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Progress Towards Clinical Diffraction Enhanced Imaging

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Disclosures

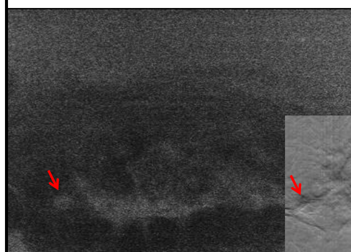
- Dr. Connor is a founder, part owner, and consultant for NextRay, Inc., which is developing a clinical diffraction enhanced imaging system.

Why phase contrast x-ray imaging?

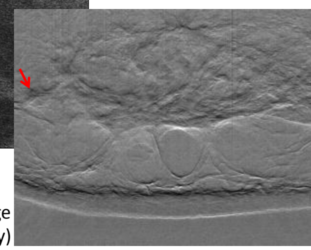
New contrast mechanisms are needed to significantly reduce patient dose or to significantly improve image contrast.

What's possible with DEI?

Mammography at ultra-low dose

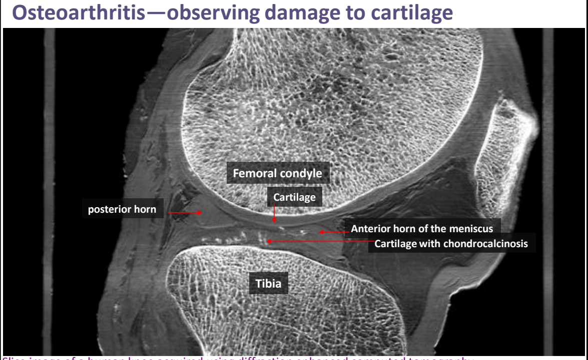


Synchrotron Radiograph
60 keV, 4 mrad (0.04 mGy)



Synchrotron DEI Refraction Image
60 keV, 4 mrad (0.04 mGy)

Osteoarthritis—observing damage to cartilage

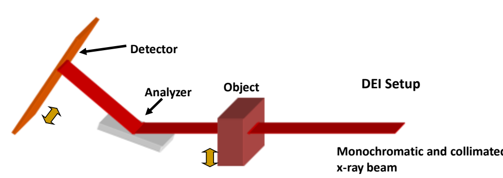


Slice image of a human knee acquired using diffraction enhanced computed tomography.

Image courtesy of Jun Li, Rush University Medical College; Li, J., Z. Zhong, et al. (2009). "Phase-sensitive X-ray imaging of synovial joints." Osteoarthritis Cartilage **17(9): 1193-1196.**

How does DEI generate phase contrast?

- Analyzer crystal converts angular shift in x-ray beam into an intensity change in an image.
- Requires the use of an x-ray beam that is:
  - **Monochromatic**
  - **Collimated**



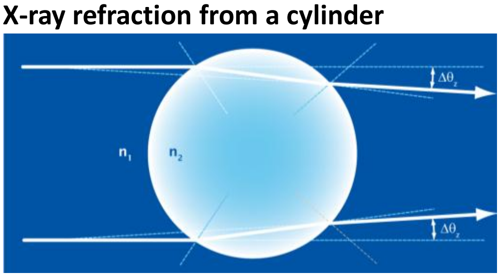
Analyzer crystal

Great for phase contrast.
Bad for flux.

DEI contrast mechanisms

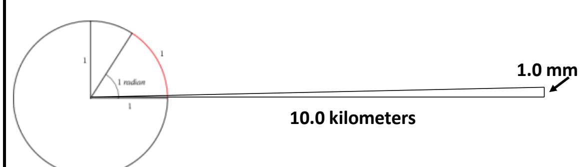
Few refracting objects.
Many refracting objects.

X-ray refraction from a cylinder



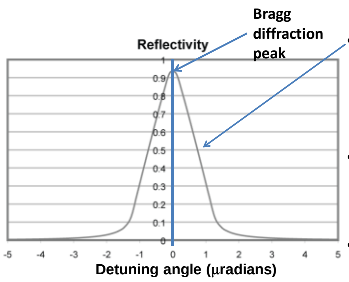
- The refraction angle, $\Delta\theta_z$, is proportional to
  - The difference in the index of refraction, Δn.
  - The x-ray energy as $1/E^2$.
- For biological tissues, $\Delta\theta$ is on the order of 10^{-7} radians.

