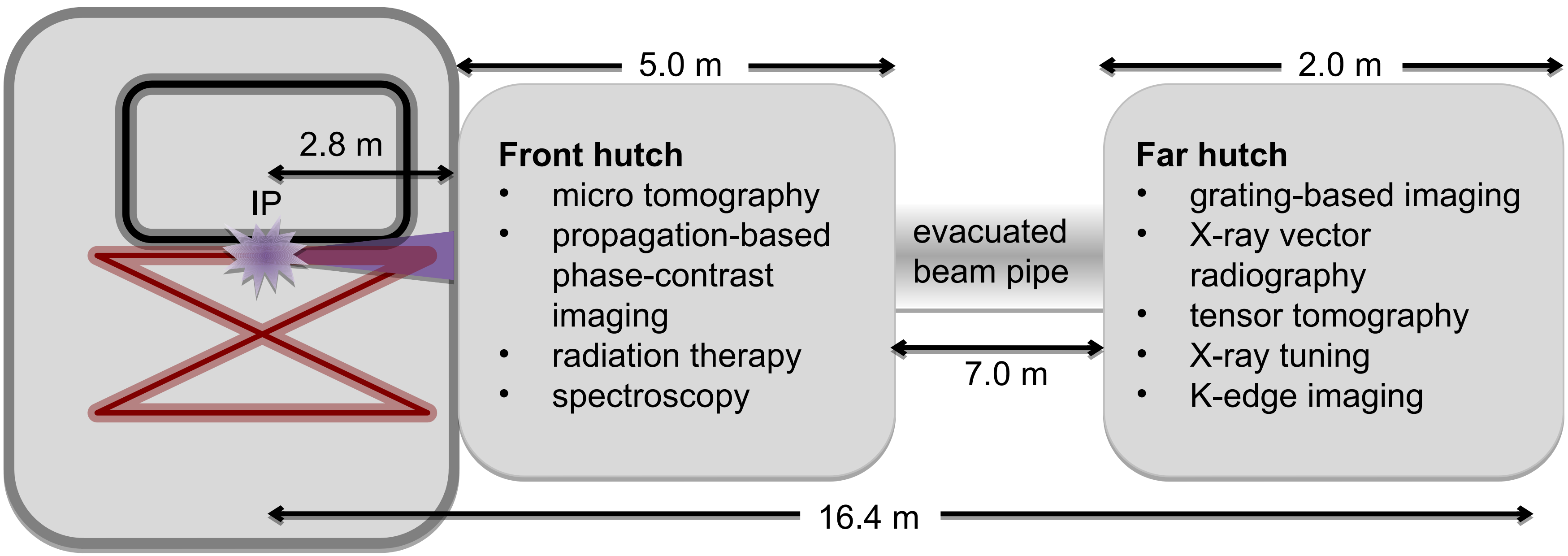

Compact Light Source

lyncean TECHNOLOGIES, INC.

Figure adapted from Eggl, Ph.D. thesis, TUM (2017)

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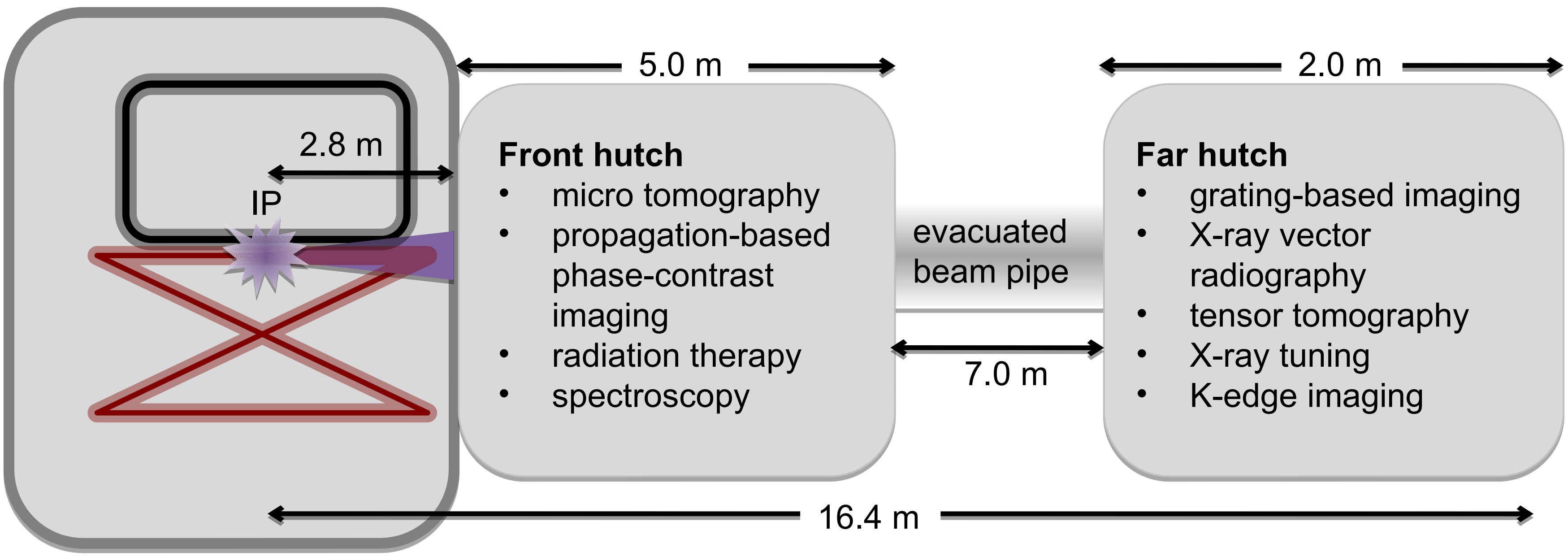

Compact Light Source

beamline with two endstations

Figure adapted from Eggl, Ph.D. thesis, TUM (2017)

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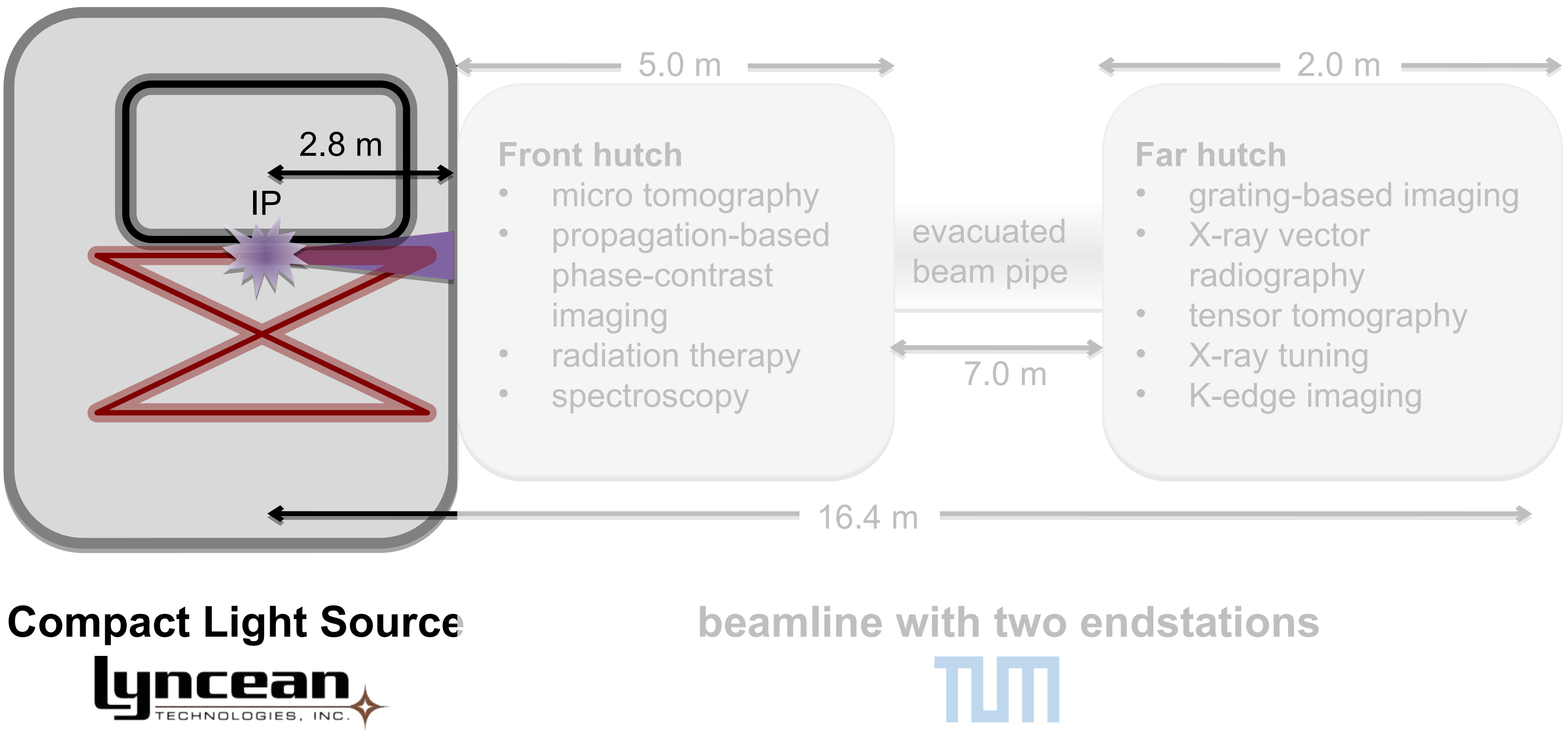
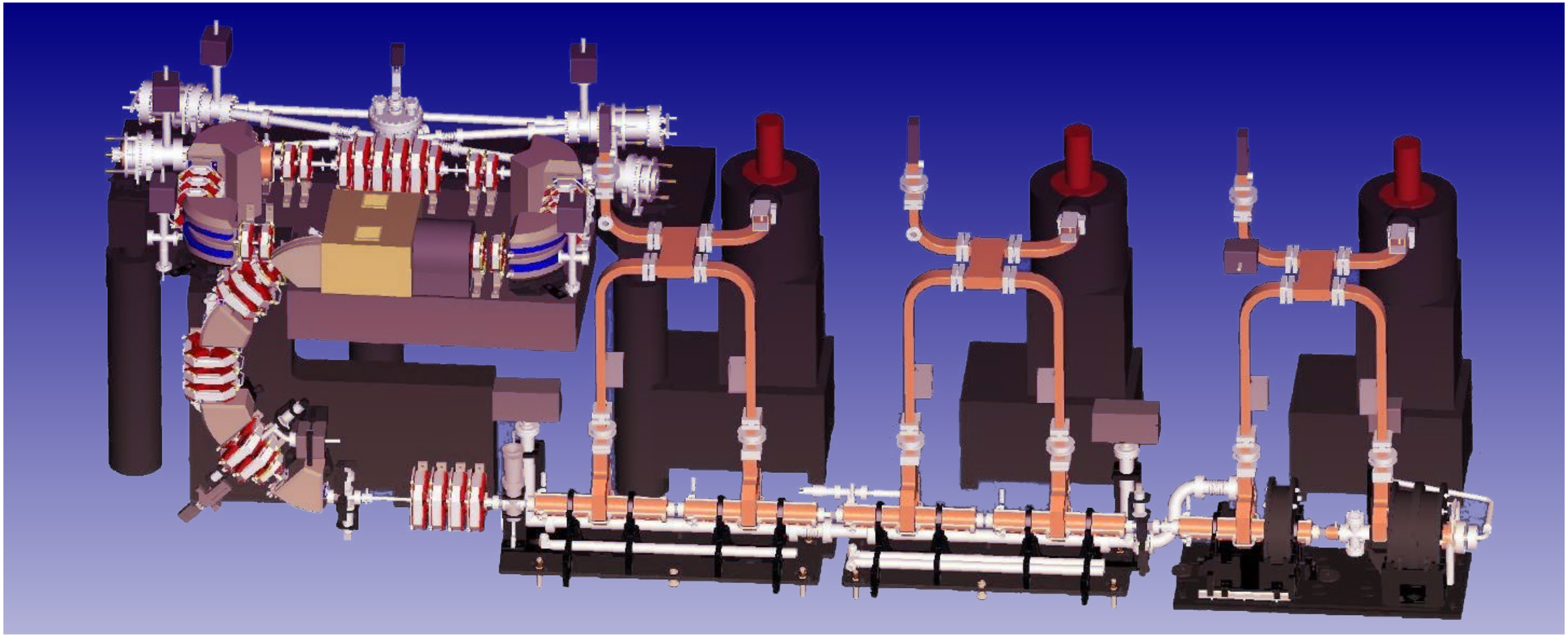
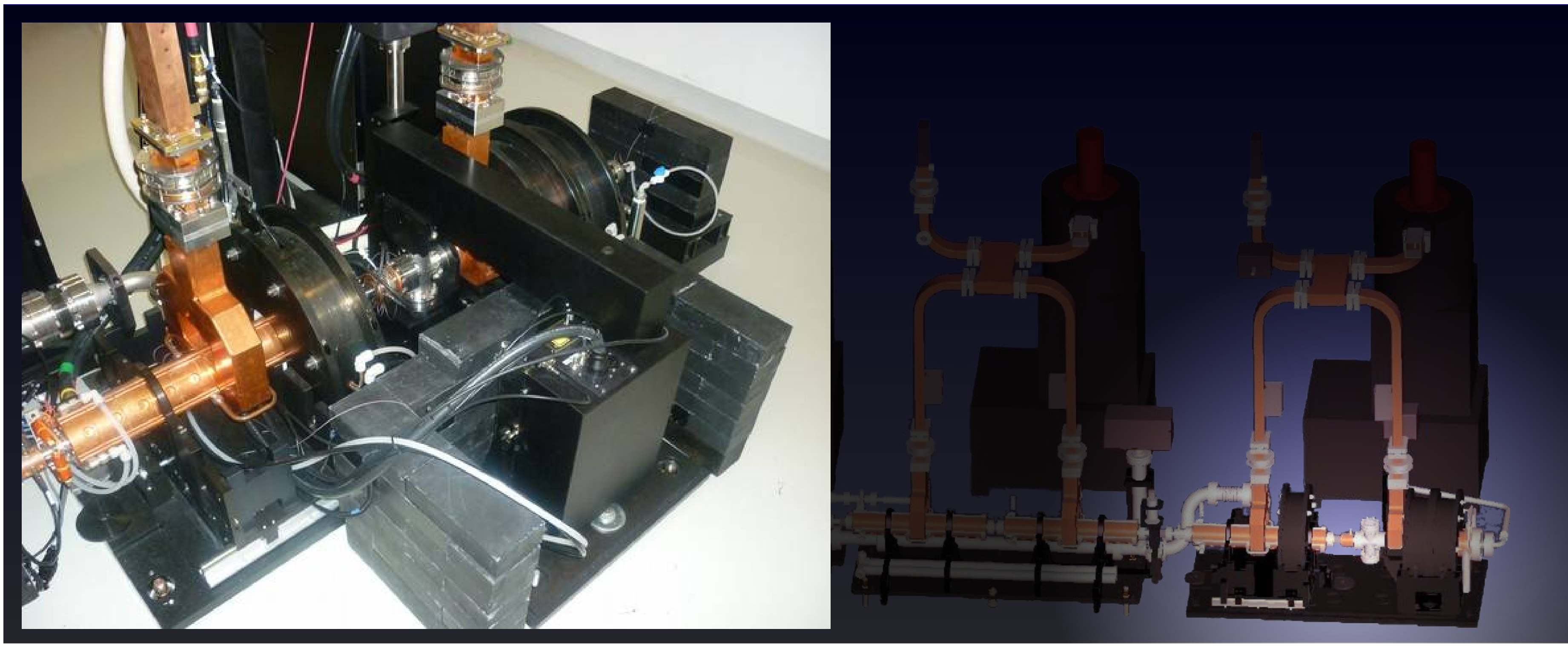


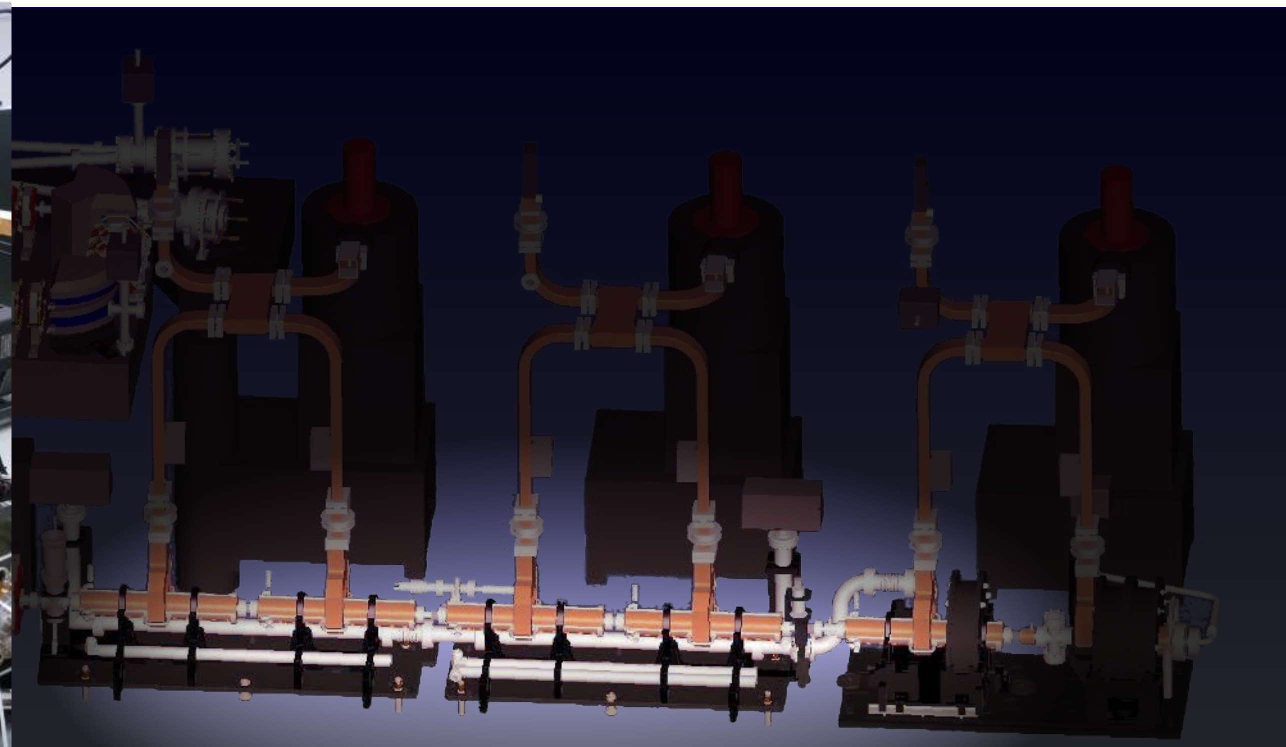
The X-ray source of the MuCLS



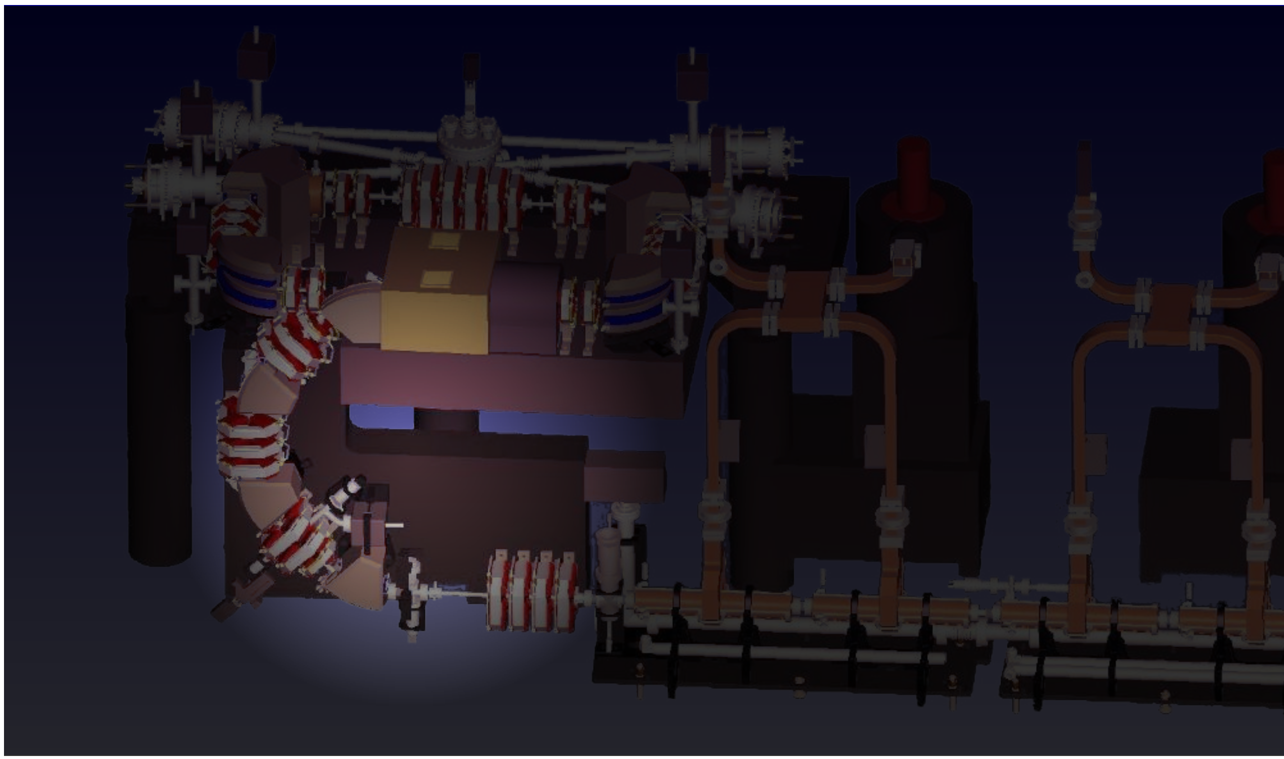
The X-ray source of the MuCLS – electron gun



