Diffraction Enhanced Imaging and Phase Contrast Imaging at the NSLSII

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I’ll do the talking

- What is DEI (Diffraction Enhanced X-ray Imaging), how is it done?
- Applications to medical imaging problems
  - Mammography
  - Osteoarthritis
  - Alzheimer’s Disease
- Towards the clinic
- Phase contrast imaging
- Limitations, Unresolved problems, NSLSII?
You’ll do the thinking

• It’s amazingly simple! ... like all great sciences

• How can it benefit my research?
  What I can see with my eyes ... I may see with x-rays
  – Inside a body *in vivo*
  – In a reaction vessel *in situ*

• Can I try the same trick?

• Worth moving to the NSLSII?
Standard x-ray imaging

- Advantage of x-rays
  - High resolution
  - Fast imaging

- Mammography
- Chest x-ray
- Fluoroscopy
- Angiography
- CT

All depend solely on absorption of x-rays for contrast

- Despite recent advances in digital x-ray, still low contrast for soft tissues (everything except bone)
ACR Phantom - Conventional and DEI

Mammography Quality Assurance Phantom
- American College of Radiology
- Simulates features of breast cancer lesions: tumor mass, spiculation, calcification

Beaml ine X15A

- Tangent arm for analyzer crystal
  Silicon 111
- Detector tth arm
- Fast shutter
  Controls exposure
- Monochromator
  Silicon 111
  Double crystal
- Sample stage for planar imaging
- Rotation stage is added for DEI-CT
- Ion Chamber
  Measures dose rate
How does DEI work?

- X-ray refraction and ultra-small angle scattering
  - on the order of micro-radians
  - not detected by conventional x-ray systems

- The analyzer’s sharp rocking curve converts angular information into intensity change

- DEI preserves the high-resolution of x-rays.

- Contrast does **not** rely on absorption of x-rays.
Refraction Contrast

- Variations of density causes x-ray refraction
- The steep slope of the rocking curve converts refraction to intensity change
Refraction contrast in Nylon fiber

Diameter

<table>
<thead>
<tr>
<th>Diameter</th>
<th>Radiograph</th>
<th>DEI</th>
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<tbody>
<tr>
<td>0.7 mm</td>
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<td><img src="image2.png" alt="Image" /></td>
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Nylon fiber simulates density variation in soft tissue

DEI does not rely on absorption

- Radiography:
  - Contrast = Absorption = Dose
  - Lower energy -> More absorption -> More dose
- DEI: Higher x-ray energy -> More penetrating power -> Lower absorption and less noise -> Lower dose
- 30 times smaller dose at 30 keV compared to 18keV
- DEI can be implemented at near zero dose by utilizing higher-energy x-rays
Breast Cancer

- Mastectomy specimen with breast cancer
- Images were compared with digital radiographs,
- 6/7 cases showed enhanced visibility of spiculation that correlated with histopathologic information

Pisano et. al., Radiology 214 (2000) 895-901
Quantitative Comparison: Spiculation

- Spiculations are due to cancer itself or the response of the host to the cancer
- Contrast quantified by measuring intensity change across spiculations
- DEI has 8 – 33 times greater contrast

Quantitative Comparison: Calcification

- Micro-calcifications vary in size < 0.05 mm to 2 mm.
- 3 mastectomies used for the study
- ~ 100 calcifications identified
- 2-7 times gain in DEI contrast

Low dose DEI with high energy x-rays

Fischer Digital Mammography System
~ 18 keV
Dose = 3 mGy

DEI, 40 keV
Dose = .02 mGy
Cartilage Imaging

DEI allows direct visualization of cartilage and assessment of damage

Simultaneous imaging: bone and soft tissues

Radiograph

Sclerotic blood vessel

Tendon calcification

Air bubbles

PP

DEI

S

M

DP

Comparison with Histology
Conceptual Design
Prototype DEI with x-ray tube
• 12 cm thick mastectomy specimen
• Compressed to 7.0 cm
• Mounted to approximate a clinical mediolateral view
• Normal radiograph acquired using a GE Senographe 2000D at 31 kV and 98 mAs.
Prototype DEI with x-ray tube