What does 10^{-7} radians look like?



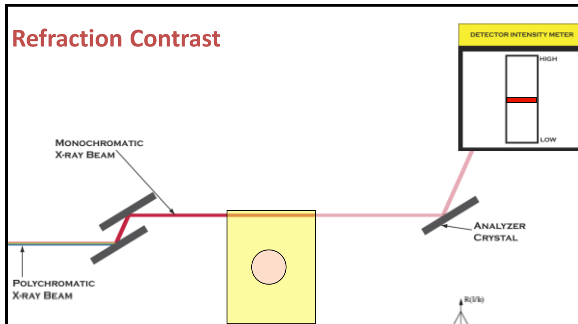
Note: Figure not drawn to scale

Reflectivity of the analyzer crystal

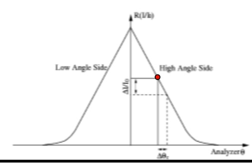


- Slope of the reflectivity profile is proportional to the x-ray energy, *E*.
- Remember that refraction is proportional to 1/E^2.
- **Thus, DEI contrast is proportional to 1/*E*.**

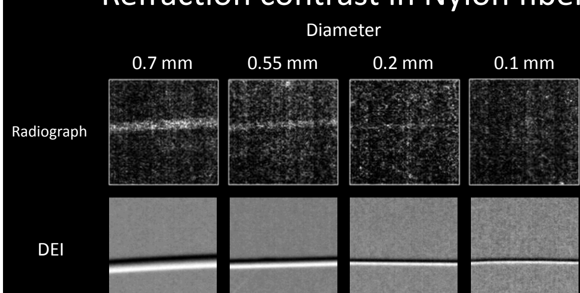
Refraction Contrast



- The analyzer crystal is on the shoulder of the rocking curve.
- Refraction causes a large change in intensity.



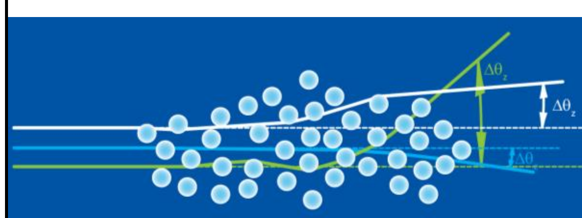
Refraction contrast in Nylon fiber



Nylon fiber simulates density variation in soft tissue.
Images are dose-matched.

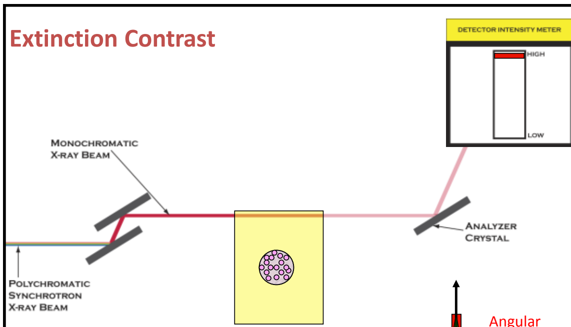
Kiss et. al., *Phys. Med. Bio.* **48** (2003) 325-340

How does extinction/USAXS work?

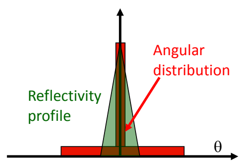


Multiple refractions from multiple structures causes an angular spreading of the x-ray beam

Extinction Contrast



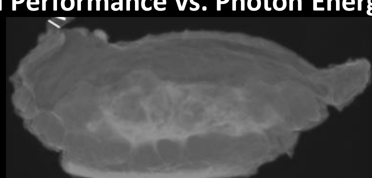
- The analyzer crystal is at the peak reflectivity point.
- Scattering causes a large change in intensity.

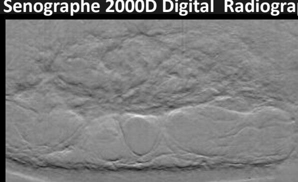


Is Clinical DEI possible?

Biggest obstacles: (1) monochromatic, (2) collimated beam.