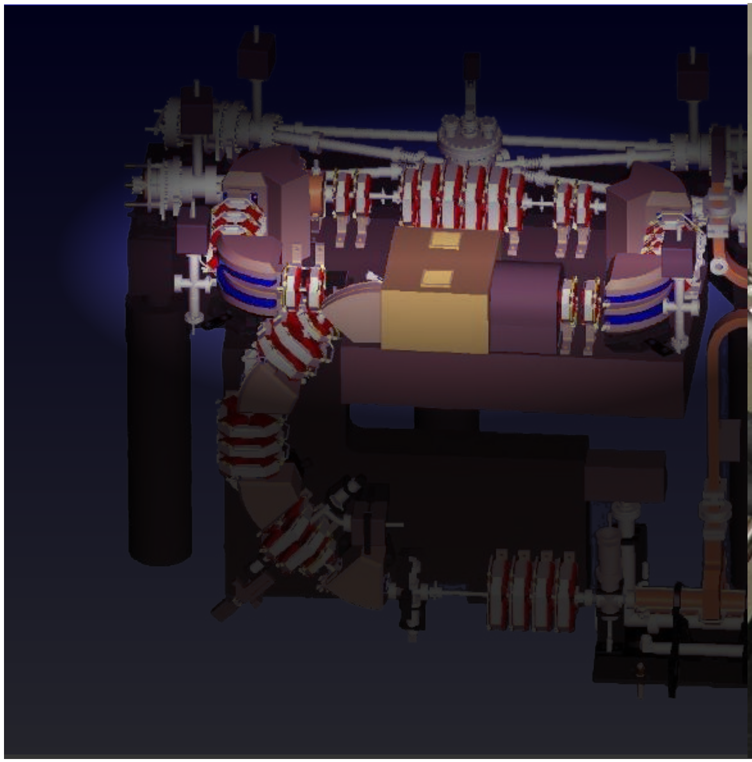
The X-ray source of the MuCLS – LINAC

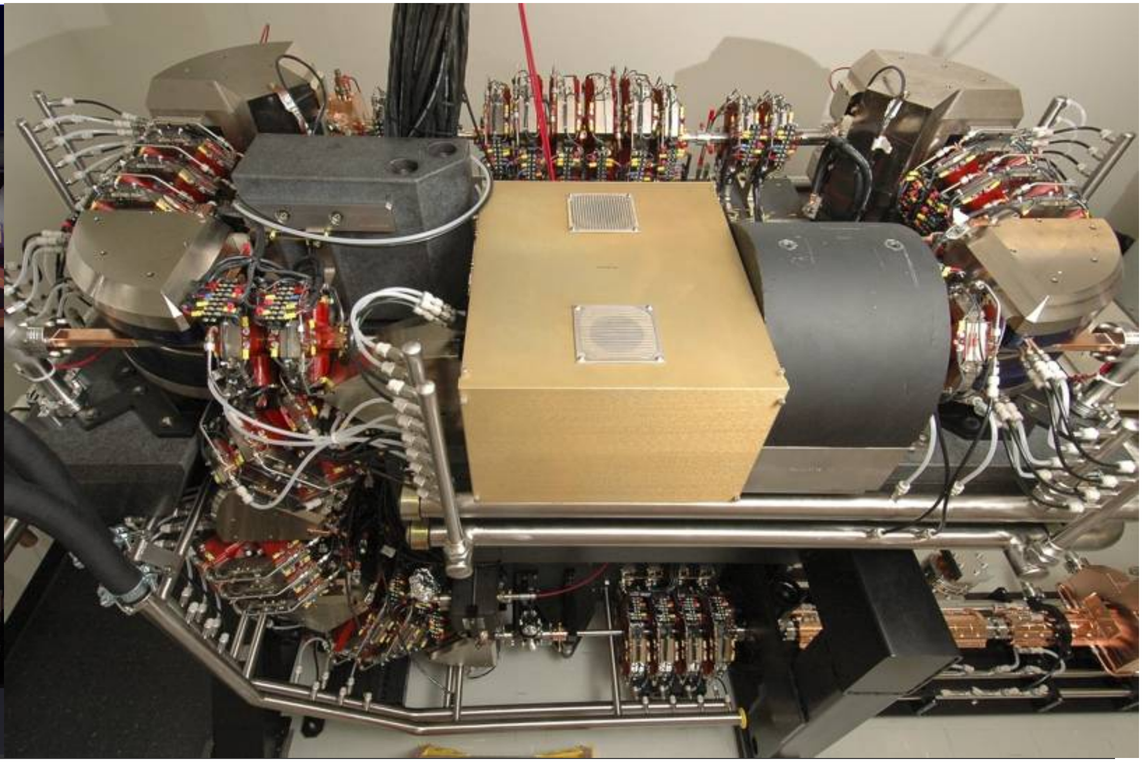


The X-ray source of the MuCLS – transport line

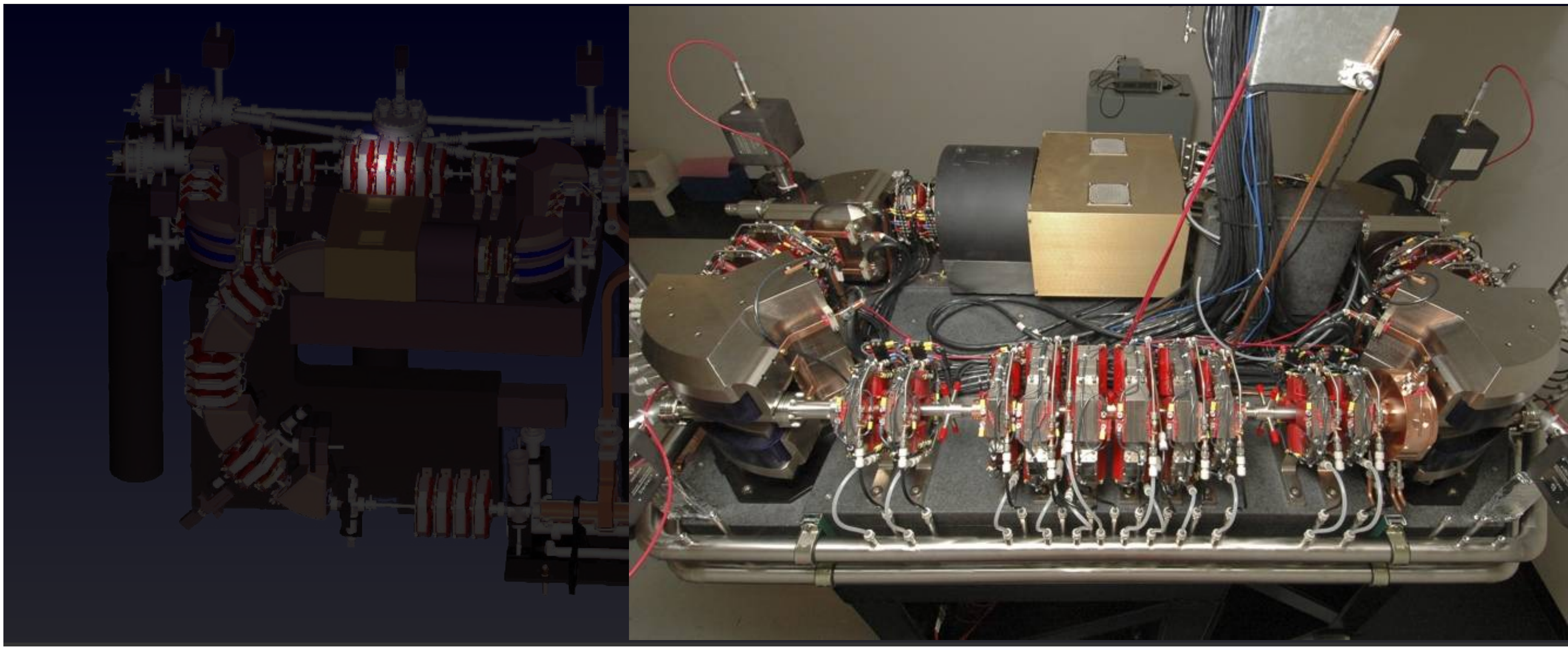


The X-ray source of the MuCLS – storage ring

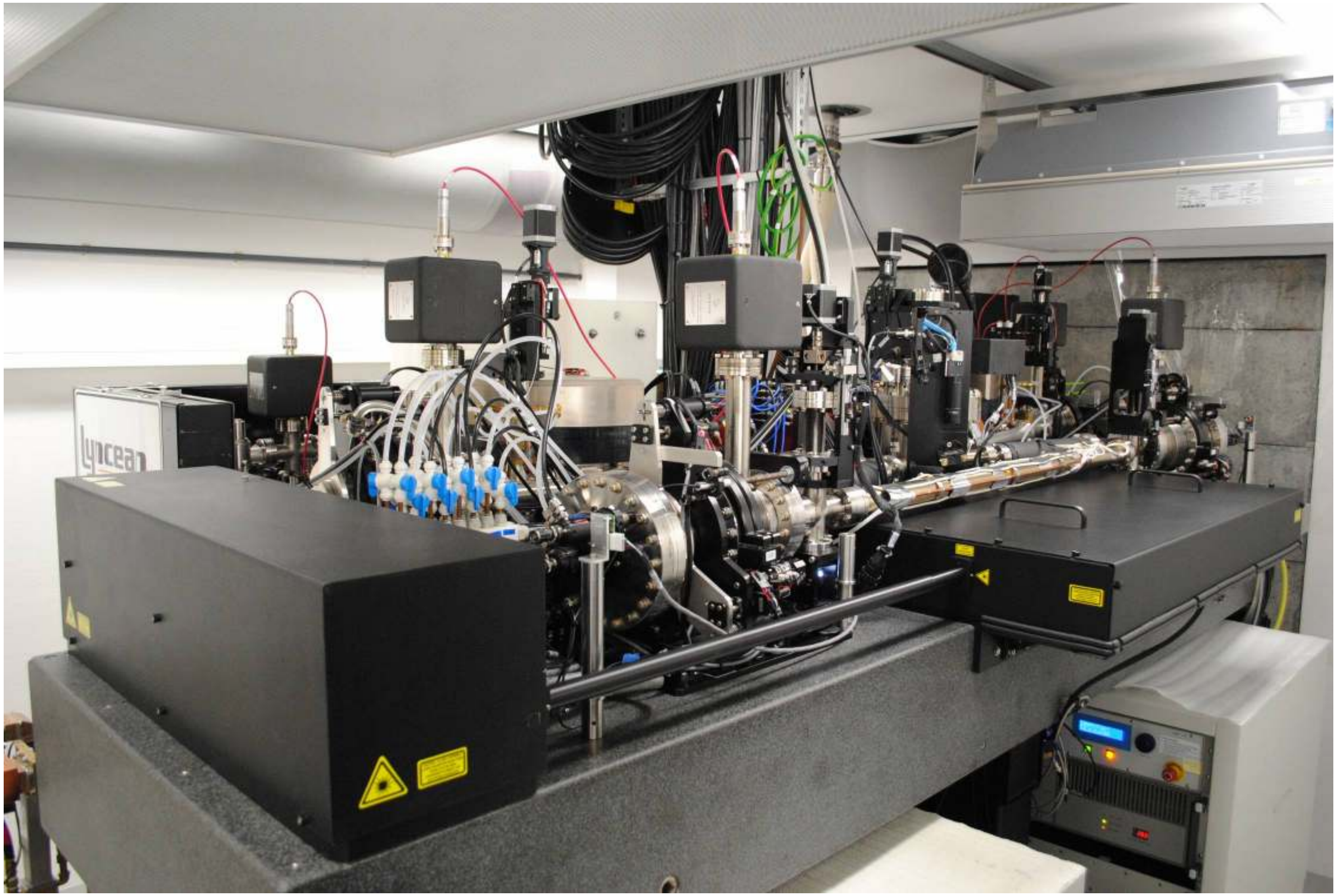




The X-ray source of the MuCLS – storage ring



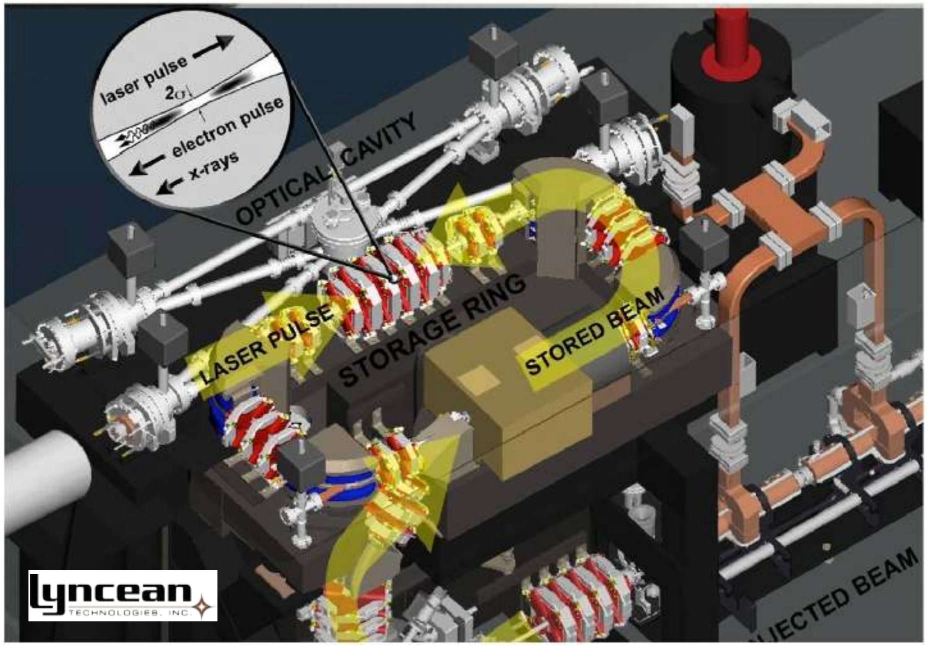
The X-ray source of the MuCLS – optical cavity



MuCLS: design decisions to optimize luminosity

maximize collision frequency

$$\mathcal{L}_0 = f_{\text{coll}} \frac{N_l N_e}{4\pi\sigma_r^2}$$



maximize electron bunch charge

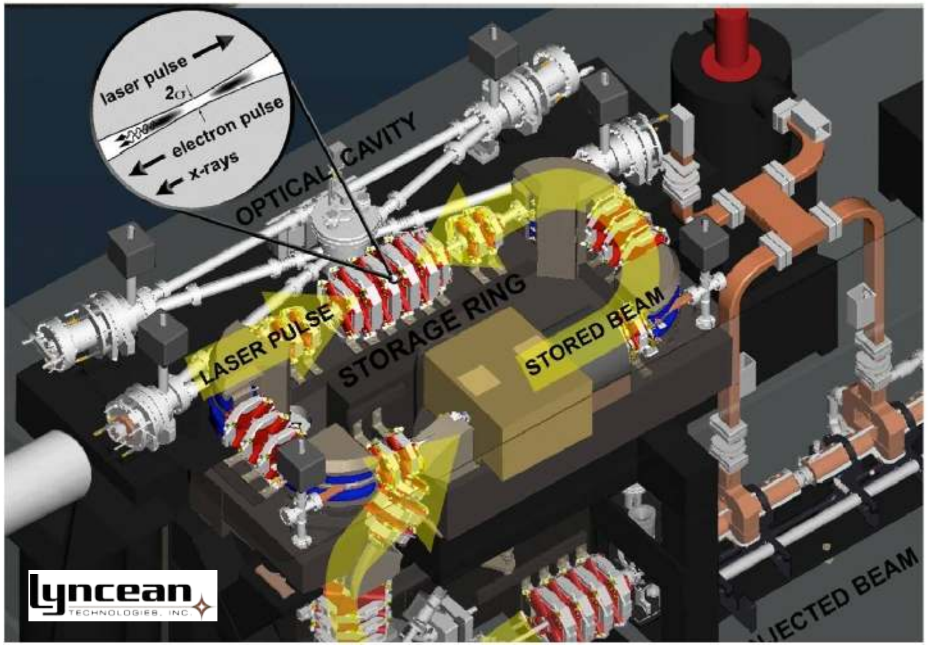
maximize laser pulse power

minimize source size

MuCLS: design decisions to optimize luminosity

$$\mathcal{L}_0 = f_{\mathrm{coll}} \frac{N_l N_e}{4\pi\sigma_r^2}$$

maximize collision frequency
→ **storage ring for electron**
→ optical cavity for laser photons
→ match round-trip time
→ $f_{\mathrm{coll}} = 65\,\mathrm{MHz}$



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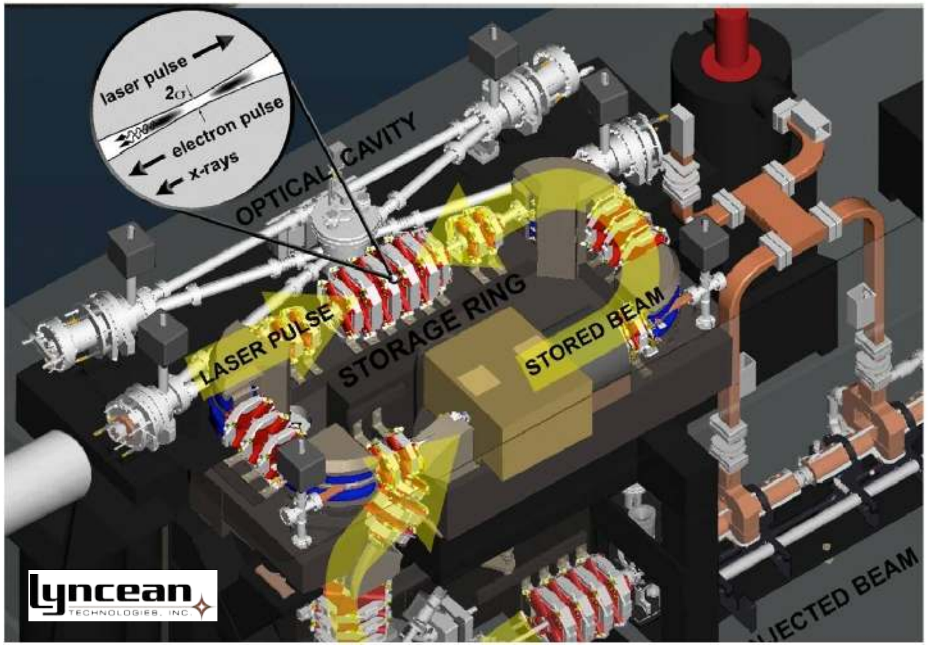
maximize electron bunch charge
→ start with low-emittance photo injector
→ refill with 25 Hz

maximize laser pulse power

minimize source size



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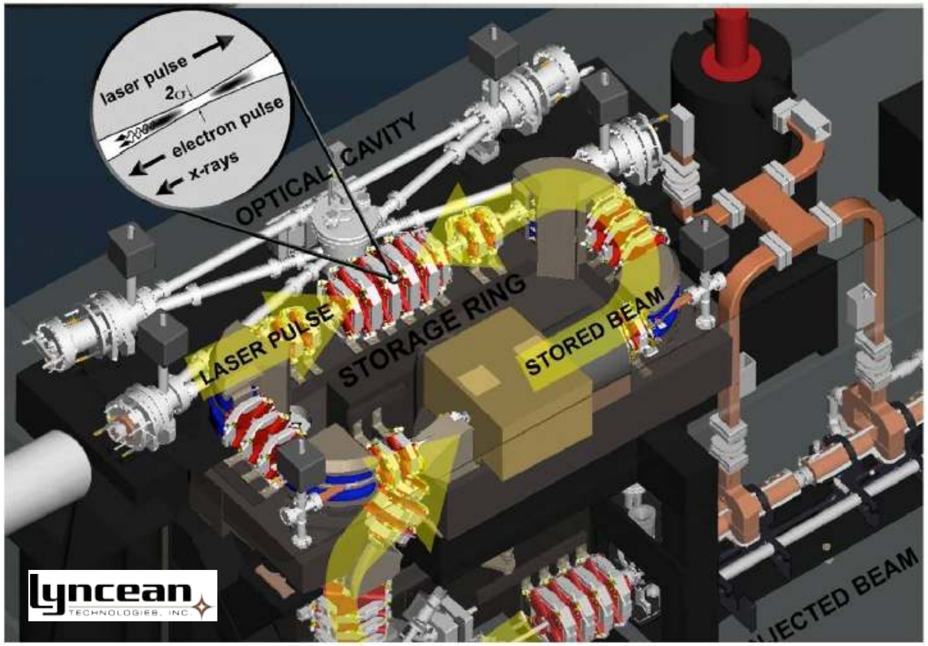
→ **enhancement cavity**
→ from ~20 W input to >300 kW stored

minimize source size



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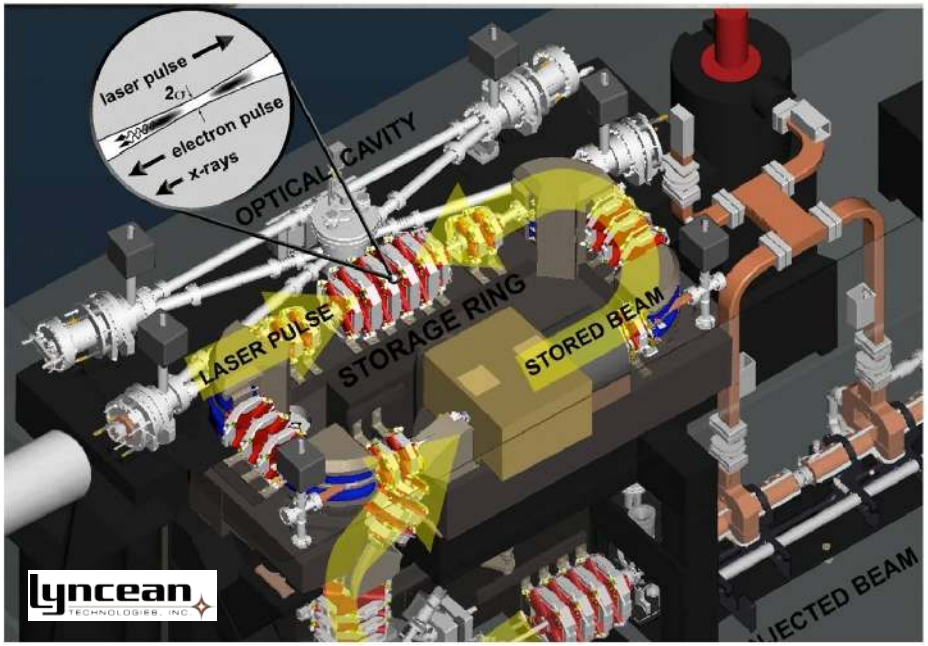
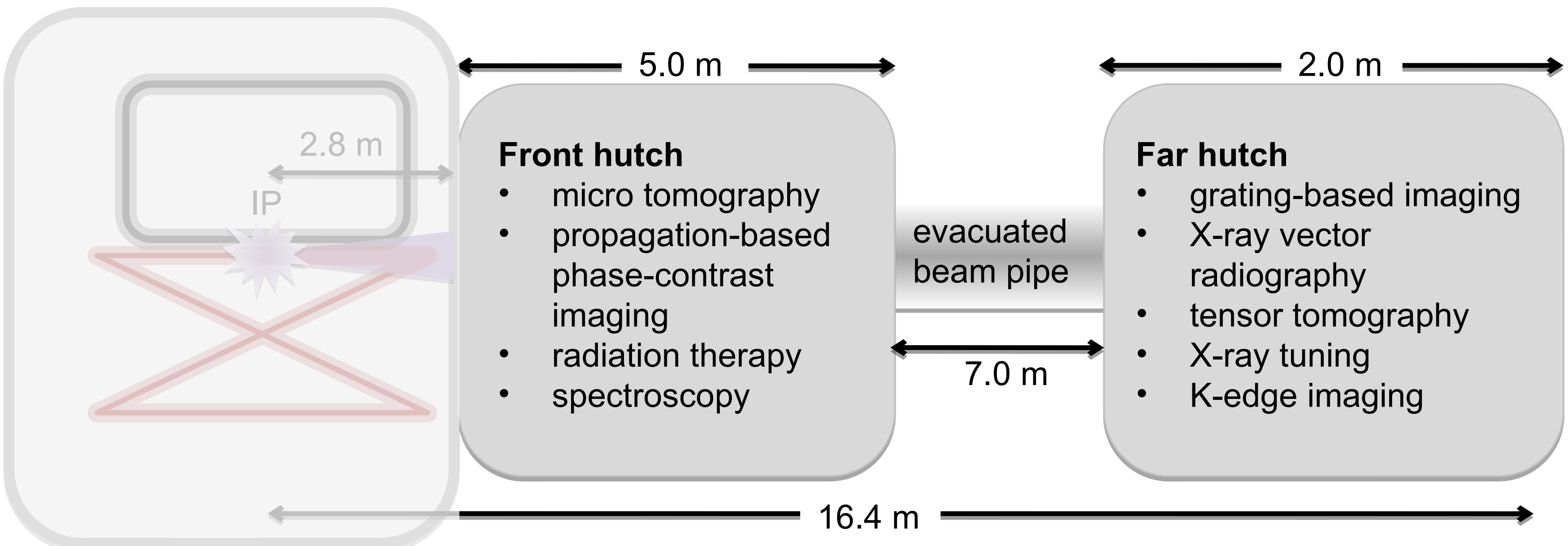
minimize source size
→ tight focusing of colliding beams
→ 25 Hz refill preserves high quality of electron bunch



What is the MuCLS?



