Synchrotron Medical Research Applications

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NSLS-II Workshop
Imaging - Nanoprobe
Breakout Session
15 March 2004
Brookhaven National Laboratory
Plan

- Imaging based on interactions:
  - Absorption imaging
  - Dual Energy Imaging
  - Computed Tomography
  - Refraction and scatter imaging
  - Phase Contrast
  - Diffraction Enhanced Imaging / Multiple Image Radiography

- Radiotherapy
  - CT Radiotherapy
  - Microbeam Radiation Therapy

- Requirements & Conclusion
Medical Research Opportunities

- COMPUTED TOMOGRAPHY
- RADIATION THERAPY
- CORONARY ANGIOGRAPHY
- MAMMOGRAPHY
- BRONCHOGRAPHY
- CARTILAGE
Interaction of X-rays with Matter

Optical Effects – index of refraction

In the x-ray energy range

\[ n = 1 - \alpha - i\beta \]

Refractive index correction is weak; \( \alpha \& \beta << 1 \)

Absorption index is weaker; \( \beta << \alpha \)
Absorption of Some Materials

Absorption Coefficient (cm²/g)

Energy (keV)

I
Xe
Gd
Pb
Bone
Water

0 20 40 60 80 100

0 10 100 1000

0.1 1.0 10.0 100.0 1000.0

Absorption Coefficient (cm²/g)
Cardiopulmonary Research

CORONARY ANGIOGRAPHY

BRONCHOGRAPHY
Iodine Absorption - Dual Energy Subtraction

- Dual energy subtraction makes use of rapid change in absorption of a contrast agent near its absorption edge.
- If images are taken near this edge, absorption of other materials in the object change very little.
- Object can be thought of as a two component system...contrast agent and rest of object.
- => take two images on each side of edge; solve for the two components.
Dual Energy Subtraction Imaging - Iodine Contrast Imaging – Coronary Angiography

Courtesy W. Thomlinson & M. Renier
Best Views-
ID17 Imaging Facility ESRF

Patient CHU_29 / ESRF_280 - Image 1
Patient CHU_29 / ESRF_280 - Image 2
Patient CHU_29 / ESRF_280 - Image 3

Courtesy W. Thomlinson & M. Renier
### Xe K-edge Imaging of Lungs

#### Energy [keV]

<table>
<thead>
<tr>
<th>Energy [keV]</th>
<th>µ/ρ [cm²/g]</th>
</tr>
</thead>
<tbody>
<tr>
<td>33.5</td>
<td>1</td>
</tr>
<tr>
<td>34.0</td>
<td>10</td>
</tr>
<tr>
<td>34.5</td>
<td>100</td>
</tr>
<tr>
<td>35.0</td>
<td>100</td>
</tr>
<tr>
<td>35.5</td>
<td>100</td>
</tr>
</tbody>
</table>

#### Attenuation Coefficient of Xe

![Diagram of Lung Structure](image)

- **Trachea**
- **Right primary bronchus**
- **Secondary bronchi**
- **Tertiary bronchi**
- **Left primary bronchus**
- **Lobes of the lung**
- **Alveoli**

**E_K = 34.56 keV**

Courtesy W. Thomlinson & M. Renier
Human Bronchography

The Sample

Giacomini, Rubenstein Gordon, O’Neil, Van Kessel, Cason, Chapman, Lavender, Gmür, Menk, Thomlinson, Zhong

Bronchography In-Vivo Rabbit Xenon K-Edge Imaging

Projection Image

Computed Tomography Image

Courtesy W. Thomlinson & M. Renier
Cardiopulmonary Physiology and Perfusion Studies

Xe perfusion studies of rabbit model system under influence of histamine

Post-Histamine

Normal Lung

8 min

30 min

Spiral CT Xe KES

Bayat et al. 2003; ESRF ID17
Mammography
Cancer in Breast Tissue

Pisano, Johnston(UNC); Sayers(NCSU); Zhong(BNL); Thomlinson(ESRF); Chapman(IIT)

Conventional  DEI - Absorption  DEI - Refraction
Synchrotron Radiography and DEI

Synchrotron Radiology Setup
- Object
- Double Crystal Monochromator
- Synchrotron Beam
- Area Detector