DEI Performance vs. Photon Energy

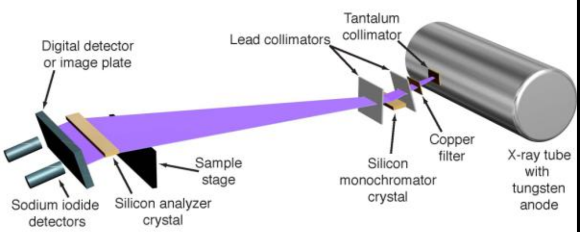

GE Senographe 2000D Digital Radiograph


60 keV DEI Refraction Image

Proof-of-principle system

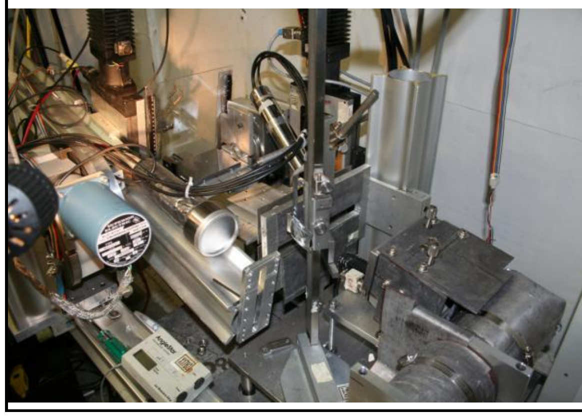
- Can x-ray tube generate sufficient flux for a clinical DEI system?
  - Built a system to measure the flux as a function of tube voltage and current.
  - Extrapolated the flux to a higher power x-ray tube source.

DEI Prototype Design

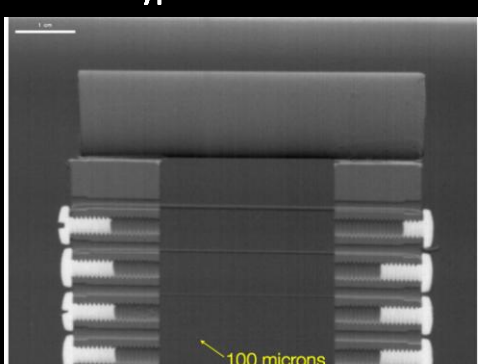


Kα1 59.318 keV
Kα2 57.982 keV

C. Parham, Z. Zhong, D.M. Connor, L.D. Chapman, E.D. Pisano, "Design and Implementation of a Compact Low-Dose Diffraction Enhanced Medical Imaging System," *Academic Radiology*, **16 (8)**, 911-917 (2009).

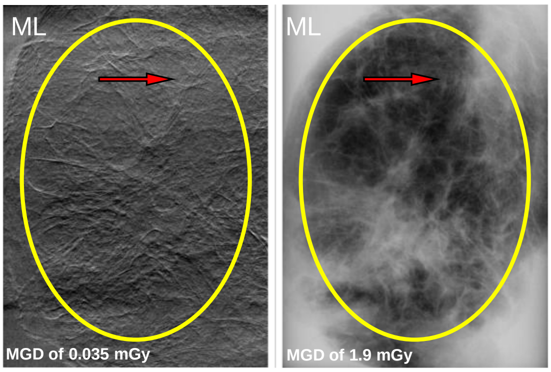


DEI Prototype Refraction Phantom



Low dose DEI prototype image of a human thumb

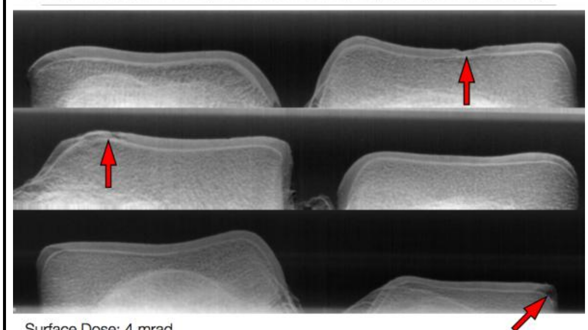
C. Parham, Z. Zhong, D.M. Connor, L.D. Chapman, E.D. Pisano, "Design and Implementation of a Compact Low-Dose Diffraction Enhanced Medical Imaging System," *Academic Radiology*, **16 (8)**, 911-917 (2009)