Compact Light Source

beamline with two endstations

What is the MuCLS?

raphy
-based
ast
rapy
y

evacuated
beam pipe

7.0 m

2.0 m

Far hutch
- grating-based imaging
- X-ray vector radiography
- tensor tomography
- X-ray tuning
- K-edge imaging

16.4 m

eamline with two endstations

Outline

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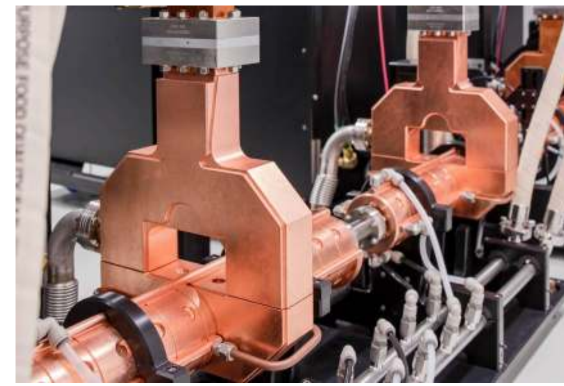
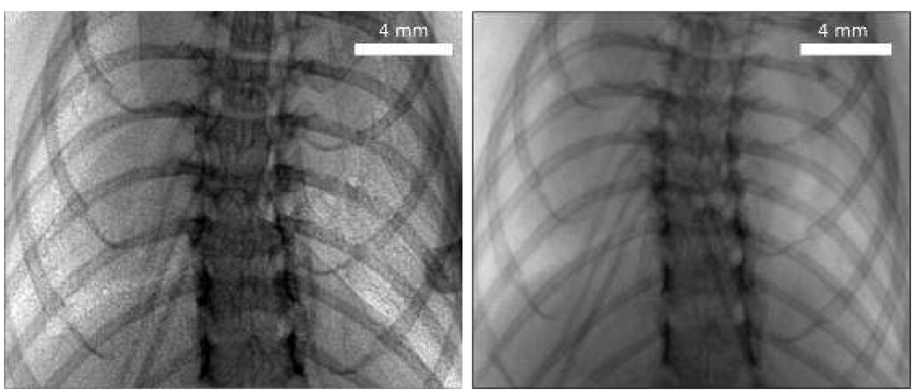
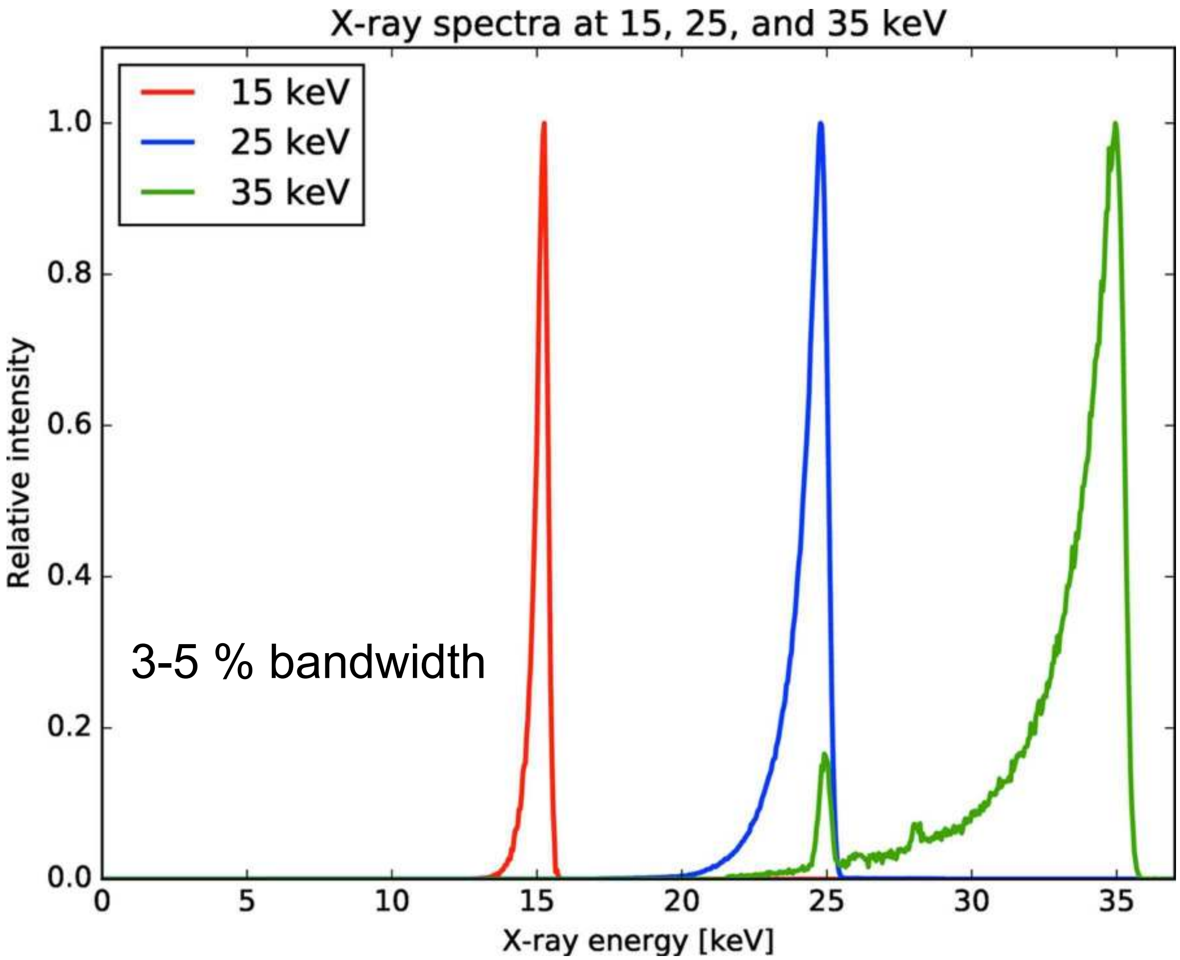




Biomedical research at the MuCLS:
- experimental setups
- selected applications

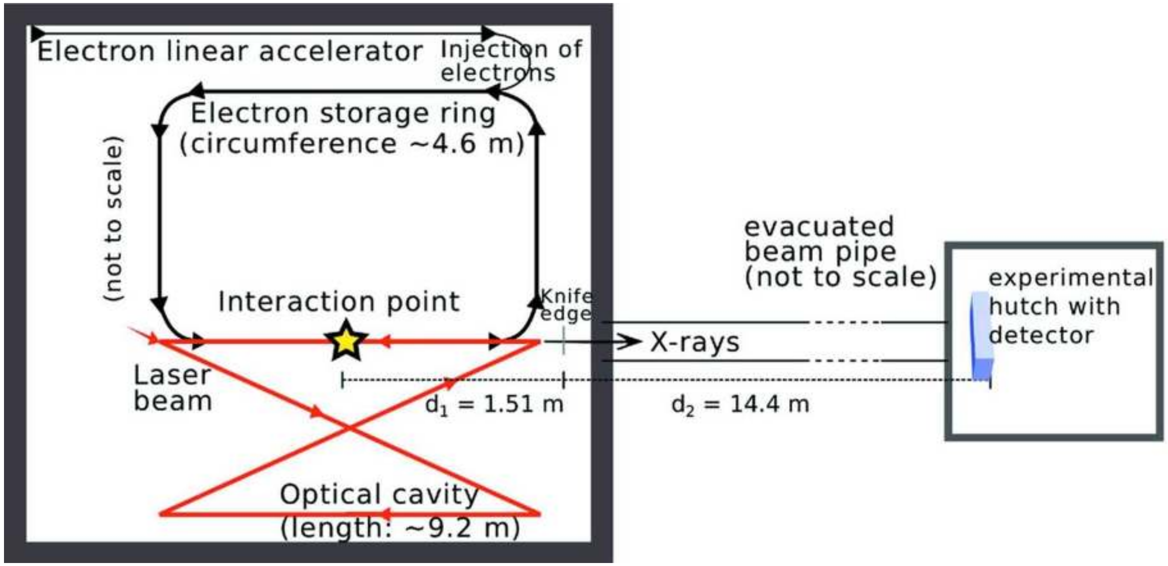
X-ray spectra at exemplary energies

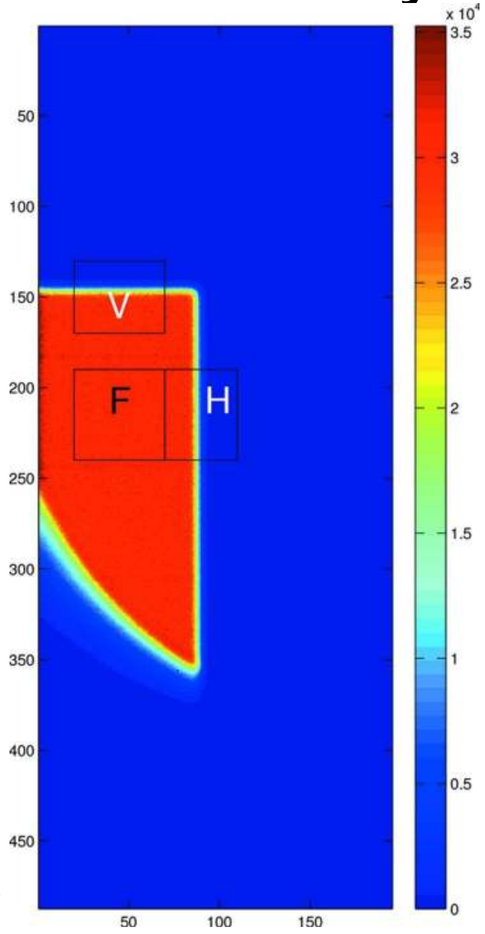


Eggl et al., J. Sync. Rad. 23, 1137 (2016)

Characterization of source parameters & stability

Hand-off runs at 15 keV, 25 keV and 35 keV





recorded at 1 Hz frame rate

work by
Elena Eggl

Eggl et al., J. Sync. Rad. 23, 1137 (2016)

MuCLS source parameters

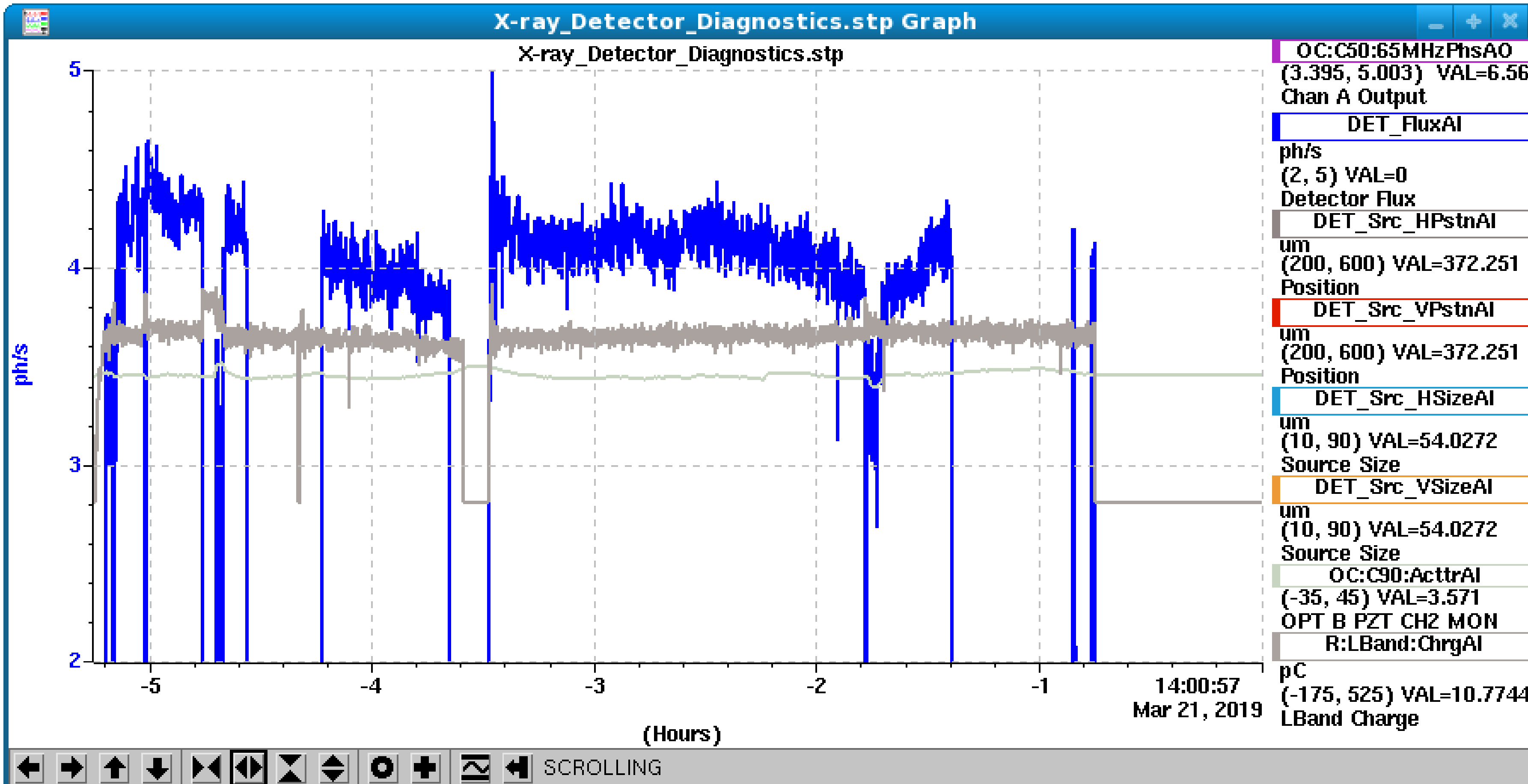
work by
Elena Eggl

Parameters measured 03 / 2017, after upgrade of laser amplifier system			
X-ray energy	15 keV	25 keV	35 keV
Flux	0.8 x 10^{10} ph/s	2.1 x 10^{10} ph/s	3.3 x 10^{10} ph/s
source sizes (h x v, rms)	51 x 46 μm^2	48 x 46 μm^2	43 x 40 μm^2
Source position stability (std. dev.)	1 µm	1 µm	1 µm

Parameters before upgrade, see Eggl et al., J. Sync. Rad. 23, 1137 (2016)			
X-ray energy	15 keV	25 keV	35 keV
Flux	0.4 x 10^{10} ph/s	1.0 x 10^{10} ph/s	1.8 x 10^{10} ph/s

values averaged over **10 min**, 90 min after starting an energy change

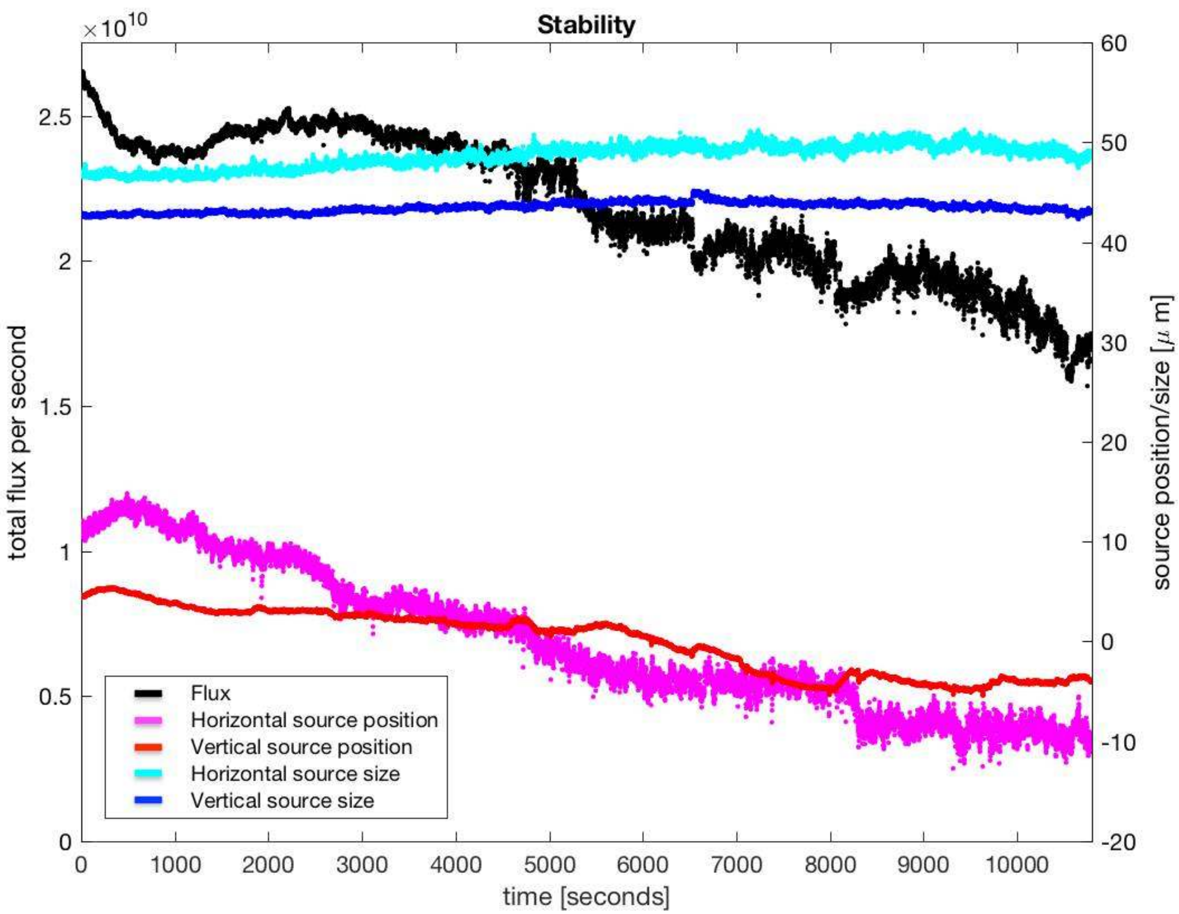
MuCLS source parameters



measured at 35 keV

Characterization of source stability

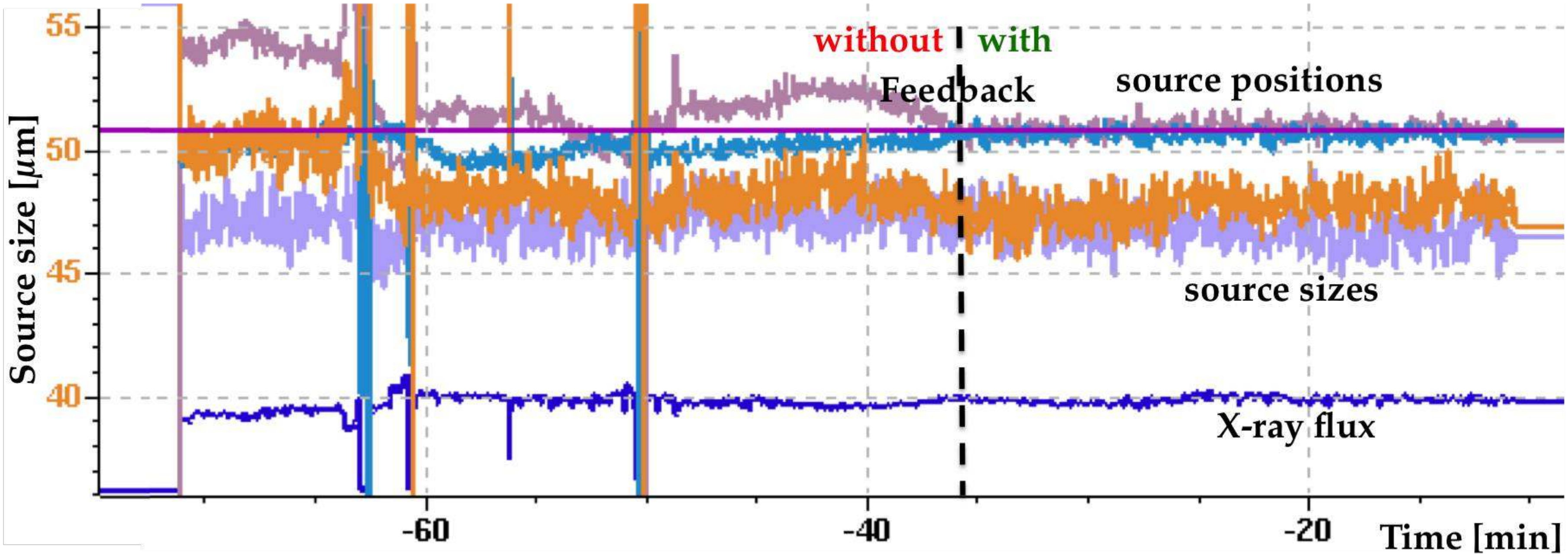
work by
Elena Eggl



3 hours without operator interaction (25 keV)	
Flux [ph/s]	2.2×10^{10}
Flux stability (std. dev.)	10%
rms source sizes [μm²]	48 x 43
Stability (std. dev.)	2%
Position stability (std. dev.)	5 μm

Eggl, Ph.D. thesis, TUM (2017)
http://mediatum.ub.tum.de?id=1360604

Improve stability: active source position feedback



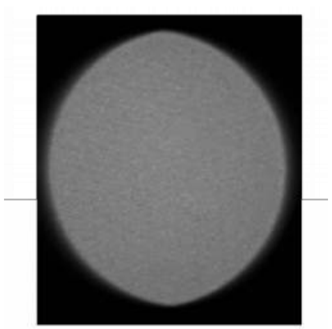
→ previous characterization used imaging detector

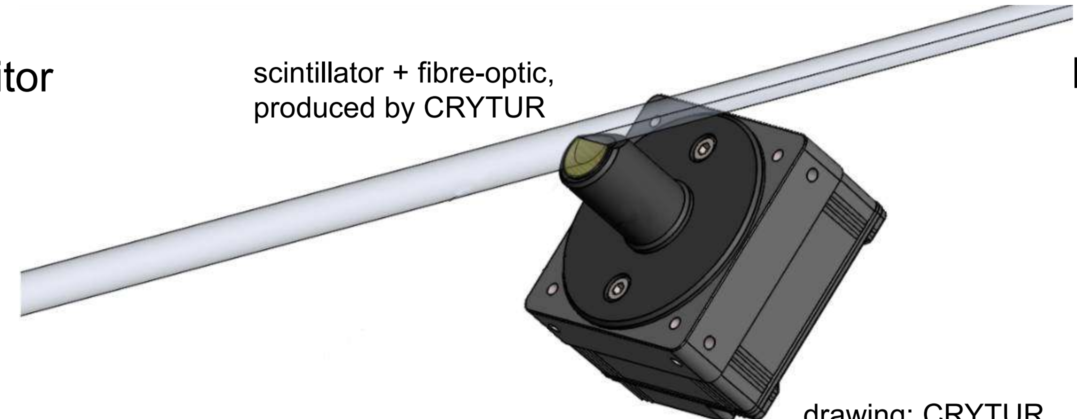
→ but: want to run characterization & feedback in parallel with experiments

work by
Benedikt Günther

Improve stability: active source position feedback

in front of beam monitor

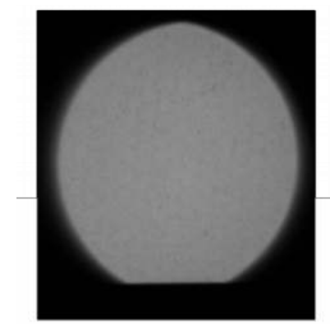




drawing: CRYTUR

Basler Ava 1600-50gm

behind beam monitor



→ intercept lower part of X-ray beam with customized detector

→ permanent knife-edge imaging + feedback

Günther et al., submitted

work by
Benedikt Günther

Summary of MuCLS parameters

Performance parameters (as of 3/2017)	
Electron beam	
Electron energy	25-45 MeV
Ring circumference	4.6 m
Repetition rate	64.91 MHz (single bunch)
Bunch length	50 ps / 1.5 cm (rms)
Bunch charge	250 pC (max. 500 pC)
Re-injection rate	25 Hz
Focus spot size	45 μm×45 μm
Laser & Laser Cavity	
Laser wavelength	1064 nm
Cavity Length	9.2 m
Repetition rate	64.91 MHz (two pulses)
Pulse length	25-30 ps (FWHM)
Drive laser power	14 W
Stored laser power	up to 140 kW
Finesse, coupling	32000 with 69%

X-ray beam	
Energy range	11-35 keV
Source size	$<$ 45 μm×45 μm
Divergence	4 mrad
Energy bandwidth	3-5%
Brilliance (35 keV)	$0.6 \cdot 10^{10} \frac{\text{photons/s}}{\text{mrad}^2 \cdot \text{mm}^2 \cdot 0.1\% \text{ BW}}$
Flux (35 keV)	$1 \cdot 10^{10}$ photons/s
Flux scaling	$\propto E_x/E_{0x}$ ($E_{0x} = 35$ keV)

Table 3.1.: Technical specifications for the MuCLS.

Eggl, Ph.D. thesis, TUM (2017)
http://mediatum.ub.tum.de?id=1360604

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Performance parameters (as of 3/2017 after laser upgrade)	
Laser & Laser Cavity	
Drive laser power	30 W
Stored laser power	$>$ 300 kW
Finesse, efficiency	32000 with 75-80%
X-ray beam	
Source size	$<$ 50 µm×50 µm
Divergence	4 mrad
Energy bandwidth	5%
Brilliance	up to $0.8 \cdot 10^{10} \frac{\text{photons/s}}{\text{mrad}^2 \cdot \text{mm}^2 \cdot 0.1\% \text{ BW}}$
Flux	up to $3.3 \cdot 10^{10}$ photons/s

Eggl, Ph.D. thesis, TUM (2017)
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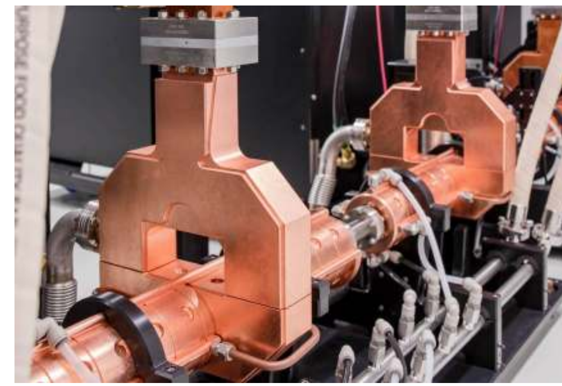

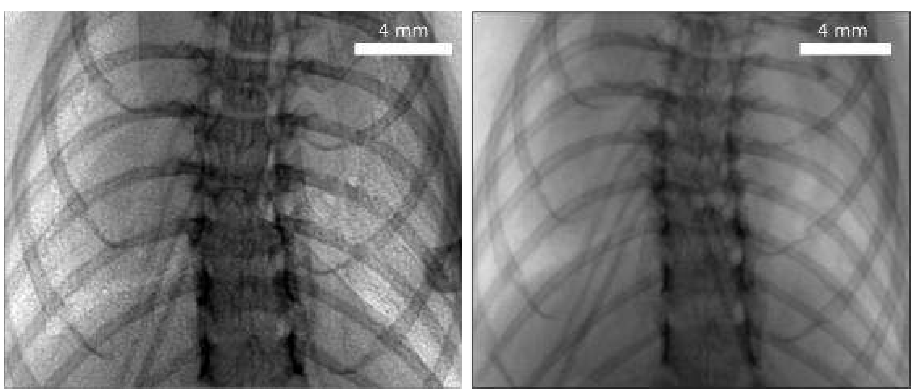

Biomedical research at the MuCLS:
- experimental setups
- selected applications

Typical MuCLS operation

<table>
<tr><th></th><th>Monday</th><th>Tuesday</th><th>Wednesday</th><th>Thursday</th><th>Friday</th><th>Saturday</th><th>Sunday</th></tr>
<tr><td>04:00</td><td></td><td colspan="4">RF startup by script</td><td colspan="2" rowspan="21">typically no operation
(usually only for
in-vivo experiments)</td></tr>
<tr><td>05:00</td><td rowspan="2">chiller startup
by script</td><td colspan="4" rowspan="3">RF warmup</td></tr>
<tr><td>06:00</td></tr>
<tr><td>07:00</td><td></td></tr>
<tr><td>08:00</td><td rowspan="6">full startup
+
~5 hours till
full thermal
equilibrium
reached</td><td colspan="4">short ebeam and X-ray startup</td></tr>
<tr><td>09:00</td><td colspan="4" rowspan="11">X-ray experiments</td></tr>
<tr><td>10:00</td></tr>
<tr><td>11:00</td></tr>
<tr><td>12:00</td></tr>
<tr><td>13:00</td></tr>
<tr><td>14:00</td><td rowspan="6">machine / setup
development
or
short X-ray
experiments</td></tr>
<tr><td>15:00</td></tr>
<tr><td>16:00</td></tr>
<tr><td>17:00</td></tr>
<tr><td>18:00</td></tr>
<tr><td>19:00</td></tr>
<tr><td>20:00</td><td colspan="5" rowspan="4">unattended experiments
or
warm standby</td></tr>
<tr><td>21:00</td></tr>
<tr><td>22:00</td></tr>
<tr><td>23:00</td></tr>
<tr><td>00:00</td><td colspan="5">warm standby (just RF off), sometimes remote maintenance work by Lyncean</td></tr>
</table>

Who operates the MuCLS machine?