Synchrotron DEI Setup
- Analyzer
- Object
Invasive Lobular Carcinoma Analysis

Found that:
- Absorption & refraction
- DEI Absorption contrast compared to radiograph was:
  - ~ 8 - 14 x higher
- DEI TOP Image has
  - ~ 12 - 33 x higher

Hasnah, Oltulu, Chapman(IIT), Pisano (UNC); Zhong(BNL)
Musculoskeletal Research

CARTILAGE

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Mouse Images

Pisano, Johnston(UNC); Sayers(NCSU); Zhong(BNL); Thomlinson(ESRF); Chapman(IIT)

Data from SRICAT 1-BM-B

18keV  30keV  DEI 30keV
Human Cartilage Imaging
Ankle Joint - Talus

Aurich, Mollenhauer, Cole, Muehleman, Kuettner (Rush); Zhong (BNL); Hasnah, Oltulu, Chapman (IIT)

Radiograph

Data from NSLS X15A
Human Cartilage Imaging
Ankle Joint - Talus

Aurich, Mollenhauer, Cole, Muehleman, Kuettner(Rush); Zhong(BNL); Hasnah, Oltulu, Chapman(IIT)

30keV

18keV

Photo

Undamaged  Slight Damage  Moderate Damage  Severe Damage

Data from NSLS X15A
Human Cartilage Imaging – Intact Knee Joint

A cadaveric knee showing articular cartilage at 30keV

Data from NSLS X15A
Multiple Image Radiography-
projection image of a foot

Red – Absorption
Blue – Refraction
Green - Extinction

Muehleman, Jun (Rush), Brankov, Wernick, Chapman(IIT);
Zhong(BNL)
Radiation Therapy

COMPUTED TOMOGRAPHY

RADIATION THERAPY
CT-Therapy

History:
1980 Mello, Norman, Solberg, Iwamoto
'Radiation dose enhancement with iodine'
1999: first ct-therapy with patients

Principle:
- Tumor loaded with a contrast agent
  (Iodine or gadolinium).
- Beam size adjusted to the tumor dimensions
- Irradiation with monochromatic x-ray beam.
- Tumor positioned at the center of rotation.
CT-Therapy Principle

X-rays

Tumor + Iodine

Bone

Brain

From Norman et al.

Dose enhancement effect; Beam crossing at the tumor & Iodine enhancement

Fig. 2. Depth dose distribution (calculated).

Courtesy W. Thomlinson & M. Renier

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CT-Therapy

- $c_1: 2.5 \text{ mg/ml}$
- Irradiation time: 60 mn

X-ray

Dose Image

$\omega: \text{180°/sec}$

• Irradiation time: 60 mn

Dose Image

Courtesy W. Thomlinson & M. Renier
Microbeam Radiation Therapy

- Has tissue sparing effect due to small dimension of x-ray beam
- Requires high dose to small area => true synchrotron application
- Uses filtered high x-ray energy spectrum
Microbeam Radiation Therapy
Mouse Brain, Visual Cortex

1mm

140Gy

25µm

4000Gy

Zeman et al, Radiat Res 15, 496, 1961
MRT of Rat Intracerebral Gliosarcomas

Fisher-344 rats bearing right frontal intracerebral 9L gliosarcomas ~4mm diameter
Treated 14 days after initiation

Histology indicates microbeam damage and health tissue in non-radiated tissue.

Synchrotron Radiation -
many opportunities for imaging and therapy

- Intense, wide energy range, small source size, polarized, pulsed
  - Small source
    - High spatial resolution
    - Coherence
  - Broadbanded radiation
    - Many absorption edges (~S to U)
    - X-ray absorption spectroscopy
    - Fluorescence XAS
    - Fluorescence Imaging
    - Dual energy imaging
    - Phase Contrast and DEI
  - Optimal imaging energies
  - Dose minimization for imaging
  - Dose optimization for therapy
## Summary of Techniques