DEI Prototype Refraction Imaging and Comparison Image taken on a GE Senographe 200D Digital Mammography System

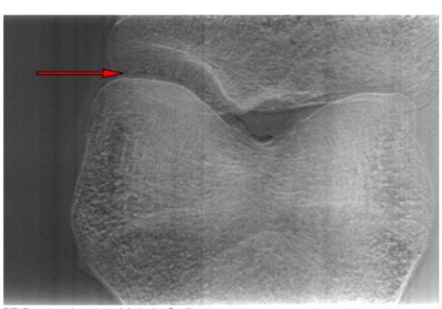
DEI Prototype Imaging of Articular Cartilage

Performed In collaboration with Jun Li, M.D. and Carol Muehleman, Ph.D., Rush Department of Biochemistry



Surface Dose: 4 mrad

DEI Prototype Imaging of the Human Knee

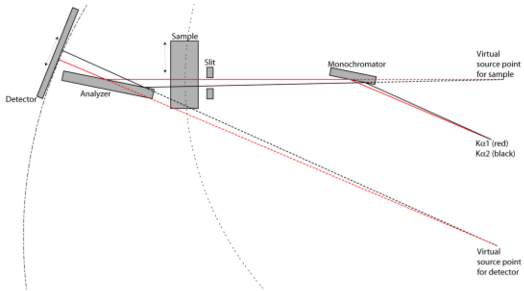


DEI Prototype Imaging of Articular Cartilage
Surface Dose: 4.0 mrad
Performed in collaboration with Jun Li, M.D. and Carol Muehleman, Ph.D., Rush Department of Biochemistry

Proof-of-principle system findings

- Measured the post-analyzer crystal system flux.
- Linear relationship between tube current and flux shown.
- For a fixed tube power, showed a higher peak voltage generated a higher flux.
- Generated the same contrast as a synchrotron-based DEI system.
- Imaging time for full-thickness breast specimen was 24 hours.

Proof-of-principle system findings



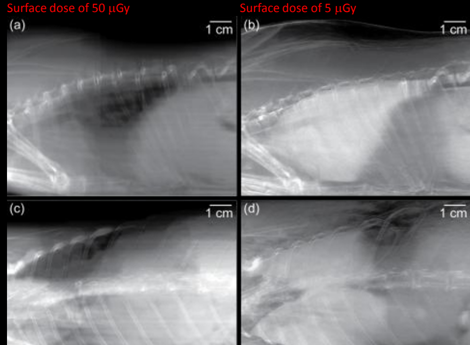
SYNCHROTRON AS WIND TUNNEL

In lieu of a functioning clinical DEI system, the National Synchrotron Light Source was used to mimic properties of a future clinical system.

Ultra-low dose infant imaging

Radiograph of rabbit chest
Surface dose of 50 µGy

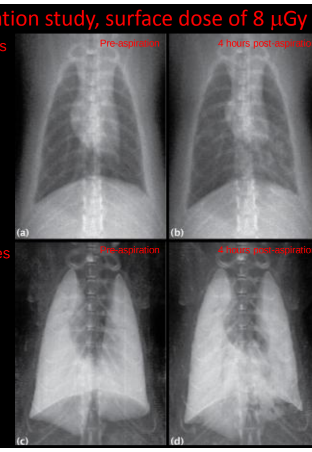
DEI image of rabbit chest
Surface dose of 5 µGy



Acid aspiration study, surface dose of 8 µGy

Radiographs

DEI peak images

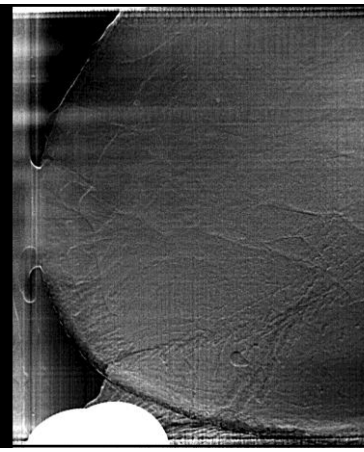


Second generation prototype

- Rotating anode tube source (fluoroscopy tube)
- Higher efficiency detector
  - Current: Image Intensifier
  - Future: Likely flat panel upgrade soon.