Who operates the MuCLS machine?

2 “expert” operators

- 1 scientist (non-permanent), 1 PhD student
- cold startup
- tricky operation conditions
- troubleshooting & small repairs
- characterization & development

Martin
Dierolf

Benedikt
Günther

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Benedikt Günther

3 “regular” operators

- PhD students with projects at MuCLS
- (mostly) warm startup
- operate the machine within normal parameters


Regine Gradl


Stephanie Kulpe


Juanjuan Huang

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Senior staff scientist:

- preparations for installation
- radiation safety
- contracts / finances


Klaus Achterhold

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Regine
Gradl

Stephanie
Kulpe

Juanjuan
Huang

Service and support contract:

- remote assistance
- quarterly service visits

lyncean TECHNOLOGIES, INC.

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Klaus Achterhold

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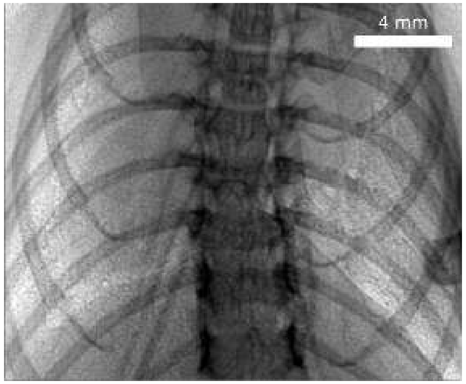

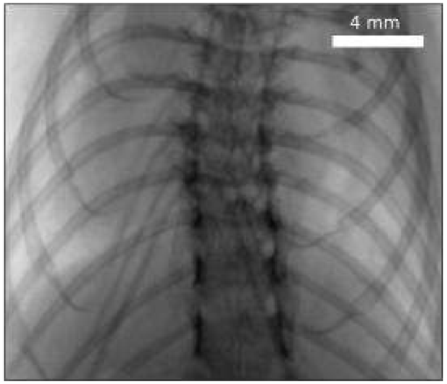

Biomedical research at the MuCLS:
- **experimental setups**
- selected applications

What can compact sources offer to users?

total flux	low		high
source sizes	small		large
typical energies	low		high
width of spectrum	narrow		broad
divergence	small		large
regular access	easy		hard
infrastructure	limited		superb
costs	low		high

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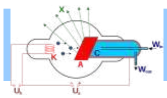
total flux	low	  	high
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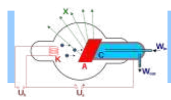

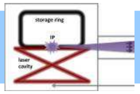

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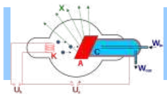
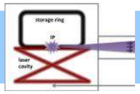
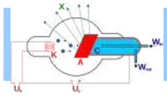
total flux	low	   	high
source sizes	small	  	large
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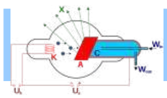
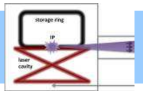
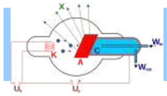
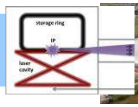
total flux	low	   	high
source sizes	small	   	large
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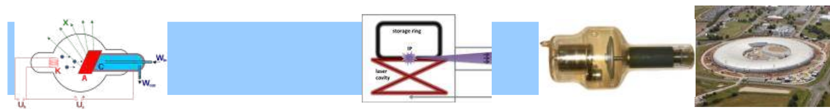
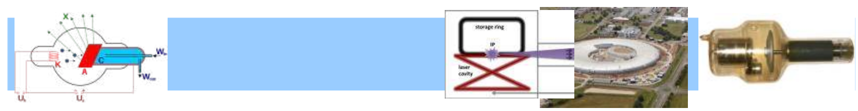
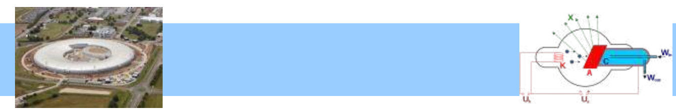
total flux	low		high
source sizes	small		large
typical energies	low		high
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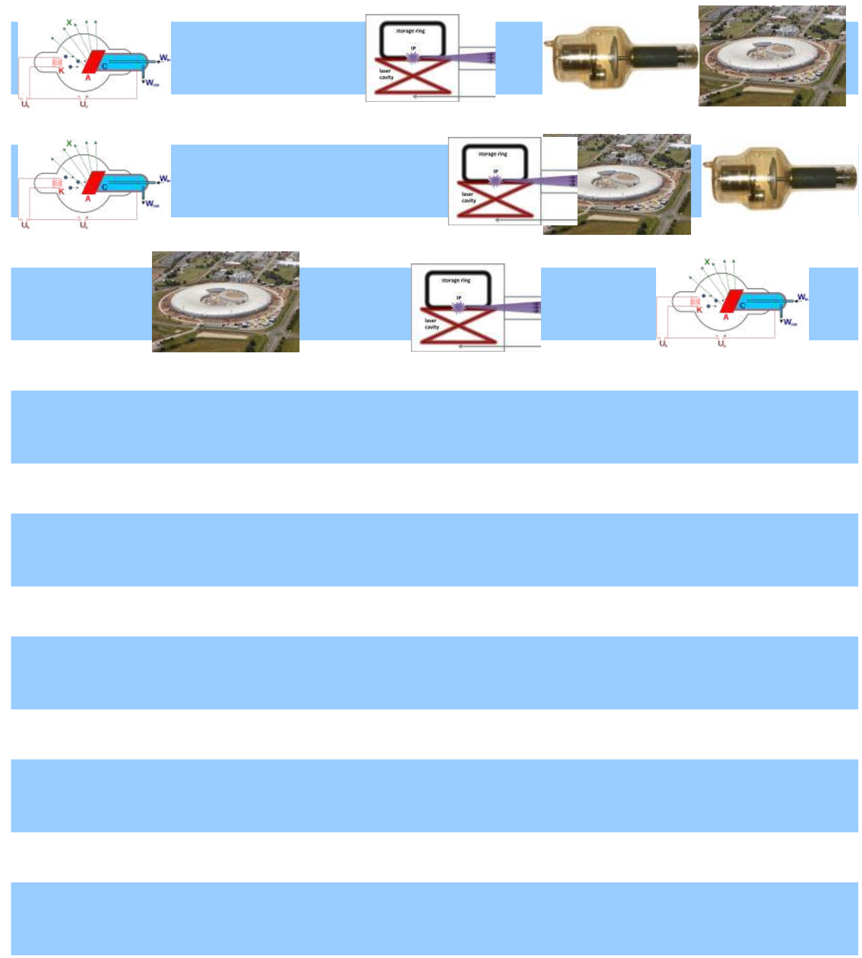
total flux	low		high
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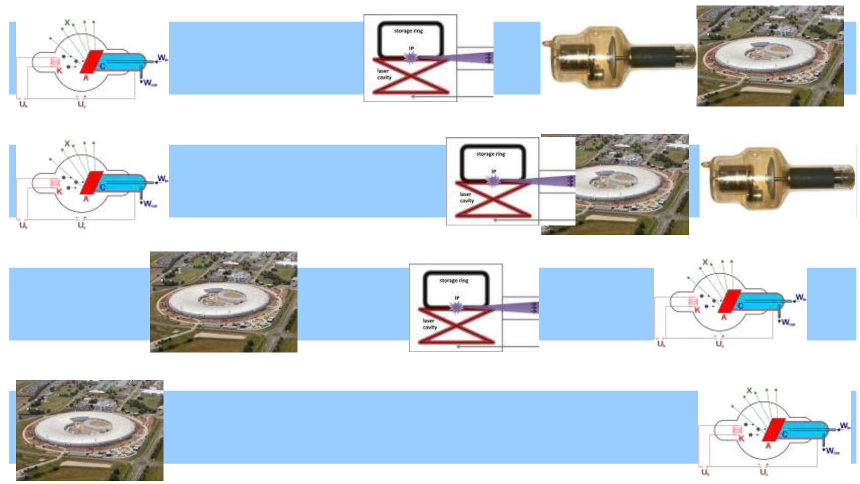

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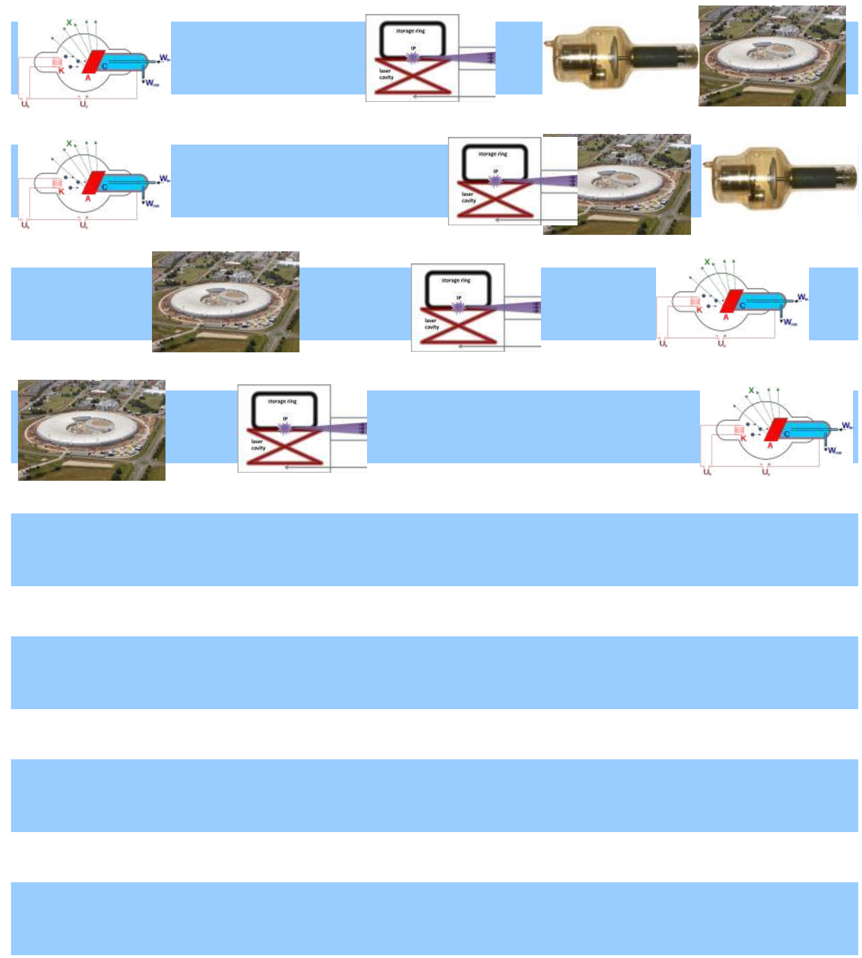

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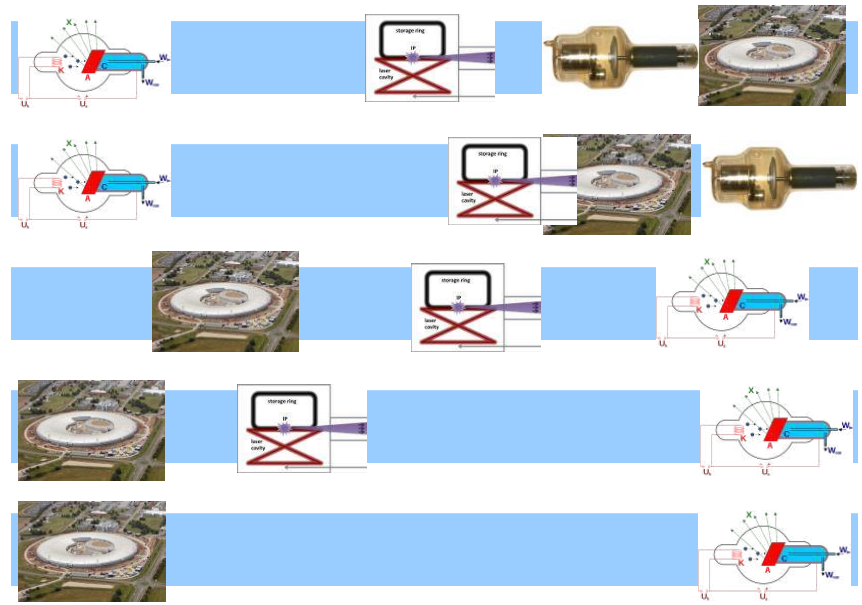

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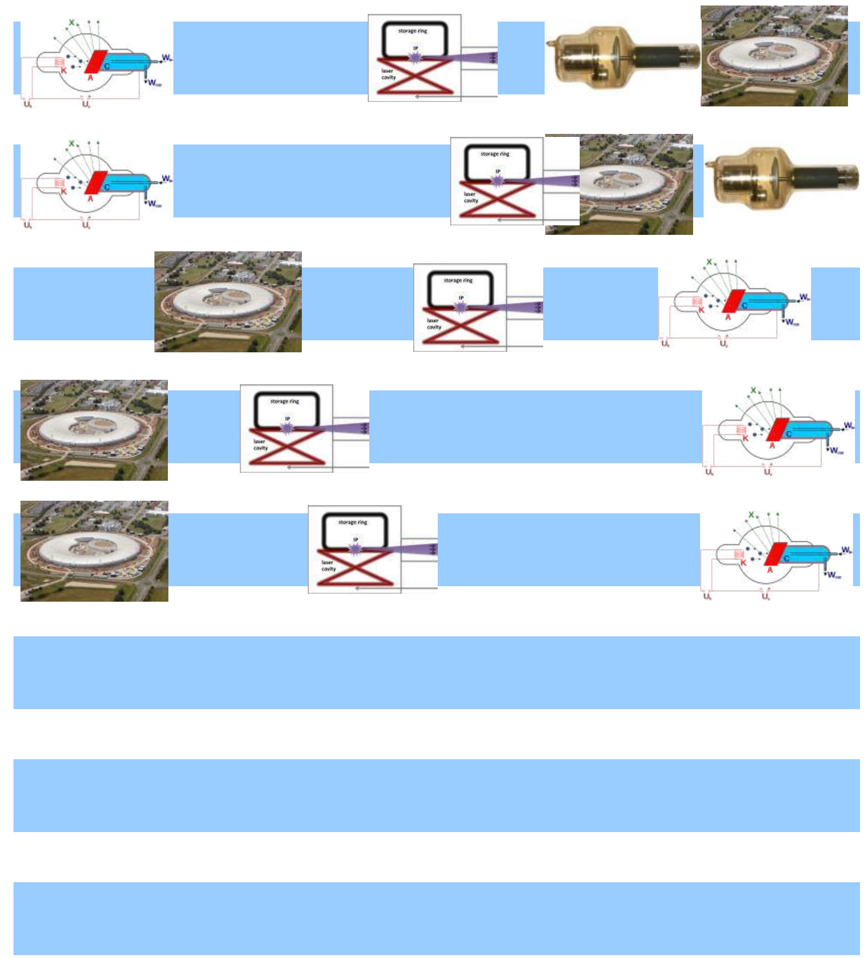

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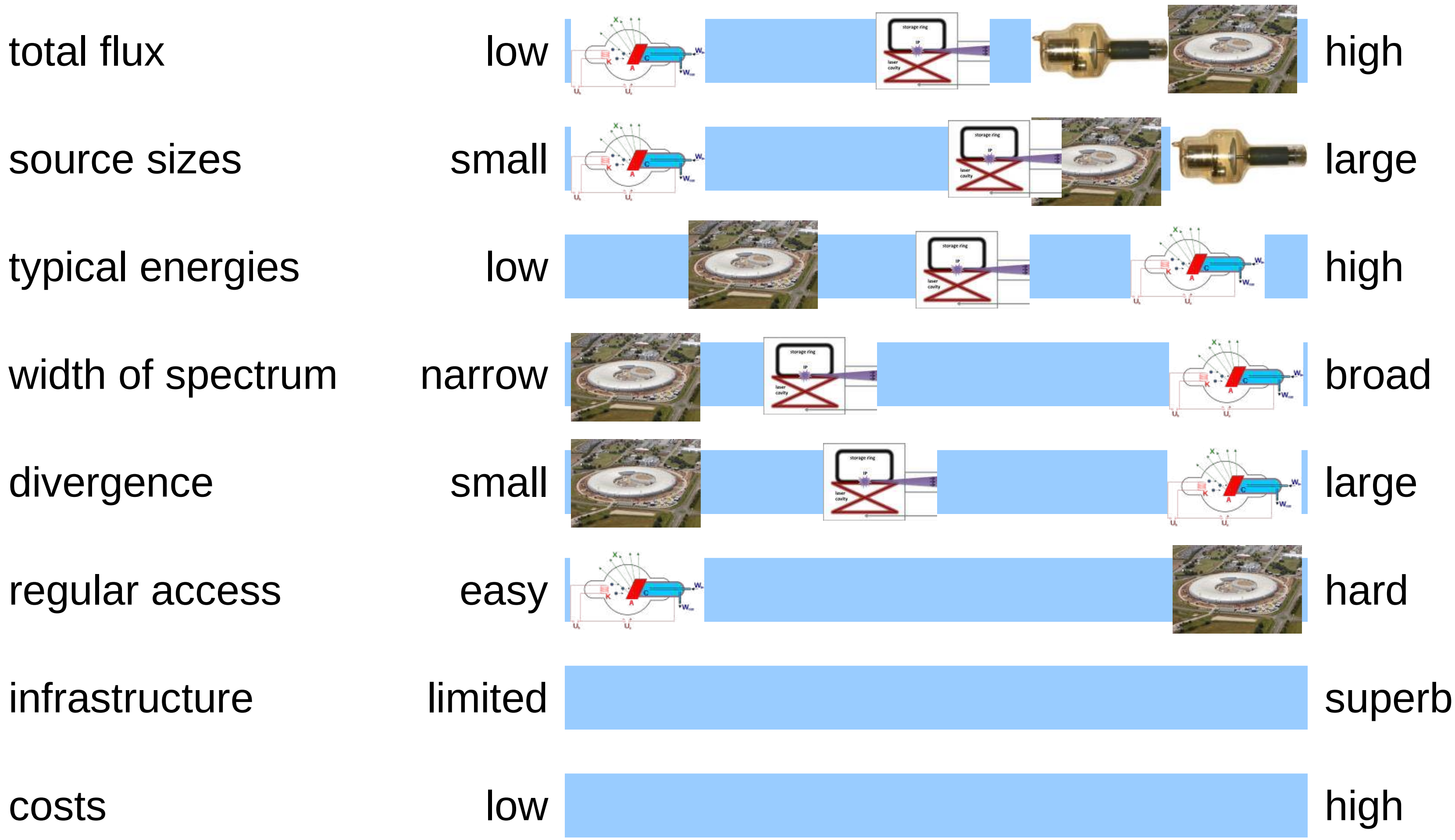

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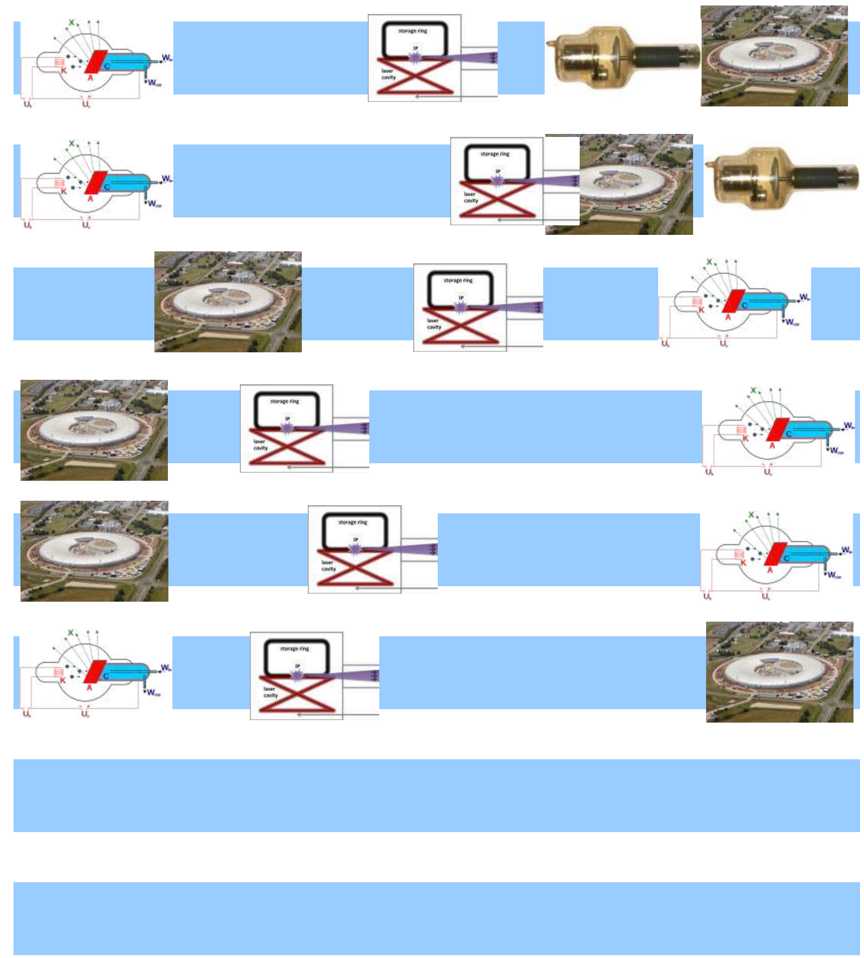

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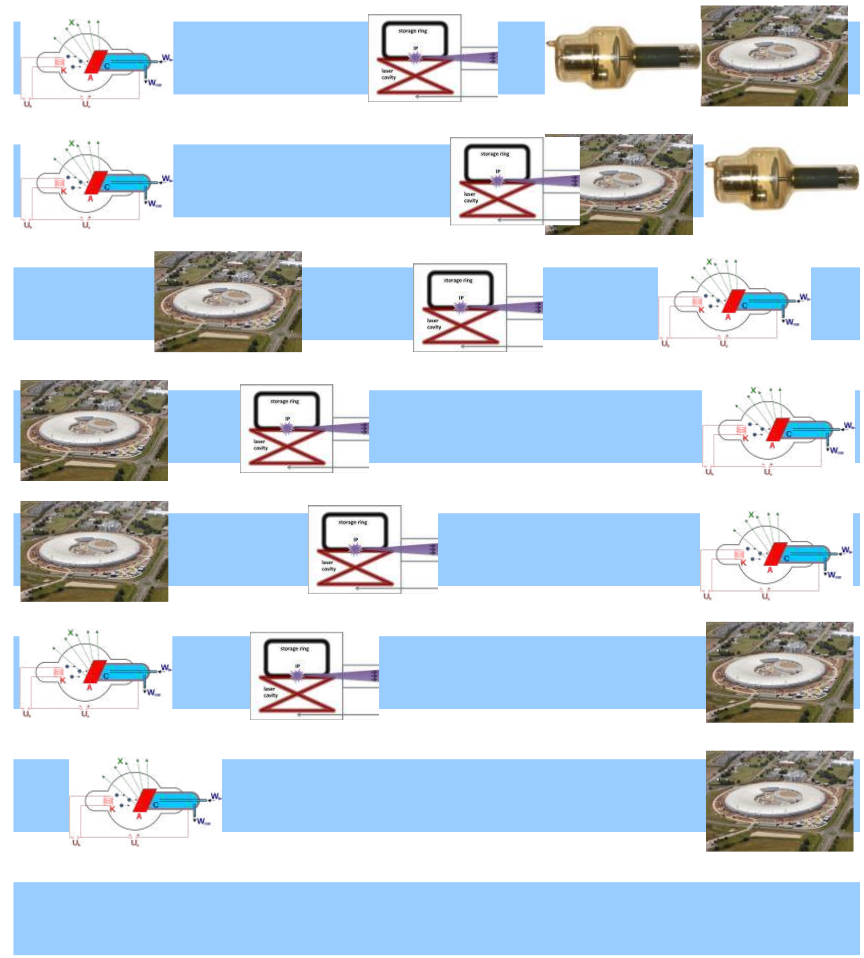