<table>
<thead>
<tr>
<th>Technique</th>
<th>Beam Width</th>
<th>Resolution</th>
<th>Energy Range</th>
</tr>
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<tbody>
<tr>
<td>KES – wide</td>
<td>200 mm</td>
<td>300 µm</td>
<td>20 – 60 keV</td>
</tr>
<tr>
<td>– narrow</td>
<td>20 mm</td>
<td>50 µm</td>
<td>20 – 60 keV</td>
</tr>
<tr>
<td>DEI – wide</td>
<td>150 mm</td>
<td>50 µm</td>
<td>20 – 90 keV</td>
</tr>
<tr>
<td>– narrow</td>
<td>15 mm</td>
<td>10 µm</td>
<td>20 – 90 keV</td>
</tr>
<tr>
<td>CT – wide</td>
<td>150 mm</td>
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<tr>
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<td>15 mm</td>
<td>10 µm</td>
<td>20 – 90 keV</td>
</tr>
<tr>
<td>CT Therapy</td>
<td>Uses the KES configuration and specification</td>
<td></td>
<td>20 – 60 keV</td>
</tr>
<tr>
<td>MRT</td>
<td>Needs high flux, high energy, minimal vibration amplitude and accurate positioning (5 µm peak-to-peak).</td>
<td></td>
<td>80 – 120 keV</td>
</tr>
</tbody>
</table>

Summary of techniques with required beam size, resolution, and spectral range required of the source. The sensitivity requirement for all techniques (both contrast agent and refraction density contrast) is approximately 1mg/cm³.
Source Specifications for CLS

Need a superconducting wiggler
- High energies
- High flux
- Wide beam

Rough schematic layout beamline showing the relative location of the MRT and Imaging facilities along with horizontal beam widths and flux requirements.
Future

- New applications
- New methods
  - Combination of existing methods – i.e. DEI and diffraction tomography?
  - Microbeam imaging?

but...

- Must be driven by medical community!
  - Significant effort into building a user group
  - Workshops, seminars, pilot experiments, MD resident programs, etc.
thank you for your attention
Other types of x-ray contrast?

Key may be in anti-scatter considerations...
i.e. UP TO 90% OF X-RAYS IN SOME DIAGNOSTIC IMAGING APPLICATIONS MAY BE OF SCATTER ORIGIN!!

Maybe we are looking at the wrong x-rays?
Can we use these scattered x-rays?
Not a new idea – i.e. X-ray Coherent Scatter Computed Tomography (CSCT)

But combining DEI with CSCT may bring a new perspective to some medical imaging problems
Rocking Curve Dependence

Rodent thorax region at 18keV

Scattering properties of some biological materials

The momentum transfer range is 0 – 0.3 Å⁻¹. (0-3 nm⁻¹).

Information and figure courtesy Dr. Ian Cunningham.
Material Specific CT Imaging based on scattering properties

Scattering patterns are used to recognize tissue types in CT mode.

These signatures are used to reconstruct image.

Information and figure courtesy Dr. Ian Cunningham.
Combined Imaging System
Reconstruction Method

“0°” projection…

Data Reduction and Processing Algorithms

CT Reconstructions

Sinograms

Filtered Back Projection

Transverse Position

Transverse Position

W/SAXS-N
W/SAXS-2
W/SAXS-1

µt

µt

W/SAXS-N
W/SAXS-2
W/SAXS-1

dρt/dz

Transverse Position

Transverse Position

0 100 200 300 400 500

0 100 200 300 400 500

W/SAXS-N
W/SAXS-2
W/SAXS-1

µt

µt

dρt/dz

0 100 200 300 400 500

0 100 200 300 400 500

Sinograms

Filtered Back Projection
Tissue Identification

Absorption – reference image

Data Reduction & Processing Algorithms:

\[ \text{Tissue}_n = \sum \alpha_{nk} S_k \]

“0°” projection…
Conclusion

Many sources of contrast available –

- Absorption
- Density or refraction
- Scattering
  - Ultra-small angle scattering – sub-pixel features such as lung
    aveoli, hair, bone trabeculae...
  - Small angle scattering – large scale molecular arrangement
    such as collagen bundles, muscle fibers...
  - Wide angle scattering – atomic and molecular arrangement
    such as atomic and molecular nearest neighbor scattering...
- Fluorescence
- Compton