DEI
Mammogram
Prototype

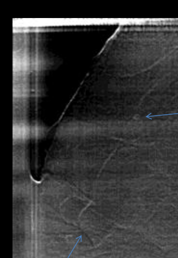
Acquisition
Parameters:
Surface dose: **4.7 μGy**
Tube voltage: 125 kVp
Tube current: 80 mA
Scan range: 50 mm
Acquisition time: 480 s



Digital
Mammogram
Hologic Selenia

Acquisition Parameters:
kVp: 28
X-ray tube current: 100
Exposure Time: 626
Body Part Thickness: 47.0
Relative X-ray Exposure: 424
Anode/Filter Combination:
Mo/Mo

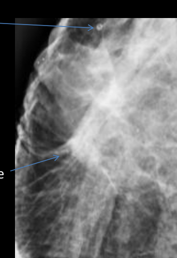
DEI Mammogram
Prototype



Calcification

Nipple

Digital Mammogram
Hologic Selenia



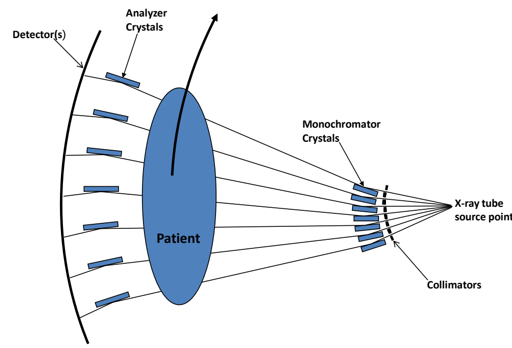
Calcification

Nipple

Preliminary findings 2nd generation prototype

- DEI contrast was maintained with the addition of a rotating anode tube source.
- Imaging time for breast specimen reduced to 3 hours (10 kW tube power at 125 kVp).
  - 480 seconds of "beam on" time from the pulsed source.
- A multiple beam approach including 10 DEI beams and a tube power of 60 kW would reduce the imaging time to **8 seconds**.

Multiple beam DEI system



WHAT NEXT?

Engineering challenges ahead

- Solution for monochromatic beam is to use high energy x-rays.
- Solution for collimated beam is to use a multiple beam DEI approach.
  - *N* beams would reduce imaging time by a factor of *N*.
  - Difficulty: Reducing size of the x-ray optics.
- Optical stability.
- Background correction in images.

Clinical challenges ahead

- Clinical trials for specific imaging applications.
  - How will clinical DEI images compare to current state-of-the-art?
  - Difficulty: Reducing size of the x-ray optics.
- Optimizing DEI imaging parameters for specific applications.
- Background correction in images.

In Summary…

- DEI has fantastic phase contrast.
- DEI optics have almost complete scatter rejection.
- Crux point is imaging time.
- Feasible path towards clinical imaging times on the order of seconds with existing technology.

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- Etta Pisano, Medical University of South Carolina
- Elodia Cole, Medical University of South Carolina
- Christopher Parham, UNC-Chapel Hill
- Zhong Zhong, NSLS
- Lisa Miller, NSLS, Stony Brook University
- Helene Benveniste, BNL Medical, Stony Brook University
- Avraham Dilmanian, BNL Medical, Stony Brook University
- Mary Kritzer, Stony Brook University
- Carol Muehleman, Rush University
- Dean Chapman, Canadian Light Source, Univ. of Saskatchewan
- Sheldon Wiebe, Univ. of Saskatchewan

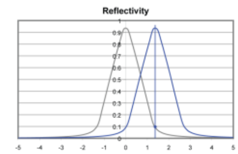
nsls IR UV X RUSH UNIVERSITY UNC BROOKHAVEN NATIONAL LABORATORY

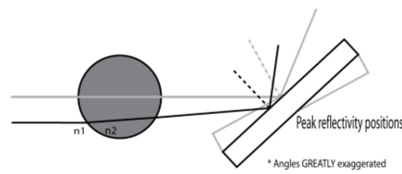
APPENDIX

Development of imaging phantom

- Goal: To develop an appropriate phantom that can be used for contrast, resolution, and contrast-to-noise ratio comparisons between different phase contrast x-ray imaging systems.