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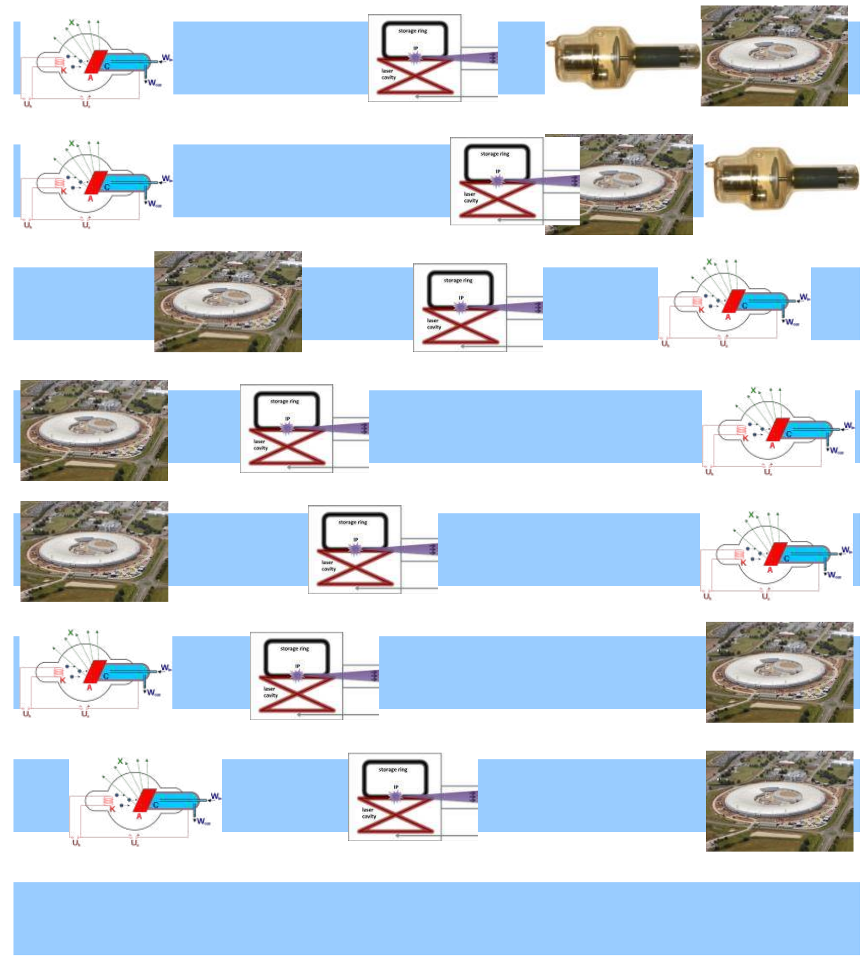

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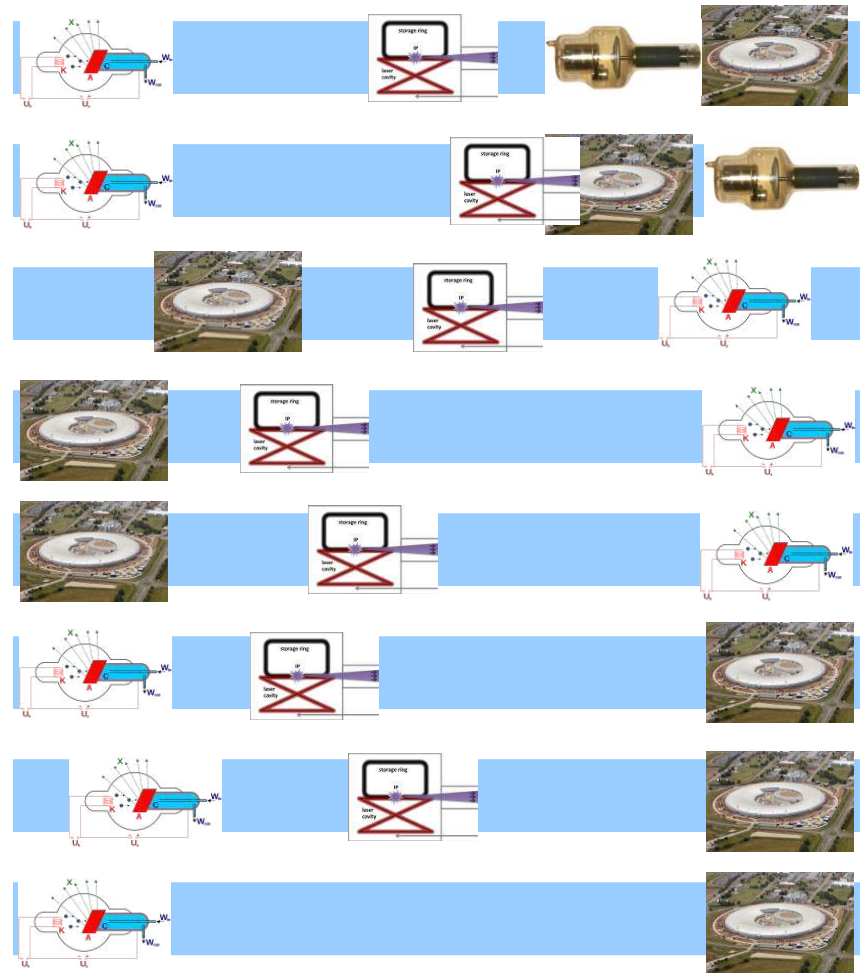

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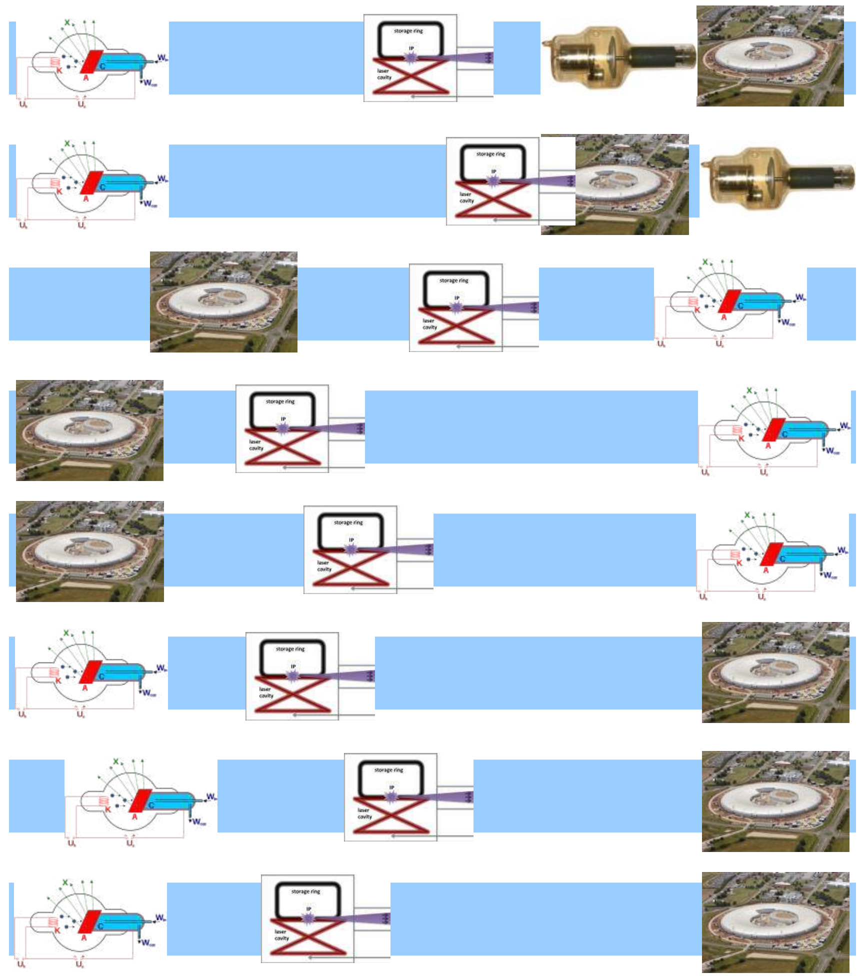

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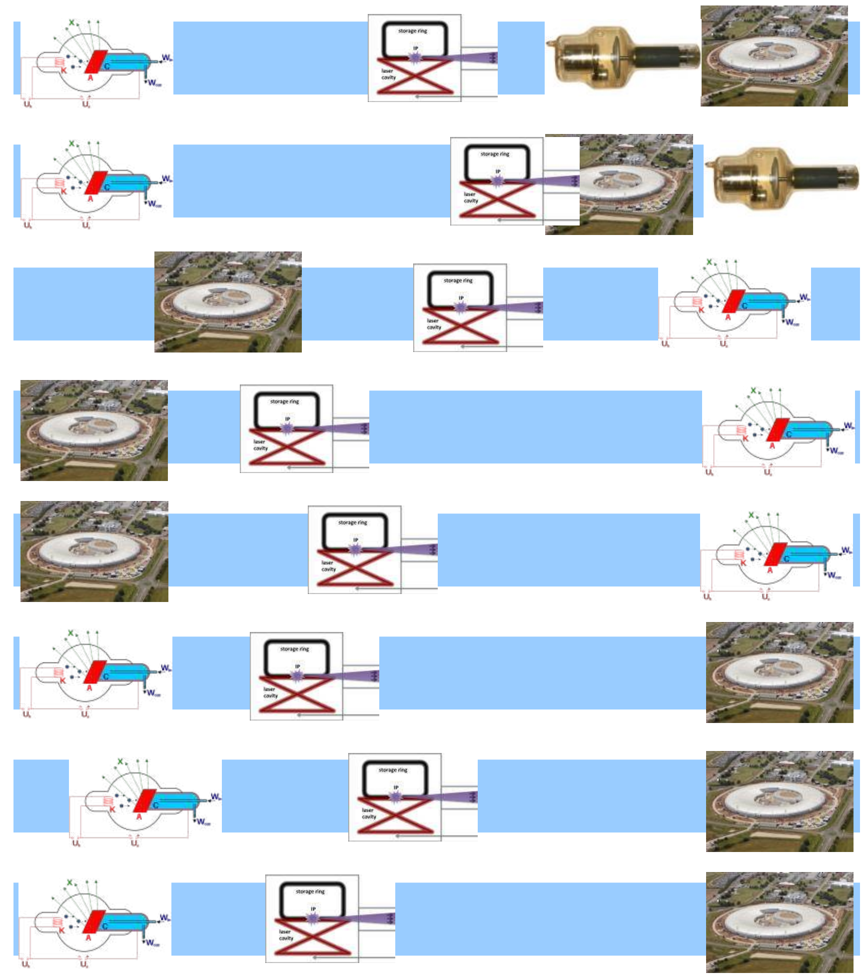

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Experimental infrastructure

two experimental hutches (sharing same beam)

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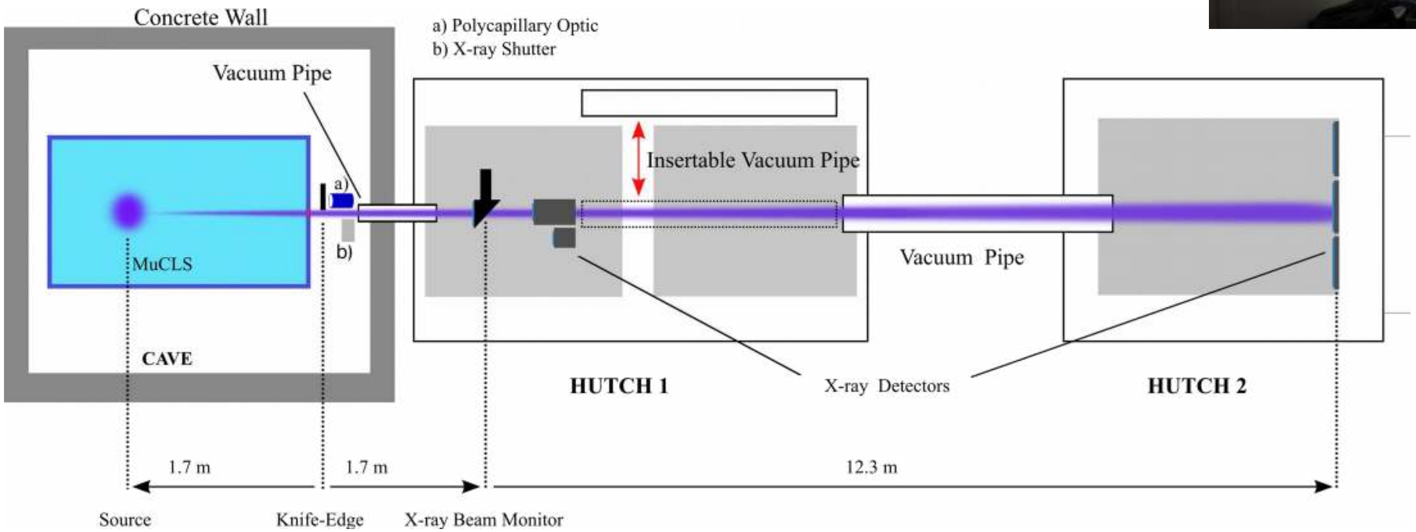

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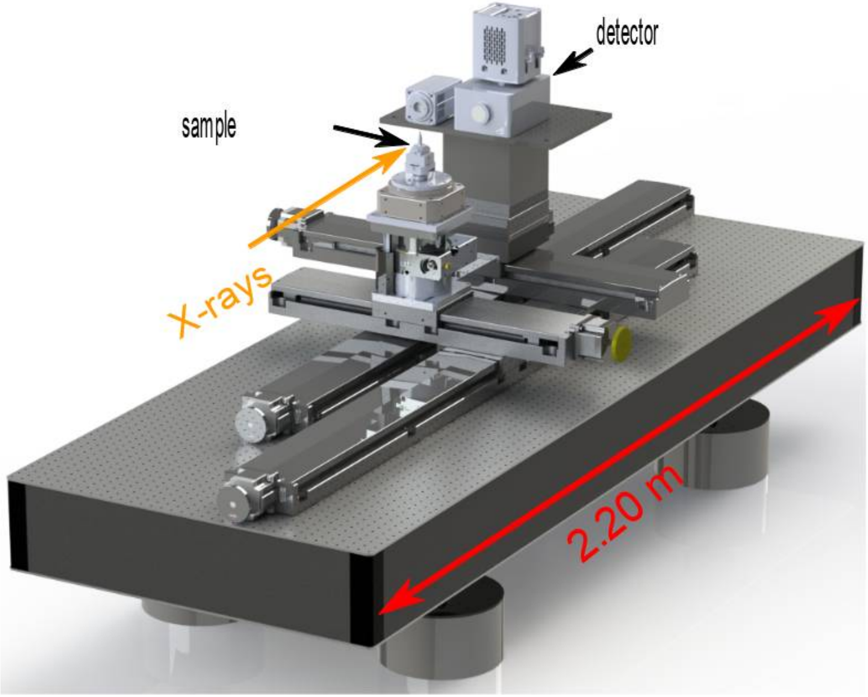
Regine Gradl



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Regine Gradl

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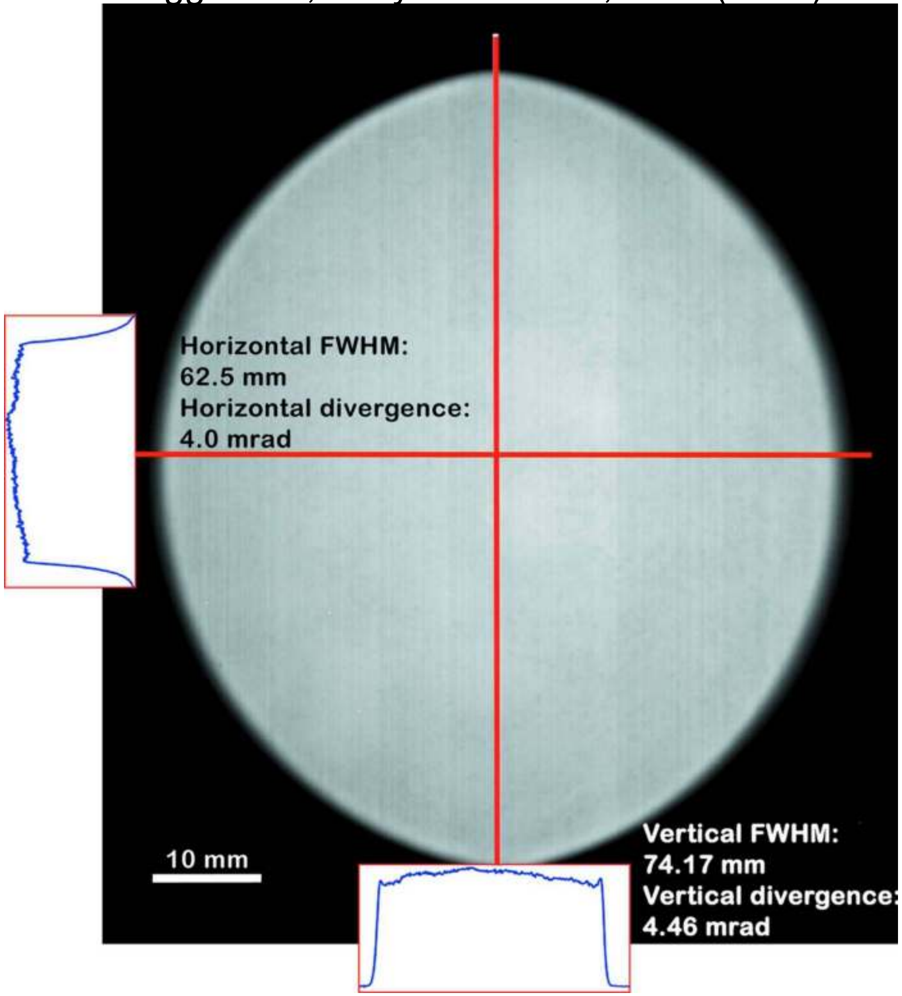
Elena Eggl

Christoph Jud

Eggl et al., J. Sync. Rad. 23, 1137 (2016)



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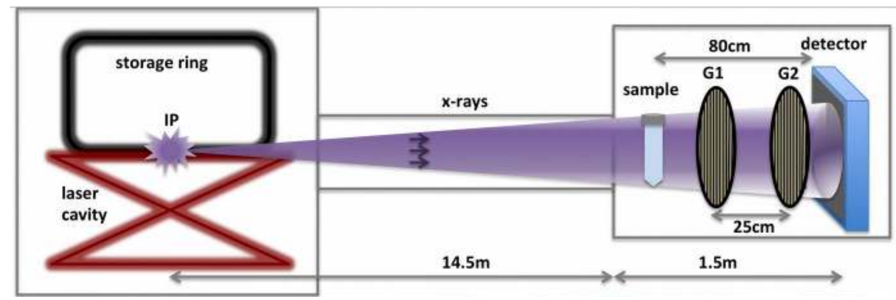

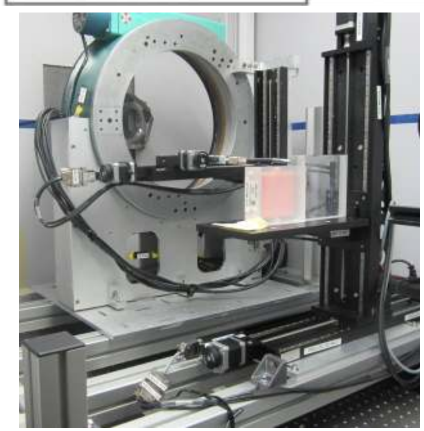

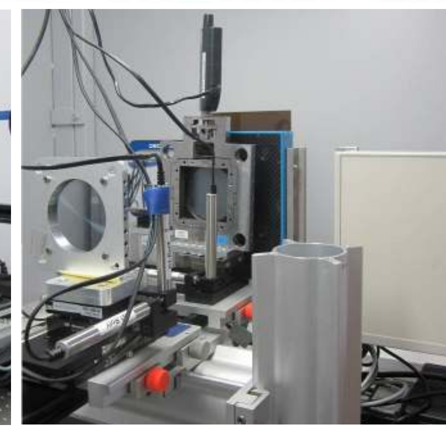

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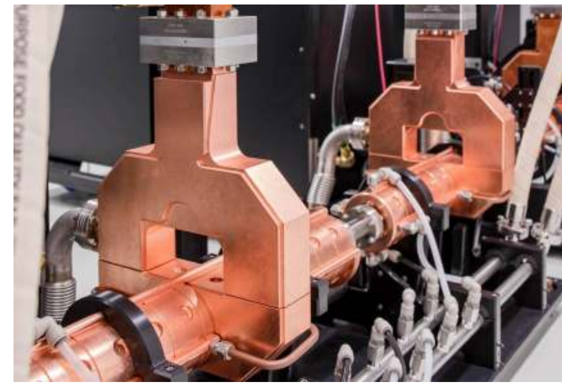
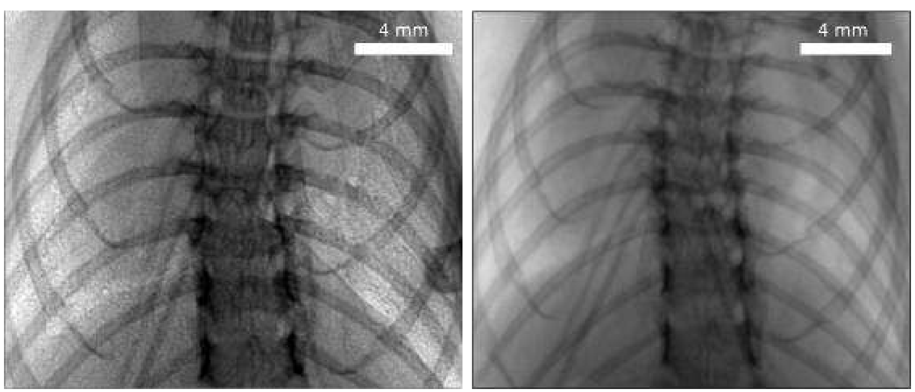
Outline

The MuCLS:
- What is the MuCLS?
- How does it perform?
- How do we operate?