DEI (15 mrad)
Absorption: Contrast proportional to feature size $w$
- Dose $\sim 1/w^4$
- 1 mGy for $w=100$ microns, $10^5$ Gy for $w = 1$ micron

DEI: Contrast independent of object size
- Dose $\sim 1/w^2$
- 0.1 mGy for $w=100$ microns, 1 Gy for $w = 1$ micron
Worldwide Efforts

- Other synchrotron facilities have developed DEI
  - Elettra, Italy, Clinical Studies
  - ESRF, France, DEICT, Large animal studies
  - HASYLAB / DESY, Germany
  - KEK, Japan
  - Spring8, Japan, dark field, interferometer
- Australian, Canadian, and ShangHai Light Sources are constructing dedicated biomedical imaging beamlines with DEI
- The NSLS is the only game in town for DEI in USA
NISL-II, High-res DEI reveals micro-structure

Currently Limited by:

- Source size \rightarrow Spatial resolution \sim 50 \text{ microns}
- Brightness \rightarrow Sensitivity \sim 0.1 \text{ micro-radians}
- The advantages of DEI are not realized for small features

High brightness of NSLS-II will allow:

- 1 \text{ micron resolution}
- 0.01 \text{ micro-radians sensitivity}
- Micro-structure in animal models, e.g., amyloid plaques in Alzheimer’s disease models

[Images of microstructures]
Proposed NSLS-II DEI Beamline

- Superconducting wiggler to enable imaging above 60 keV
- Sample environment more appropriate for live animals (humans included)
- Part of biomedical research suite
- Incorporate:
  - Lessons learned at Trieste, ESRF, Spring8
  - Lessons that will be learned at CLS and Australian Light Source and Shanghai Light Source
Phase Contrast Imaging

ENERGY RANGE:
• 8 – 30 keV (or higher)

SPATIAL RESOLUTION:
• 1-5 μm

CONTRAST MECHANISM:
• X-ray refraction
• Propagation-based edge enhancement

MODE(S) OF OPERATION:
• Real-time imaging
• 3D tomography (μ-CT)
• Sample thickness: 0.5-10mm

Description. Phase contrast imaging (PCI) is a relatively new imaging modality being used extensively only after the availability of 3rd generation synchrotron sources. Instead of the traditional absorption contrast, phase contrast imaging exploits the real-part of the refraction index and makes use of a larger distance between sample and an area detector which allows direct intensity contrasts due to wave propagation. Since PCI's contrast mechanism does not rely on the absorption of the subject, it is ideally suited for biological imaging, especially for real time or quasi real-time imaging of living small animals.
Phase-Contrast Imaging

UNIQUE CAPABILITIES:

• Better contrast for biological and biomedical imaging than conventional absorption radiography
• High throughput with robotic sample changer
• At higher x-ray energies, the phase contrast reduces radiation dose to the subject
• 3D (tomographic) imaging can be performed in quasi–real–time
• Zoom–in tomography allows detailed high resolution studies of region of interest (ROI) after initial survey of the specimen at lower resolution and with a larger field of view

RECENT EXAMPLES:

• (Below) The leaf cross–section is a 'phyllode' from an Acacia tree that is very widespread in Western Australia. This leaf came from a tree growing on a mine stock pile of ore that is rich in Cu and Zn. The tomogram illustrate the vascular network within the leaf, the calcium oxalate crystals that have grown within it (dense bright particles) and the leaf tissue. In the figure below, the horizontal dimension is ~ 2 mm (Courtesy of R. Hough, CSIRO, and F. DeCarlo, APS)
Phase-Contrast Imaging

RECENT EXAMPLES:


BENEFIT FROM NSLS–II:

• Fast 3D tomographic imaging of living small animals through phase–contrast imaging (PCI)
• Long beamlines >300m can be accommodated at NSLS–II for advanced full-field medical imaging and therapy
Summary

• Advantages of DEI:
  – Low dose
  – Refraction and extinction provide new contrast
  – High spatial resolution
• Refraction highlights tumor boundaries and cartilage-> Early diagnosis of breast cancer and osteoarthritis
• Refraction by Amyloid plaques is visible to DEI -> Assessment of Alzheimer’s Disease drugs
• Phase contrast imaging uses refraction too, and can offer high-speed, high-resolution, 3D images.
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Thank you for your Attention!