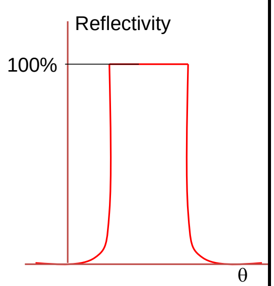
Effect of refraction on rocking curve



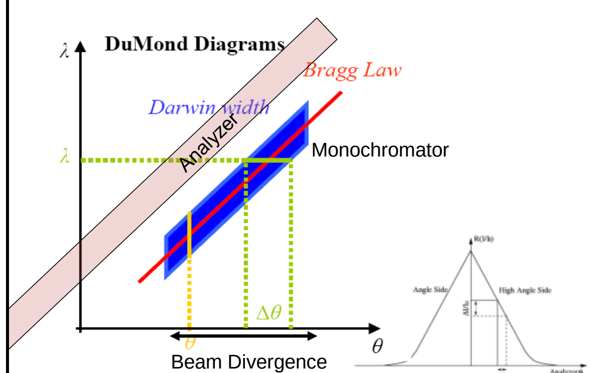


Diffraction by Perfect Crystals

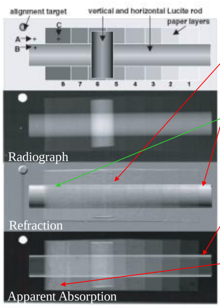
- The reflectivity as function of crystal's angle is the rocking curve
- For perfect crystals, the rocking curve is roughly rectangular.
- Peak reflectivity ~100%
- The width (Darwin width) is on the order of micro-radians
- 1 micro-radian is the angle subtended by 1 mm at a distance of 1 km



Analyzer Rocking Curve



DEI in Presence of Scatter



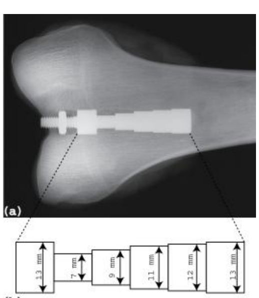
- Refraction image only sensitive to refraction in the vertical plane along the direction of beam propagation.
- Refraction signal decreases in presence of ultra-small-angle x-ray scattering (USAXS).
- In regions of high refraction, apparent absorption image has an edge-enhancement effect.
- If there is a lot of USAXS, apparent absorption increases significantly.

Images from Oltulu, et al, J. Phys. D: Appl. Phys. **36** (2003) 2152–2156

BONE GROWTH ASSESSMENT

Increased contrast imaging of hard tissue features

Stepped implant experiment



- Images taken at 40 keV using [333] diffraction.
- Human distal femur was used.
  - 13 mm diameter hole was drilled into the bone.
  - Stepped implant was press-fit into the drill hole.
- Peak, -0.8 µrad, and +0.8 µrad images were obtained.

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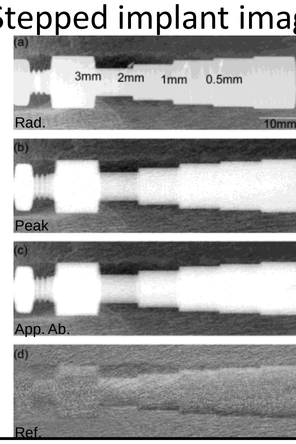
Stepped implant images



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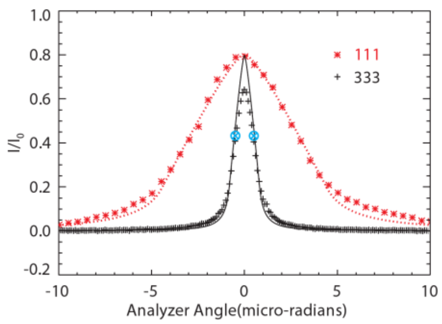
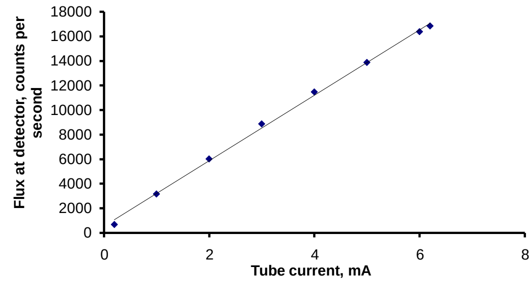
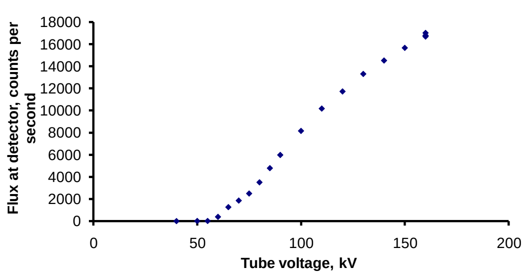
Measured reflectivity profile