Biomedical research at the MuCLS:
- experimental setups
- **selected applications**

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Respiratory imaging using inline phase contrast

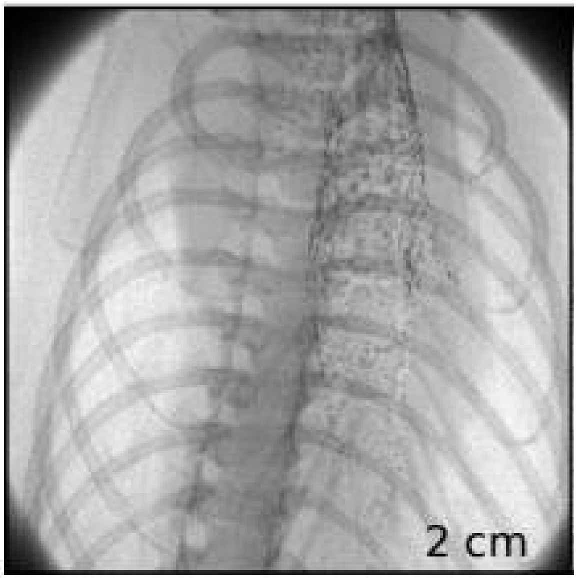
Work by

Regine Gradl

Kaye Morgan

see also Gradl et al., Scientific Reports 7, 4908 (2017)

Respiratory imaging using inline phase contrast



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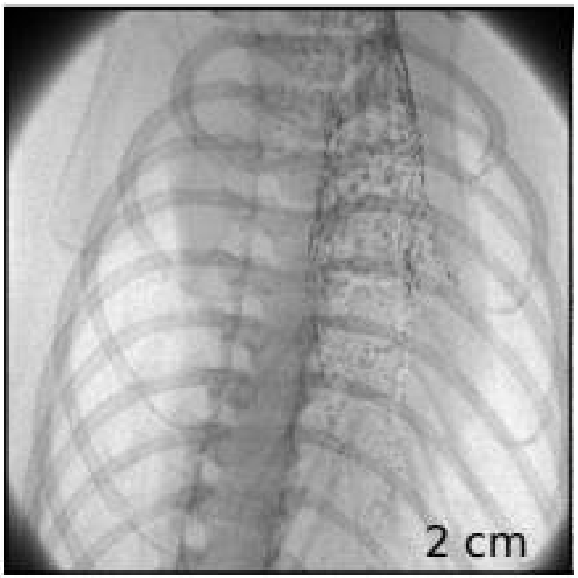

increasing sample-to-detector distance

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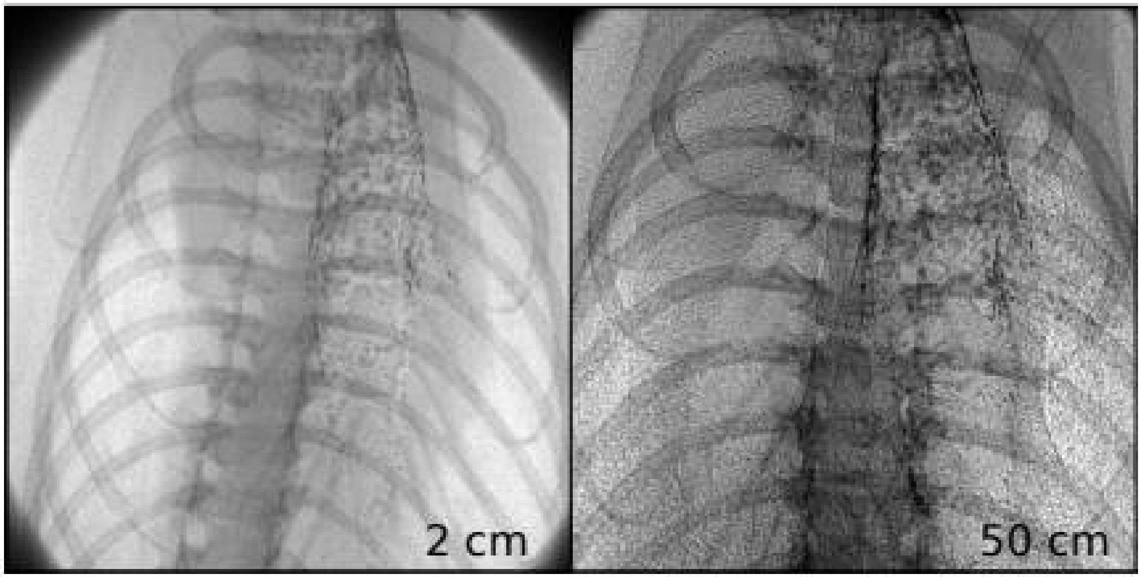

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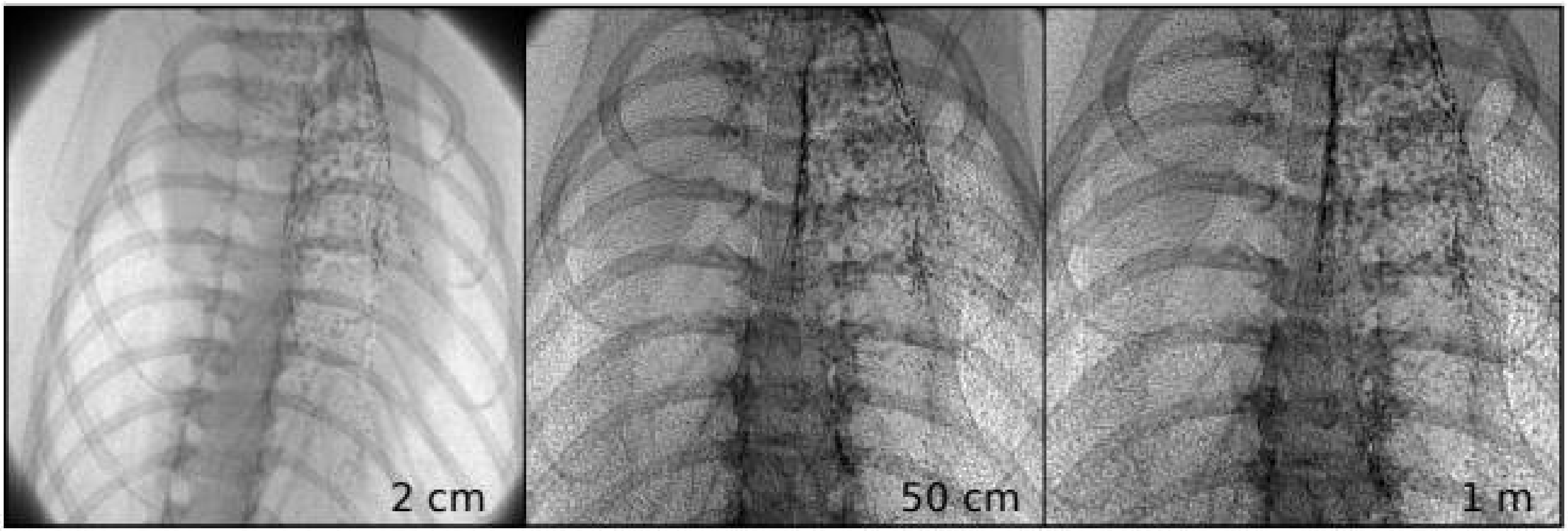

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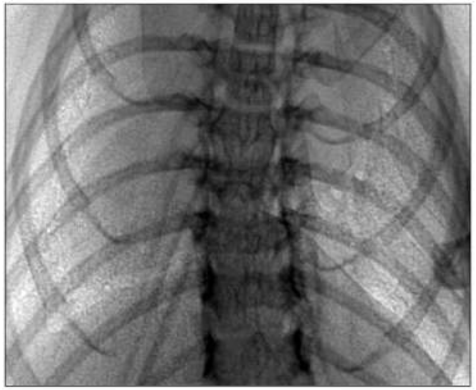
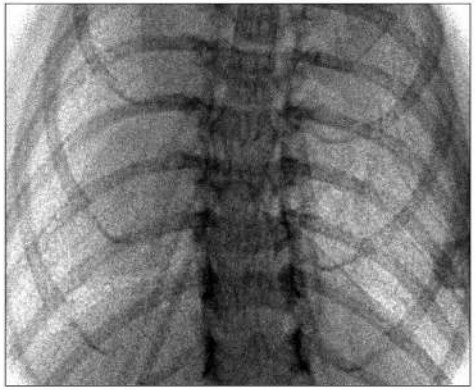
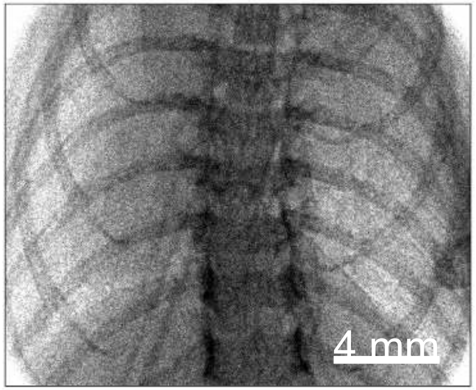
exp. time = 10 s



exp. time = 1 s



exp. time = 0.1 s



exp. time = 0.05 s

Lung imaged with 13 µm detector pixel size and 1.5 m propagation distance

✓ exposure time can be reduced to 0.05 s

Gradl et al., Scientific Reports 7, 4908 (2017)

Respiratory imaging: mucociliary clearance

Work by

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Kaye Morgan

In collaboration with

Women's and Children's Hospital
ADELAIDE

David Parsons, Martin Donnelley

Klinikum rechts der Isar
Technische Universität München

Melanie Kimm, Helena Haas, Nathalie Roiser

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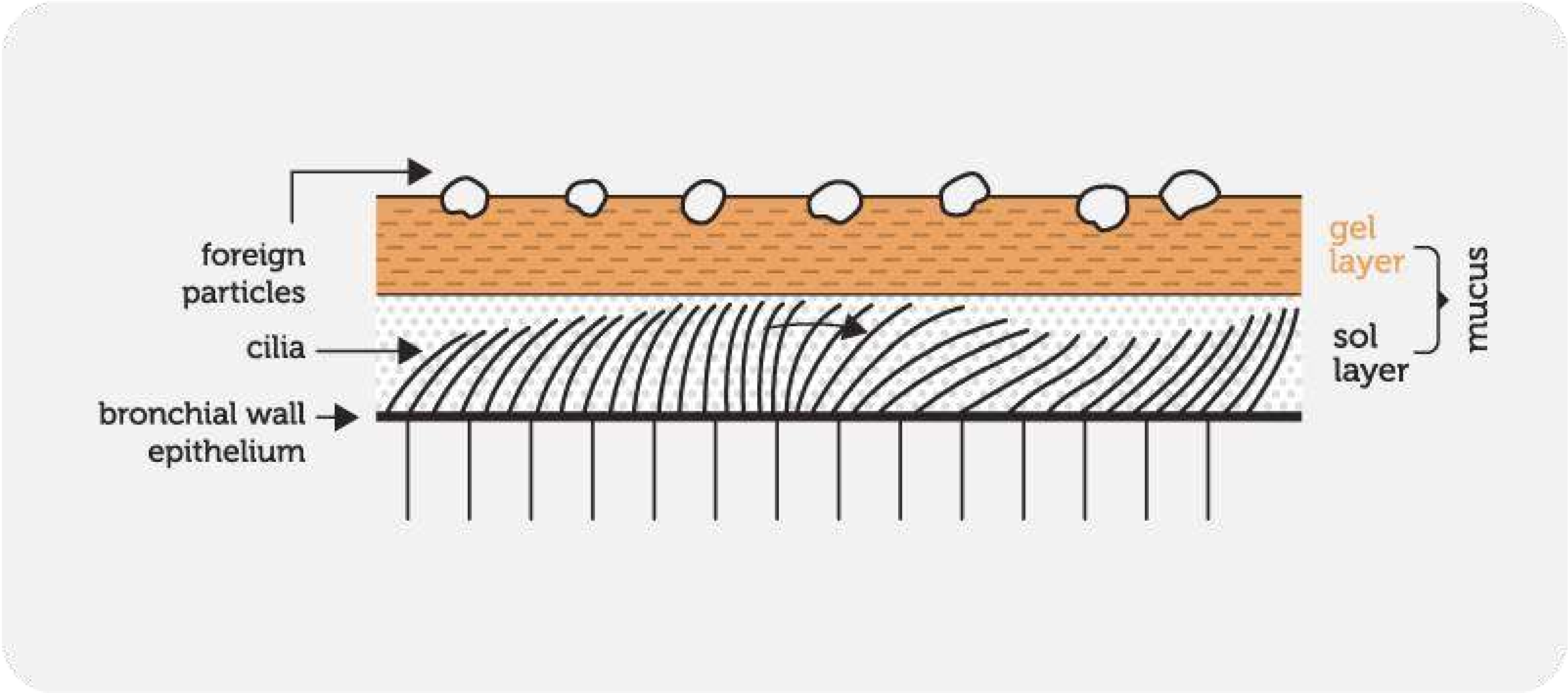

http://bronchiectasis.com.au/physiotherapy/principles-of-airway-clearance/airway-clearance-in-the-normal-lung

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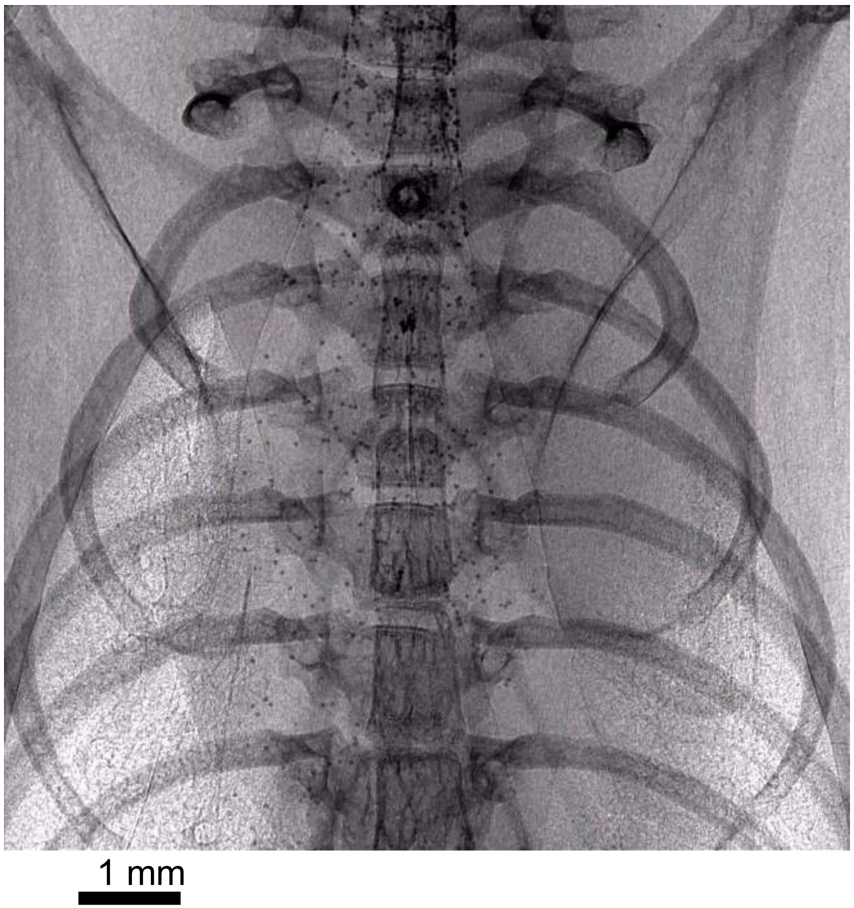
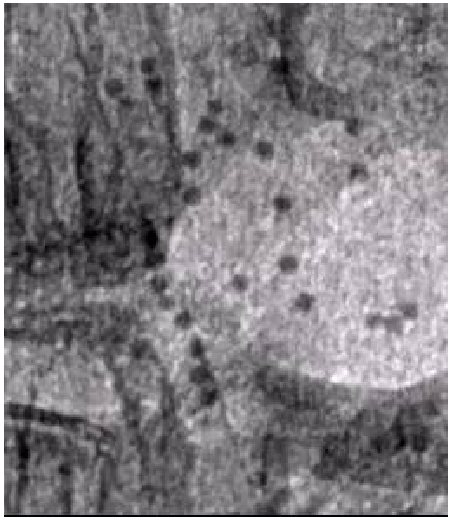


75 um glass beads to mimic inhaled debris

hypertonic saline nebulisation



Gradl et al., to be submitted

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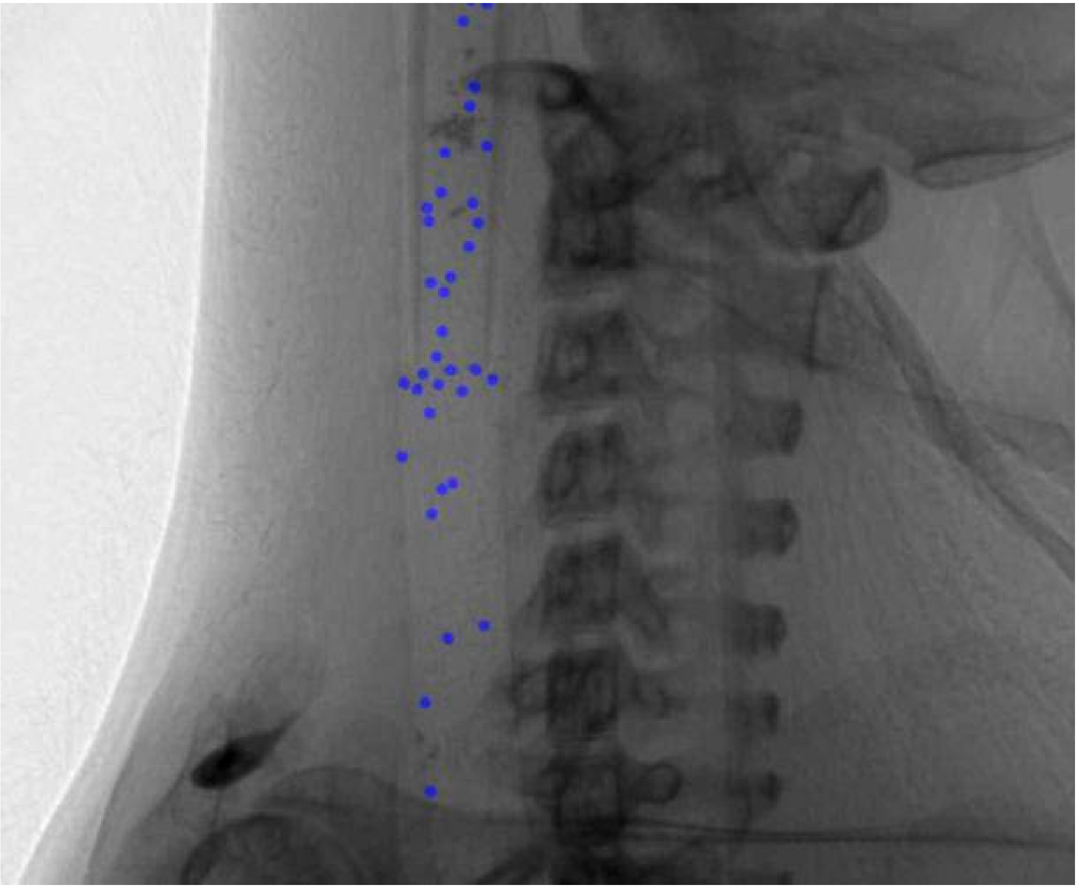

tracking analysis:
Martin Donnelley,
WCH Adelaide

Gradl et al., Scientific Reports 8, 6788 (2018)

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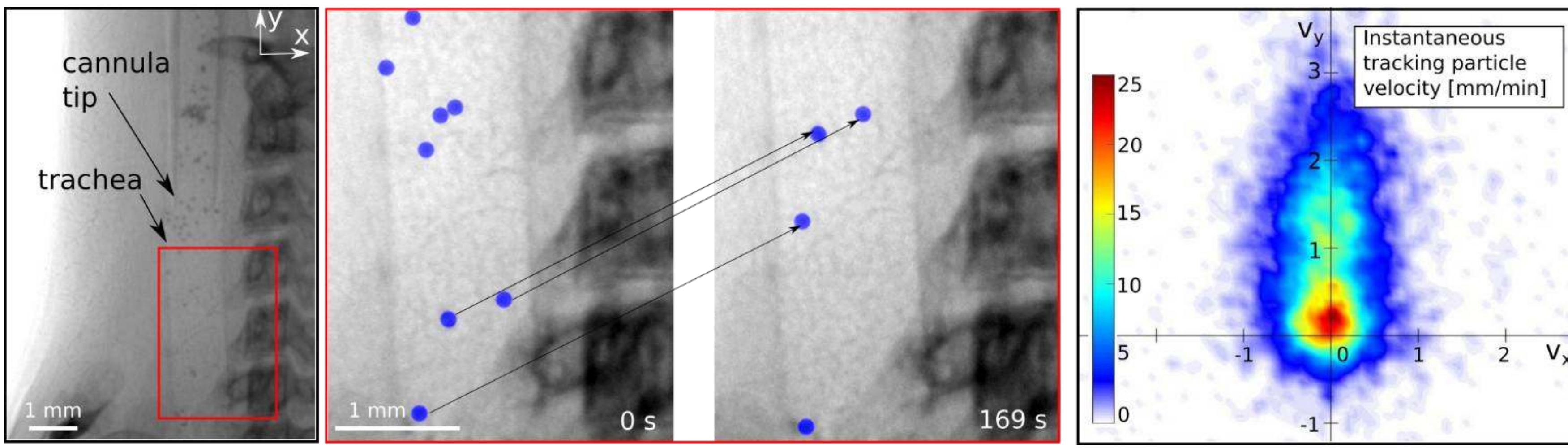

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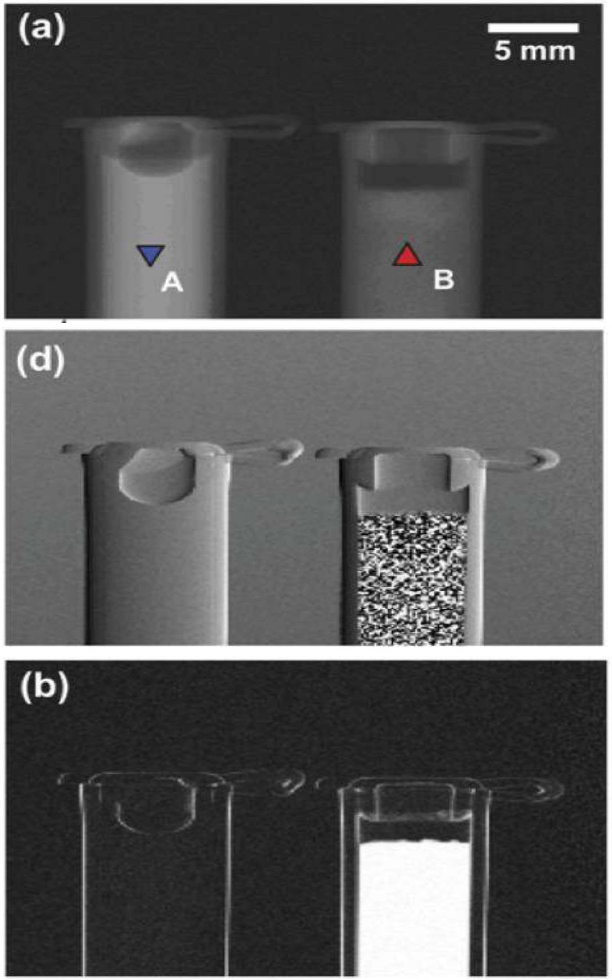
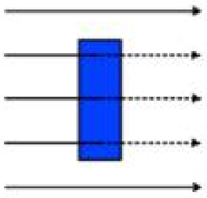
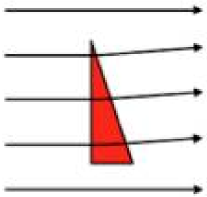
Grating-based imaging: bone anisotropy