Measured flux for constant voltage



Measured flux for constant power



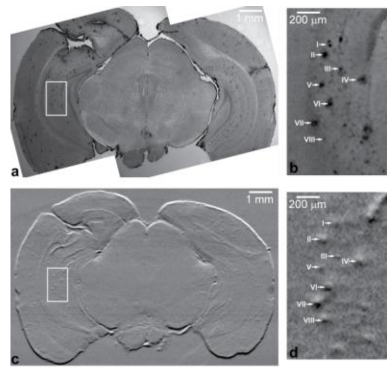
IMAGING OF AMYLOID BETA PLAQUES

Synchrotron-based high contrast and high resolution soft tissue imaging with diffraction enhanced computed tomography

Methods

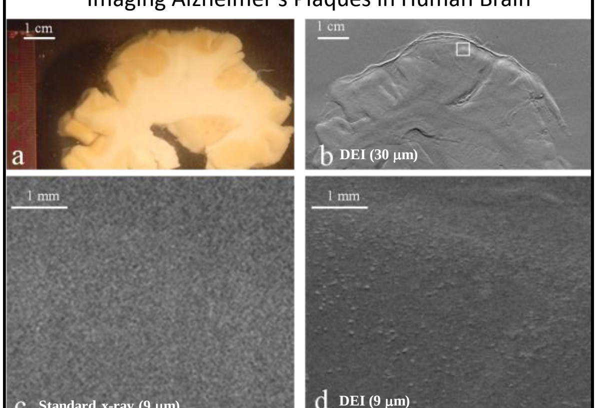
- Brains of Alzheimer's disease-model mice and wild-type mice were imaged at NSLS beamline x15a.
- Monochromator and analyzer crystals were aligned to the 20 keV, silicon [333] reflection for maximum soft tissue contrast.
- Full sets of projection images were taken at the +/-FWHM/2 points on the reflectivity profile.
- Projection images were combined to form refraction projection images.
- Refraction projection images were processed with filtered backprojection to create an array of 2D cross-sections of the brains.
- After imaging was completed, the brains were then physically sectioned and immunostained to show the plaques.

Histology and refraction slice comparison



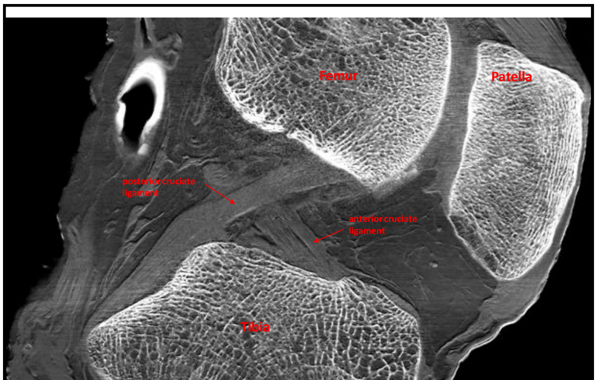
- (a) and (b) are how we've been able to see the amyloid beta plaques for the last 100 years.
- (c) and (d) refraction CT slice images from the corresponding section of the same brain.

Imaging Alzheimer's Plaques in Human Brain



CARTILAGE IMAGING

High contrast imaging of soft tissue structures at the synchrotron



Slice image of a human knee acquired using diffraction enhanced computed tomography.

Image acquired by Jun Li, Rush University Medical College, and Dean Connor and Zhong Zhong, NSLS, Brookhaven National Lab