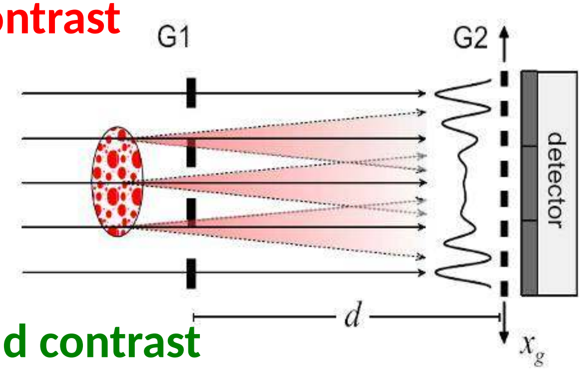




Absorption contrast



Phase contrast



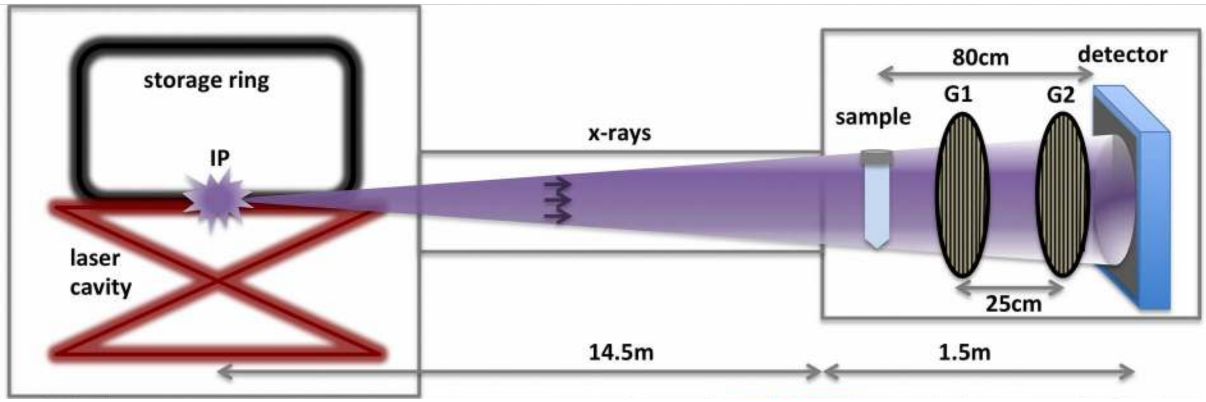
Dark-field contrast

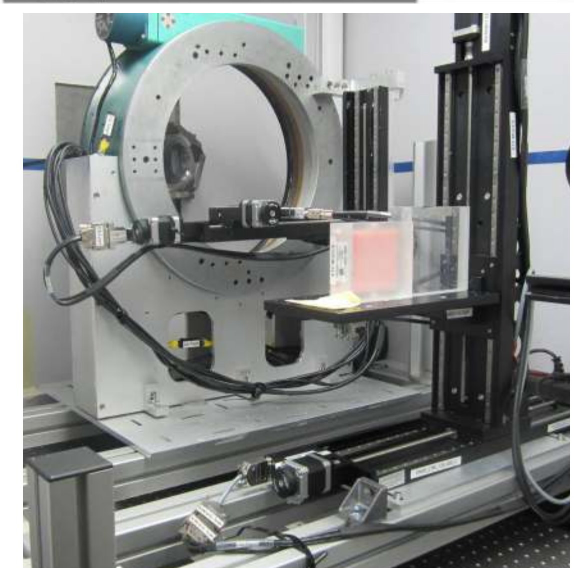
Grating-based imaging: bone anisotropy

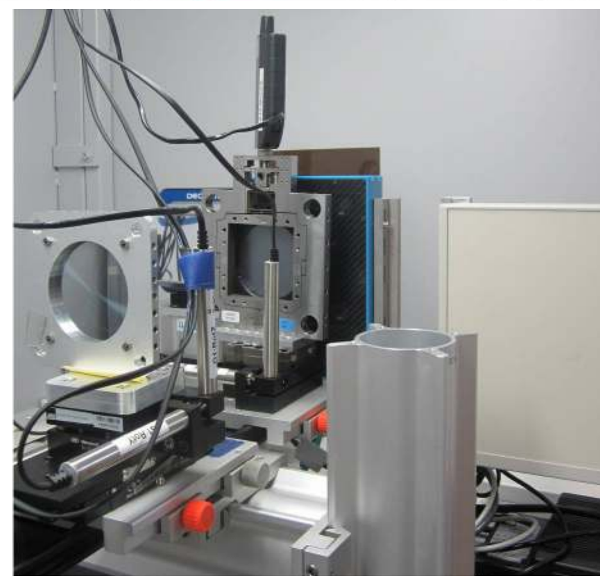
Work by

Christoph Jud

Grating-based imaging: bone anisotropy







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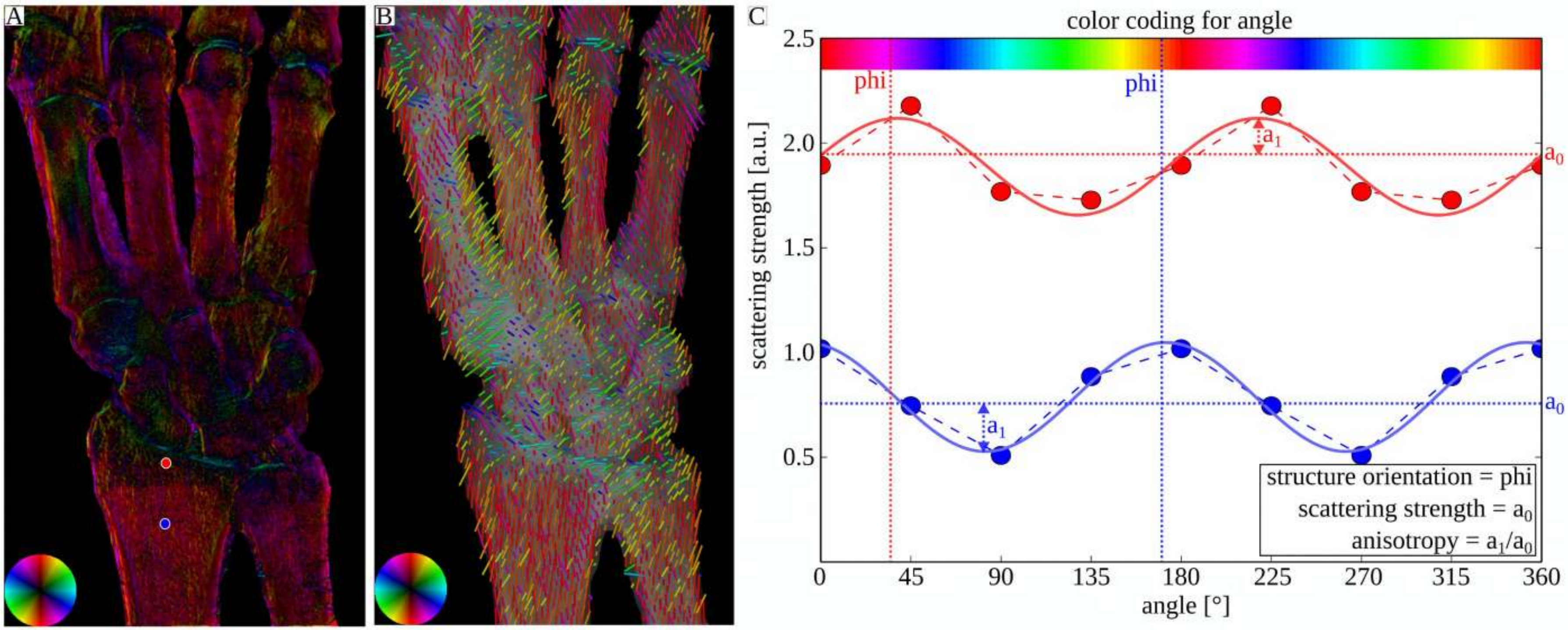

Work by

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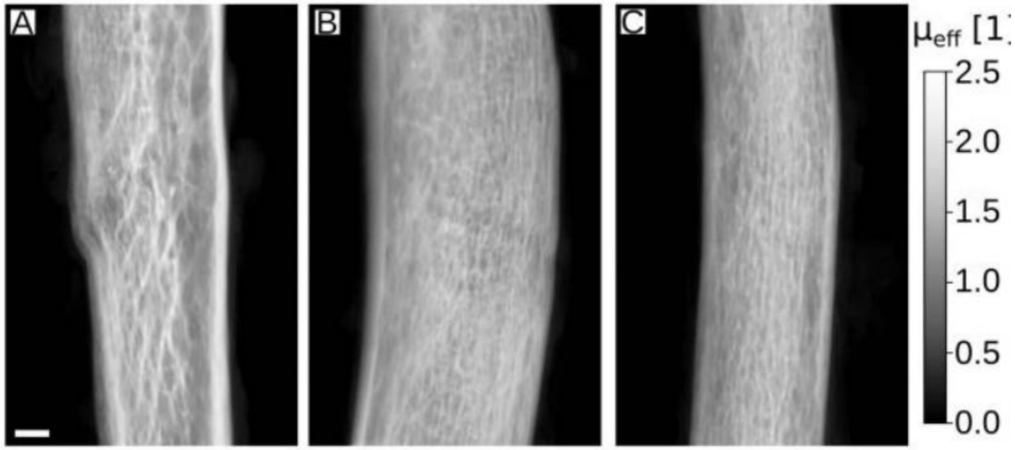
gratings → detect preferential direction of scattering

Jud et al., Scientific Reports 7, 6788 (2017)

Grating-based imaging: bone anisotropy

detection of radiographically occult fractures in an ex-vivo porcine rib model



Work by

Christoph Jud

Jud et al., submitted

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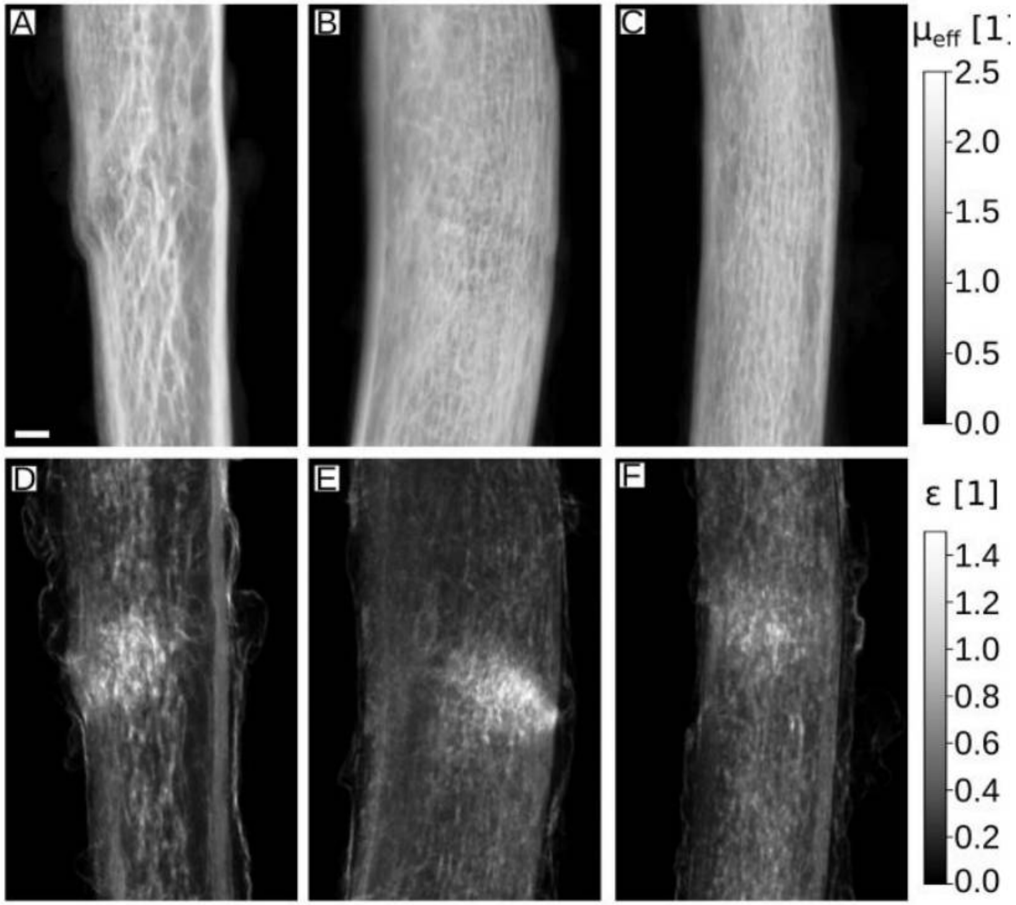

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Work by

Christoph Jud

Mammography @ MuCLS

Work by

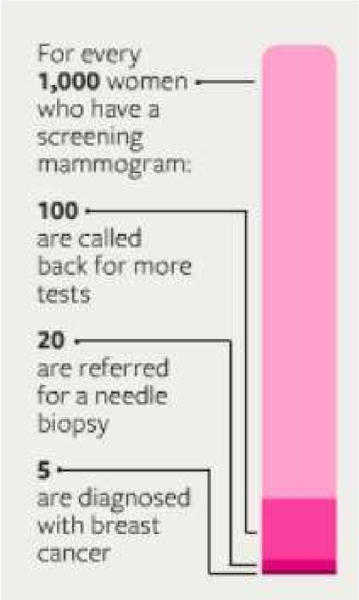

Elena Eggl


Lisa Heck


Julia Herzen

Mammography @ MuCLS – motivation

- Breast cancer screening: Mammography
  - low soft-tissue contrast
  - dose sensitivity
  - false-positives → unnecessary invasive procedures



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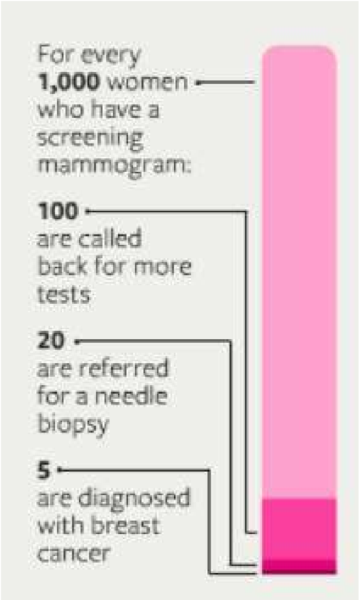

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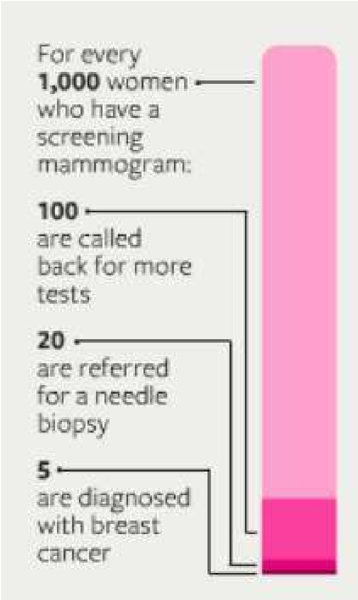

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@ MuCLS:
combine advantages
& avoid disadvantages

Work by


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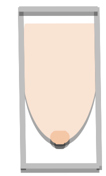
Mammography @ MuCLS – study design

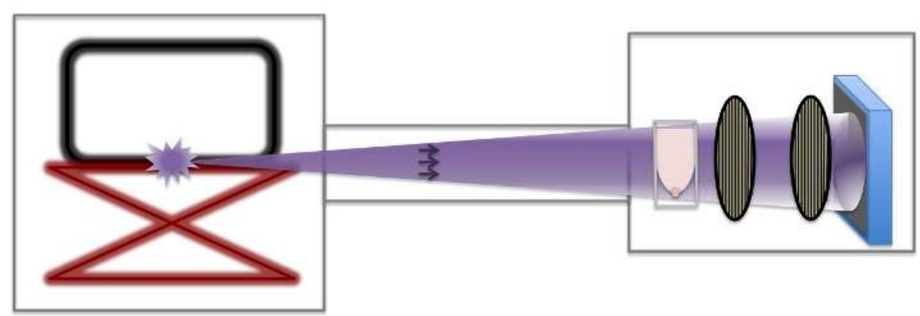
Goal: dose-compatible grating-based mammography at the MuCLS

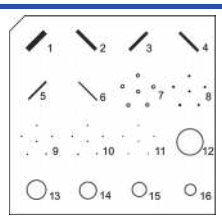
mammography → positive diagnosis
→ mastectomy → fix in sample holder



Compare ex-vivo mammography

Clinical vs. MuCLS

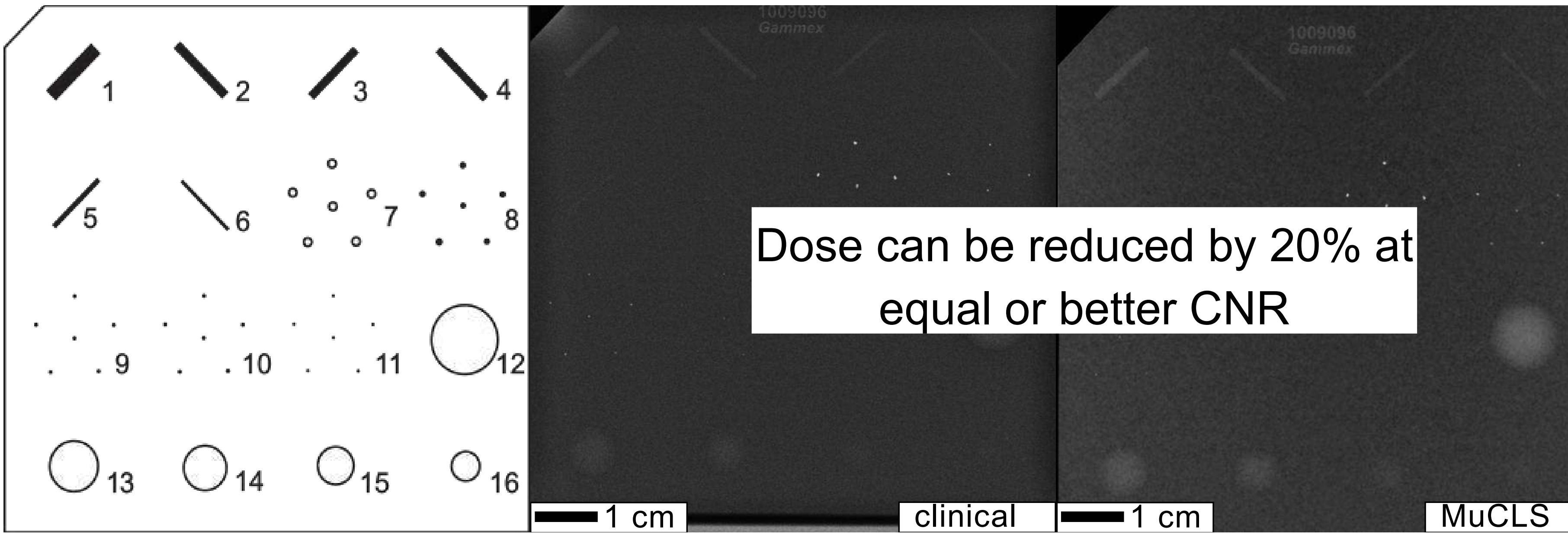




Quantitative analysis for a mammographic accreditation phantom (contrast-to-noise ratio analysis)

Mammography @ MuCLS – results

Gammex phantom | Clinical, 2 mGy | MuCLS, 2 mGy



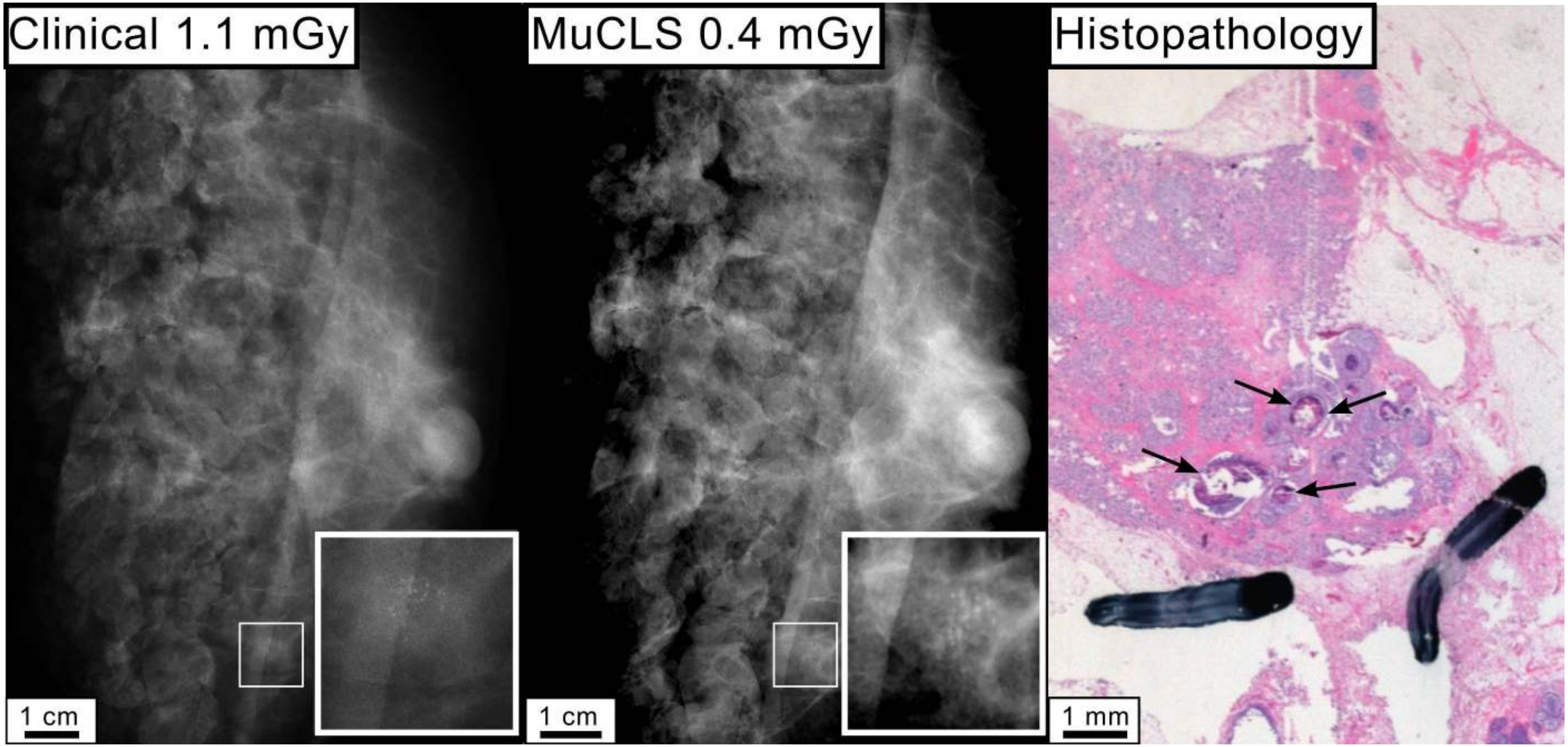
Dose can be reduced by 20% at equal or better CNR

ACR requires to resolve
4 fibrils
3 groups of microcalcifications
3 tumor masses

MuCLS vs. Clinical (equal dose):
Fibrils: CNR +88%
Calc.: CNR +20%
Masses: CNR +106%

Eggl et al., Scientific Reports 8, 15700 (2018)

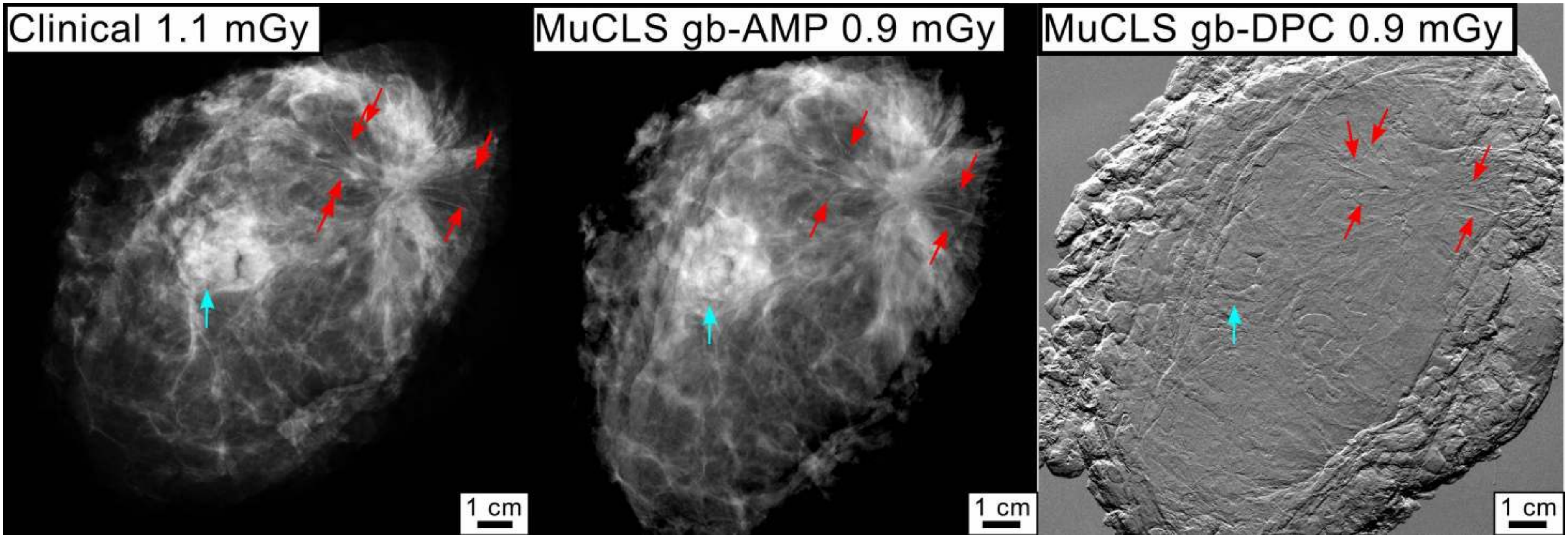
Mammography @ MuCLS – results



Equal detection of microcalcifications at reduced dose

Eggl et al., Scientific Reports 8, 15700 (2018)

Mammography @ MuCLS – results



Improved delineation of tumorous lesions in DPC image

Eggl et al., Scientific Reports 8, 15700 (2018)

Applications exploit source properties of MuCLS

narrow tunable spectrum
- CT without beam hardening
- K-edge imaging / angiography
- spectroscopy

low divergence / high flux density
- radiation therapy studies
- fast (dynamical) imaging
- high-resolution imaging

partial coherence
- propagation-based phase contrast
- grating-based phase contrast (2 gratings only)

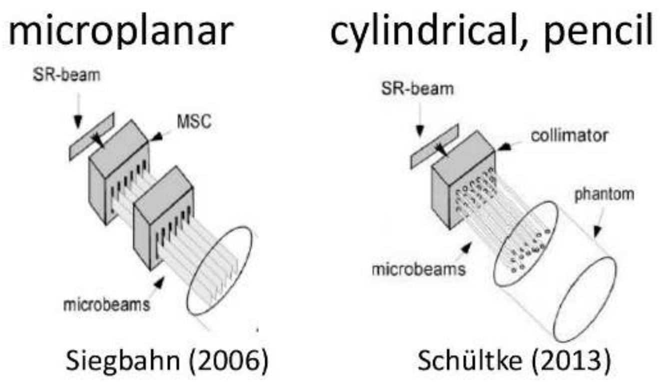
Microbeam radiation therapy studies

work by
Karin Burger

Microbeam radiation therapy studies

General idea:

irradiation with small beamlets (<100 µm)
instead of broad beams
→ spare skin / heathly tissue area
→ improved recovery of irradiated healthy tissue



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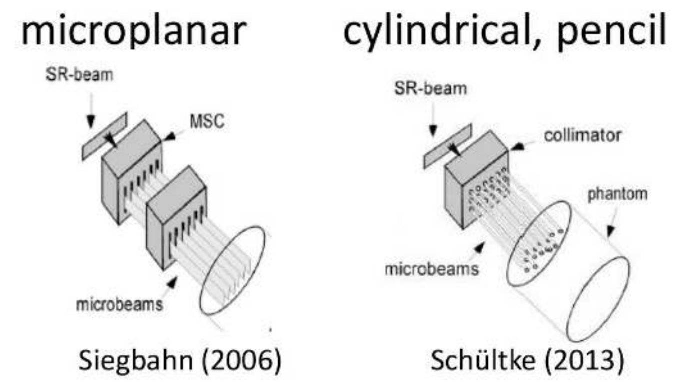

Technical requirements:
high dose rates & small beam divergences
→ mainly limited to synchrotron radiation so far

→ investigate at Munich Compact Light source
- in-vitro cell studies
- in-vivo small-animal tumor models

work by
Karin Burger

Microbeam radiation therapy studies

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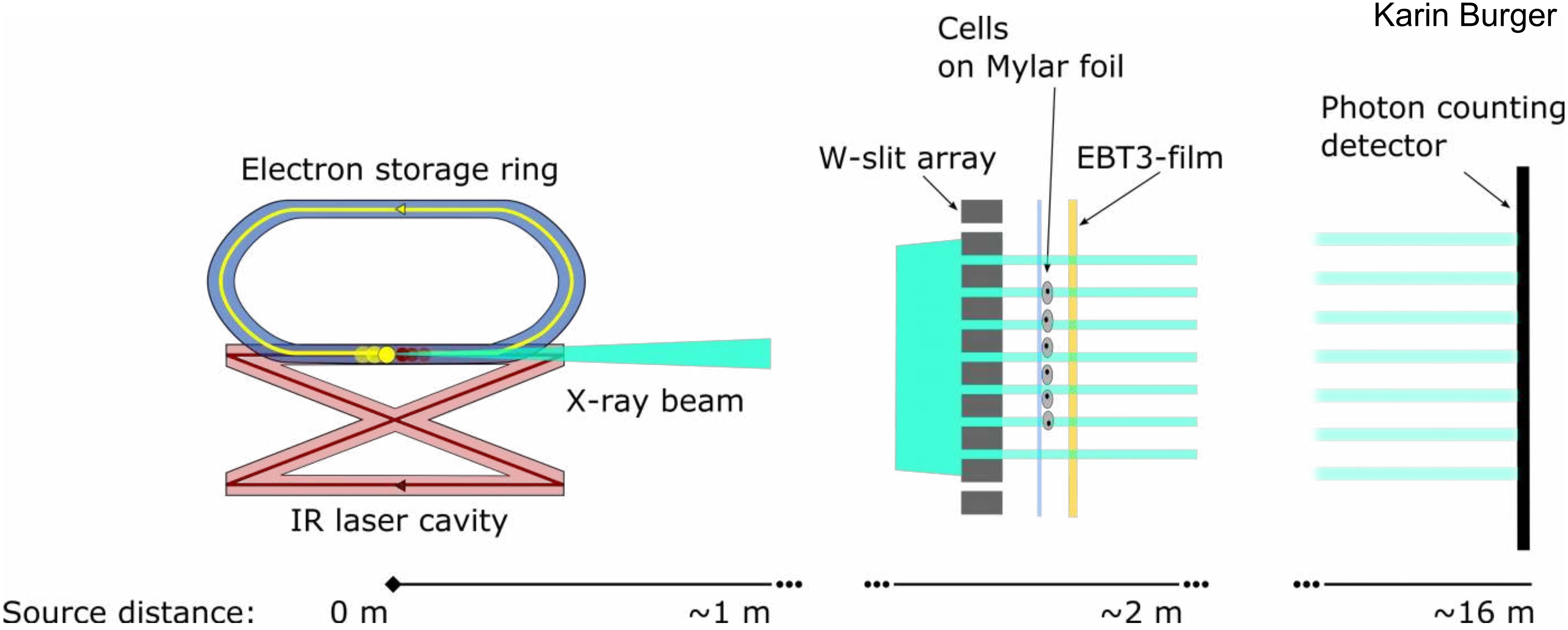
Experimental setup



Burger et al., PLoS ONE 12, e0186005 (2017)

Microbeam radiation therapy studies

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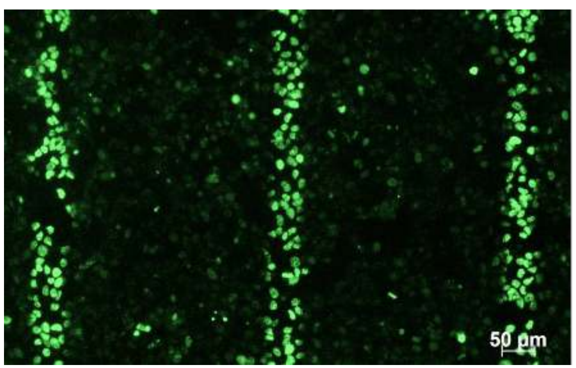
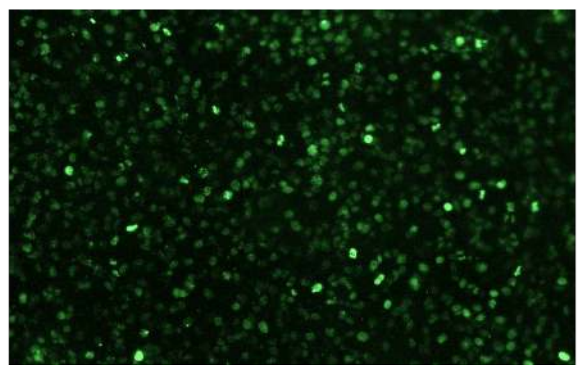
gamma-H2AX staining of DNA double-strand breaks in HeLa cells

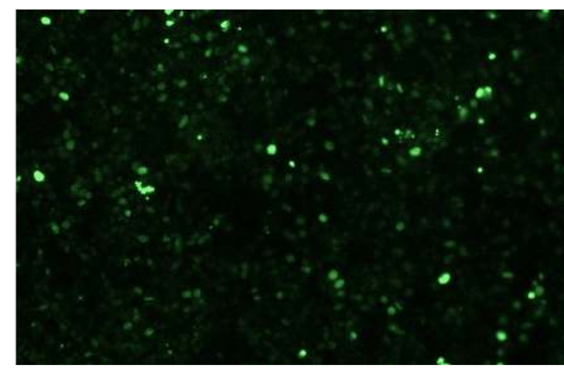
2 Gy mean (~14 Gy peak)



2 Gy mean homogenous



not irradiated



→ MuCLS provides required beam parameters

Burger et al., PLoS ONE 12, e0186005 (2017)

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Coronary angiography at MuCLS

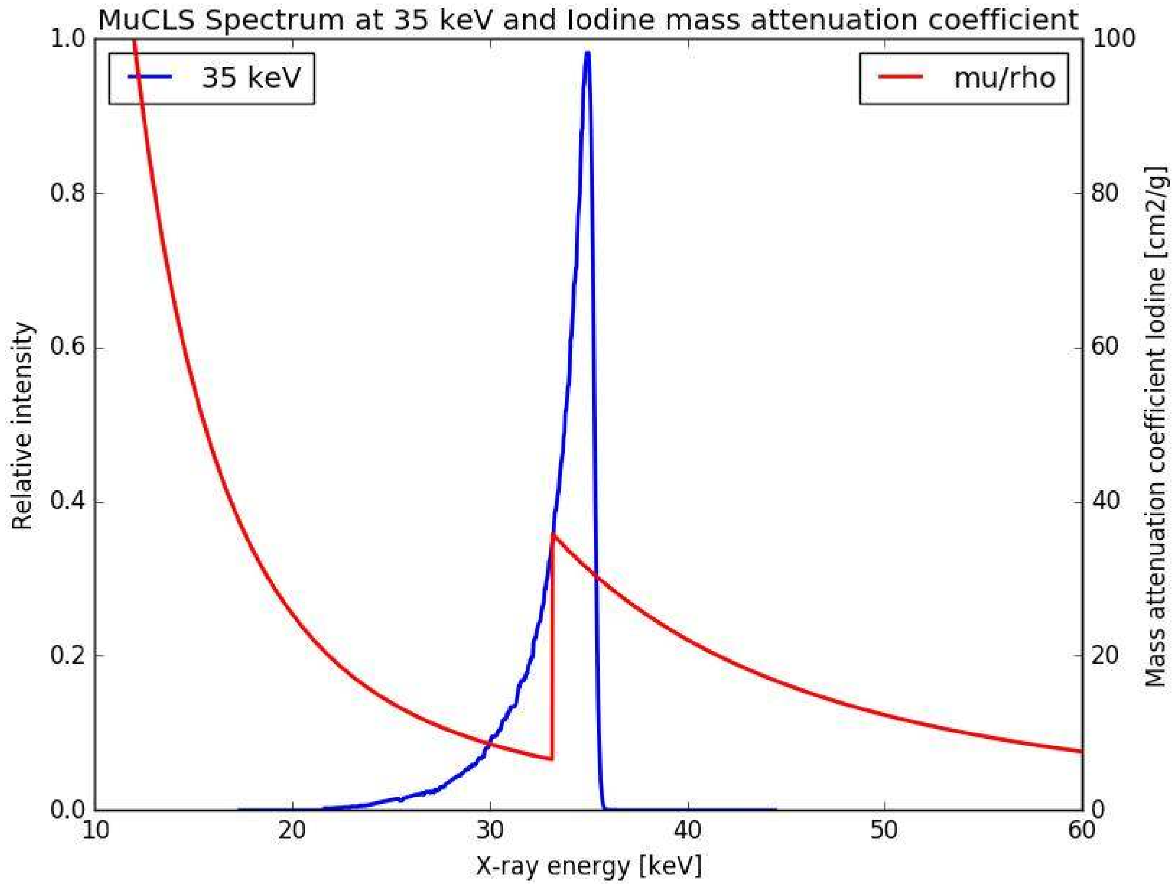
Work by


Elena Eggl


Stephanie Kulpe

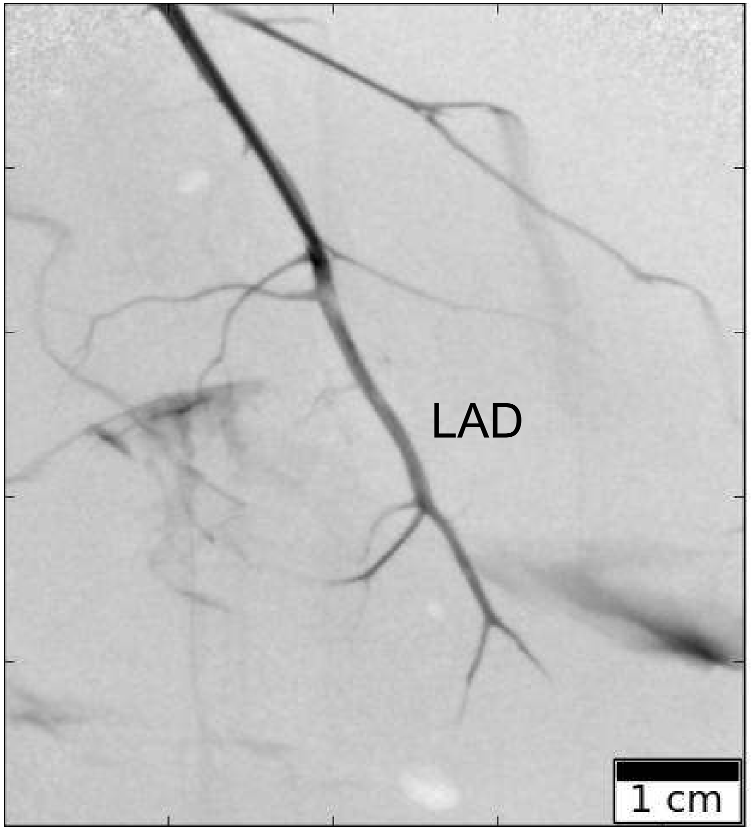

Daniela Pfeiffer

Coronary angiography at MuCLS



Eggl et al., Scientific Reports 7, 42211 (2017)

Coronary angiography of a pig heart



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One step further: K-edge subtraction imaging

Work by

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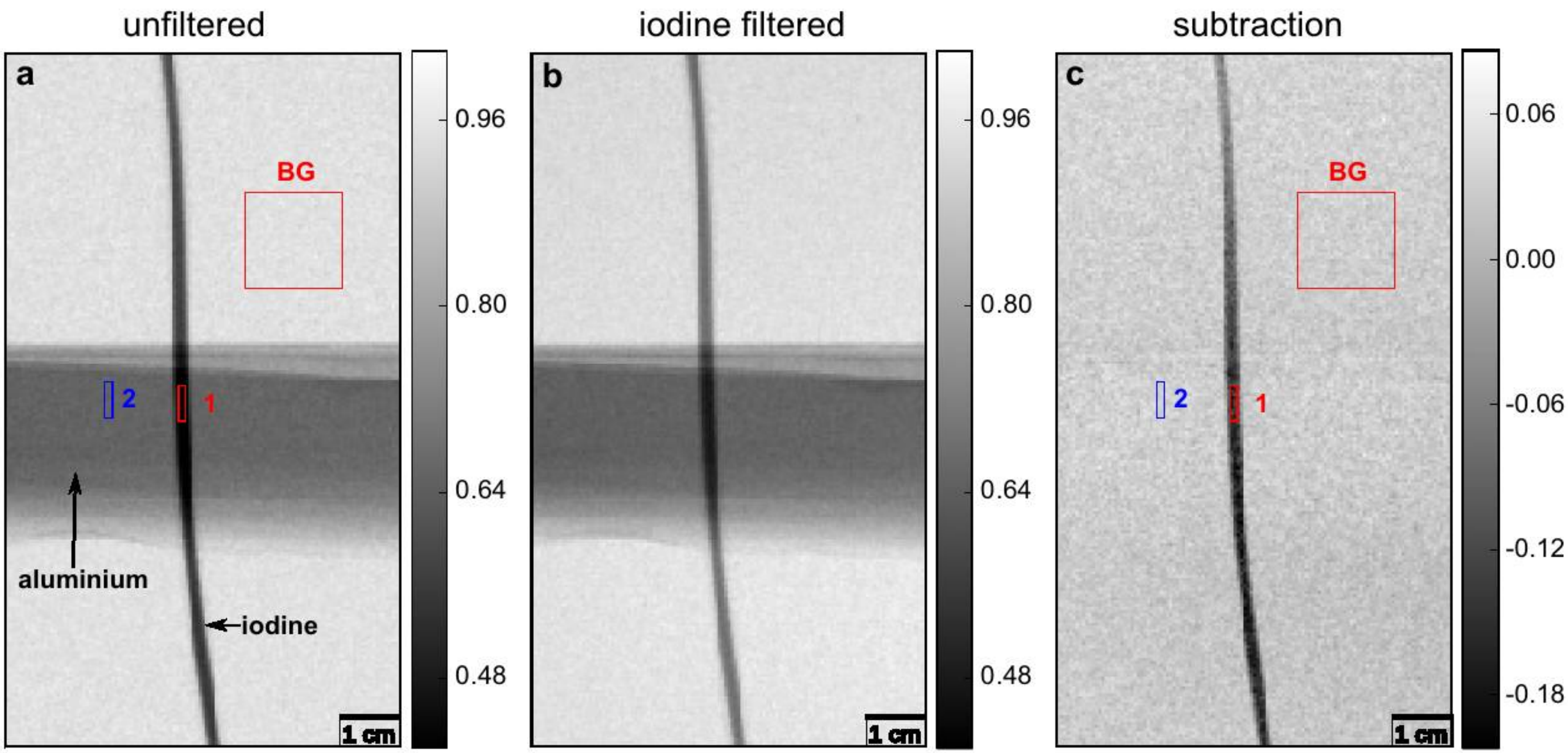

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Kulpe et al., PloS ONE 13, e0208446 (2018)

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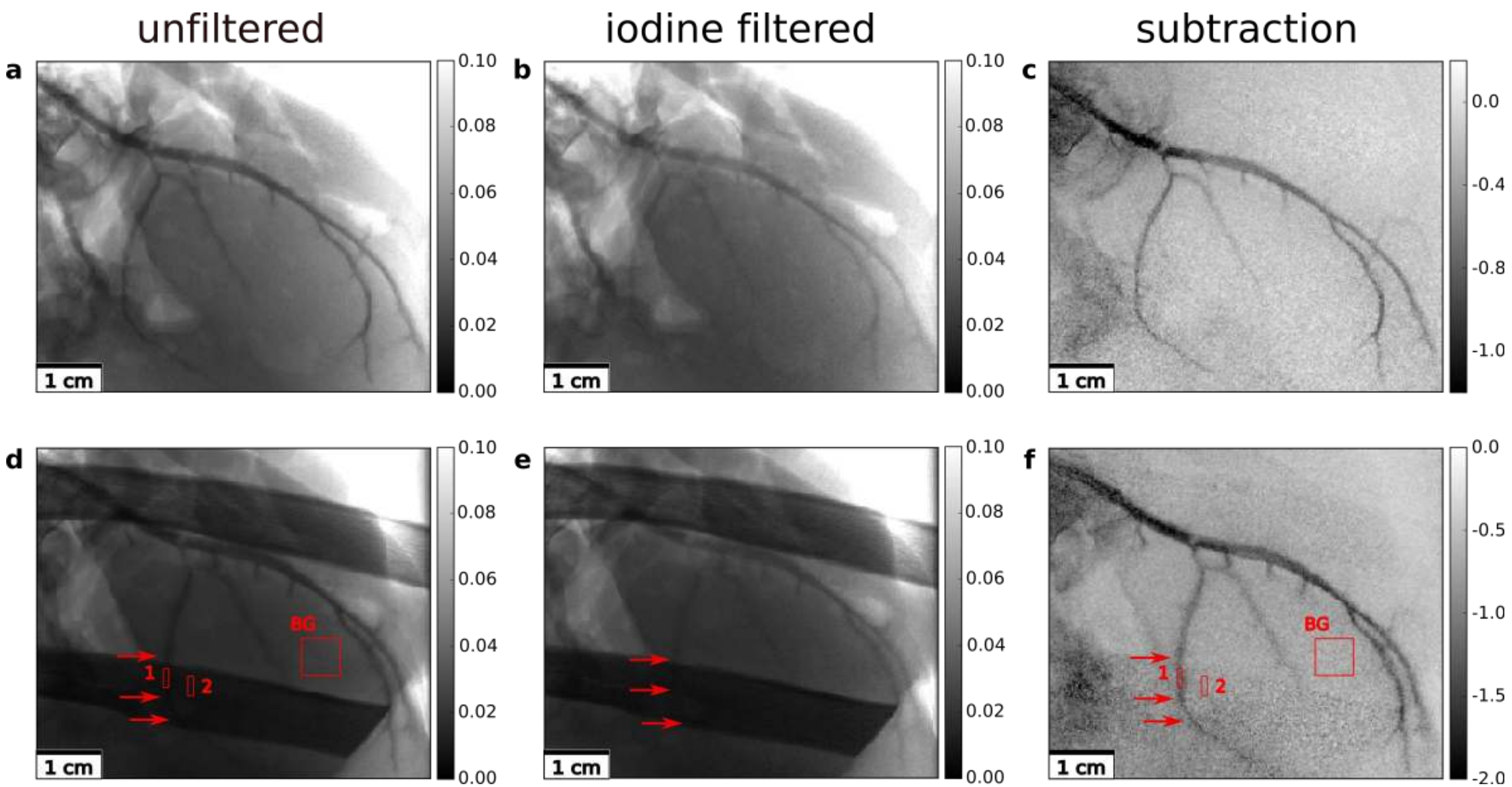

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Absorption spectroscopy at MuCLS

Work by

Juanjuan Huang

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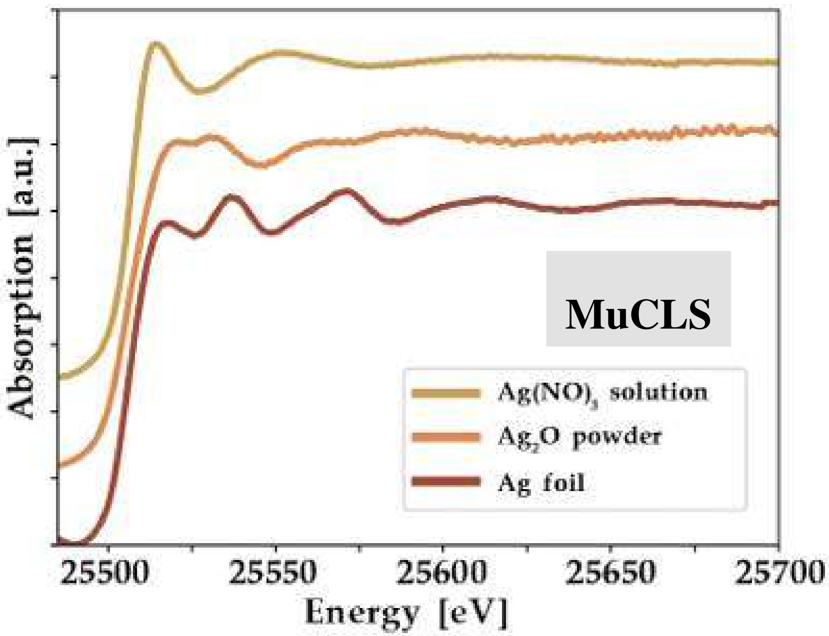


Work by

Juanjuan Huang

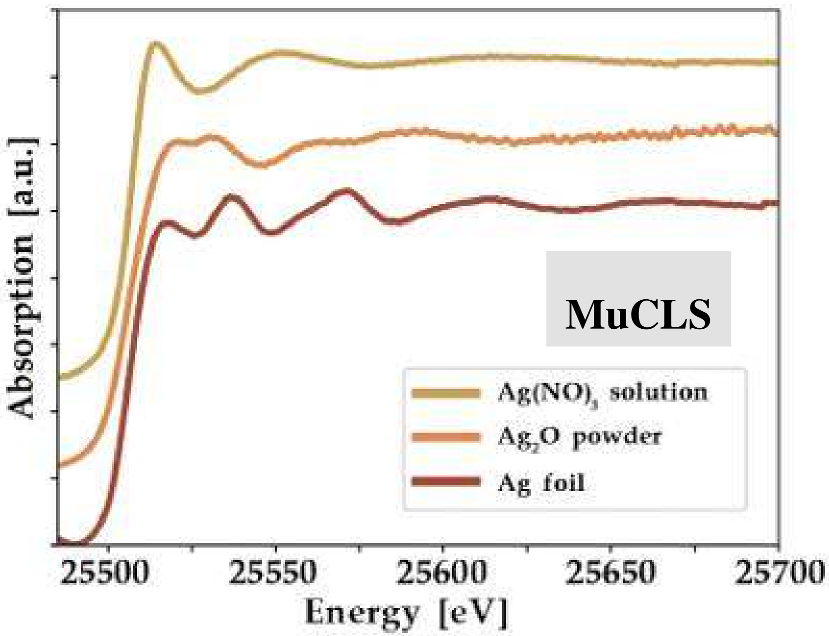
Energy resolution

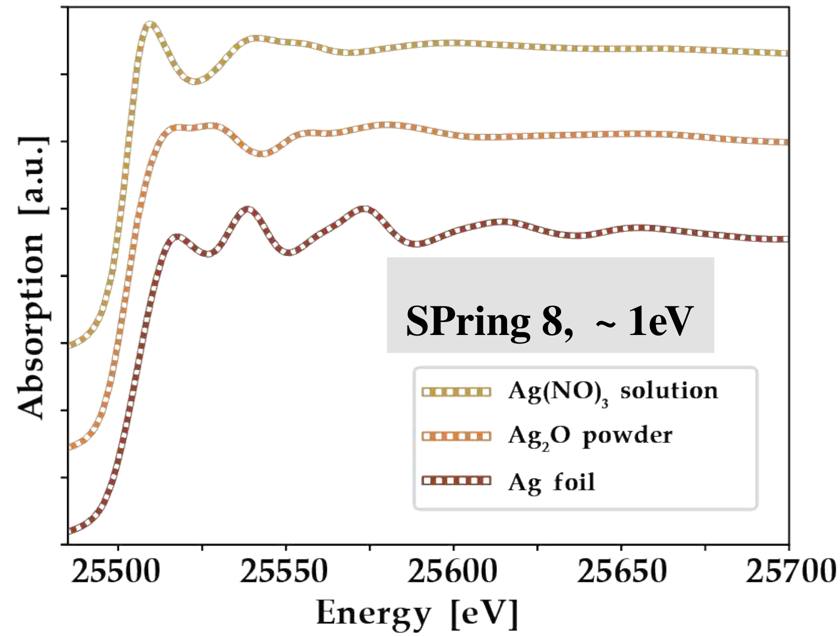
~ 2.24 eV @ 26 keV

Huang et al., to be submitted

Absorption spectroscopy at MuCLS

Reference taken at
QXAFS, BL14B2, SPring8,
courtesy: *Dr.* Yitao Cui





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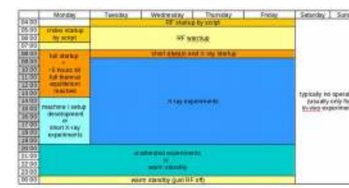
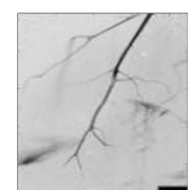
Conclusions

MuCLS: a lab-sized synchrotron facility based on an inverse Compton scattering source

In day-to-day use for experiments



Focus on experiments that exploit special (for lab source) properties



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IAS TUM Institute for Advanced Study

NHMRC

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+ many more people at the Chair of Biomedical Physics

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Martin Groß,
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X-ray experiments from a user perspective

As long as parameters are as required
→ **Users usually do not want to care about details of X-ray generation**

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Lessons learned

- long scans (computed tomography)
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