

Taking Time, Risk, and Cost Out of Drug Discovery

Applications of Diffraction
Enhanced Imaging to
Osteoarthritis Drug Research

EnPro-351

Executive Summary

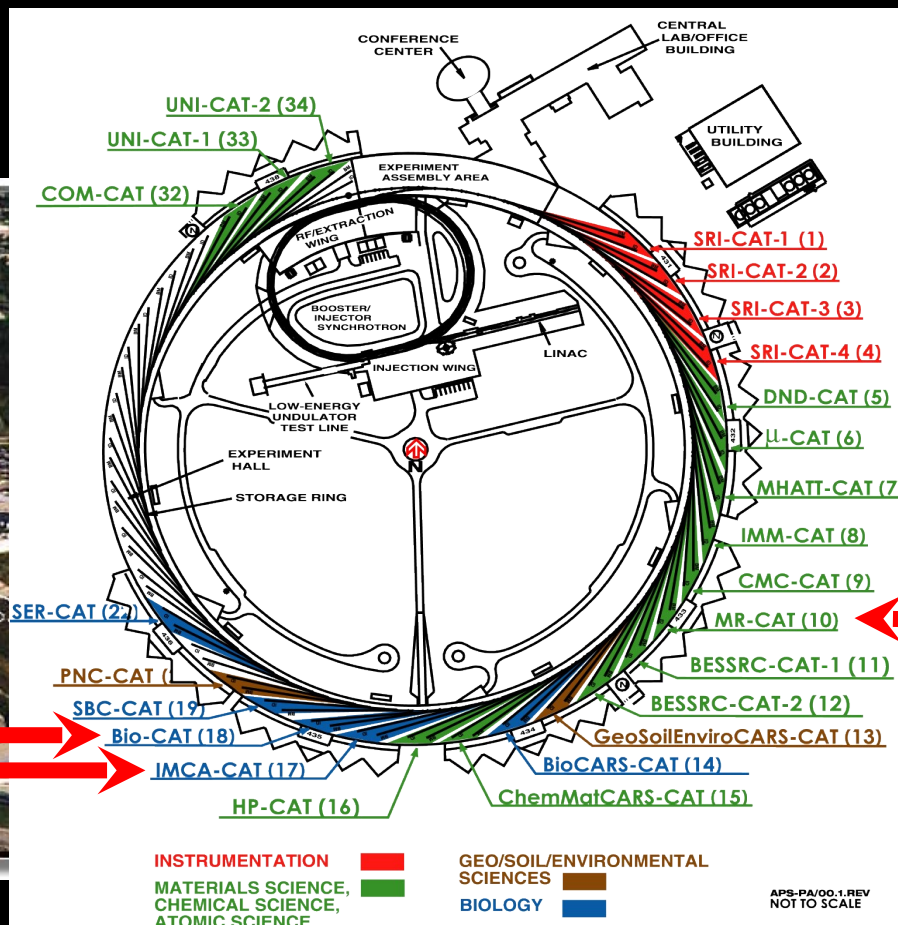
- Propose a consortium of university, medical school, national laboratory, and drug company to develop an improved x-ray technology that will improve drug development in osteoarthritis (OA)

Background

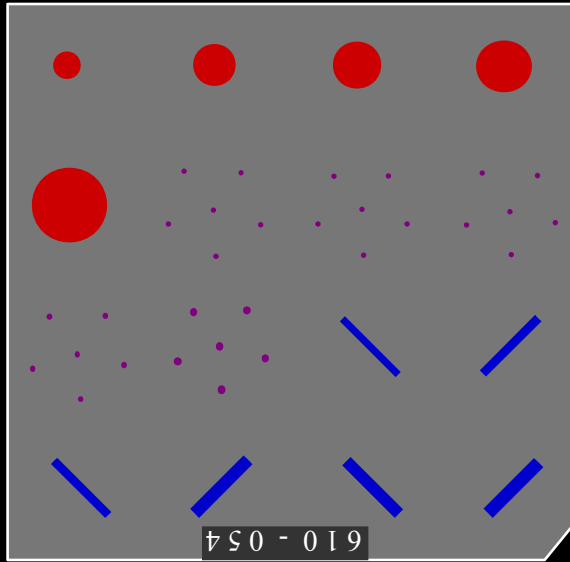
- IIT conducts major on-going research efforts in the use of synchrotron radiation
- Diffraction Enhanced x-ray Imaging (DEI) was developed by researchers at IIT for application in mammography
- An unexpected result was the discovery that DEI imaged tissue previously undetectable by x-rays
 - ◆ Cartilage is invisible to conventional x-rays and thus limits OA research

What's a Synchrotron?

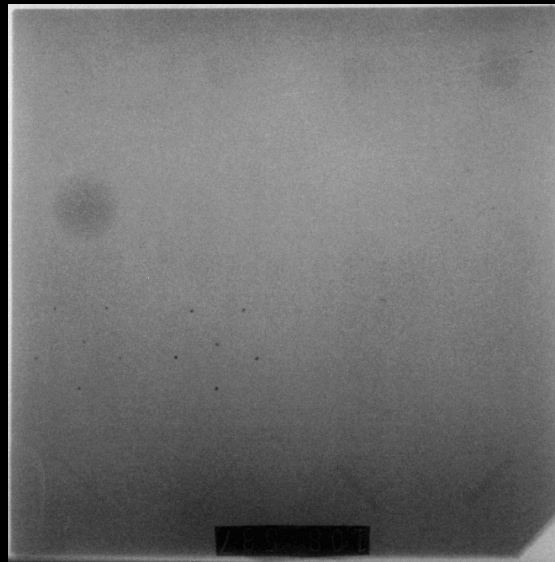
■ Synchrotron



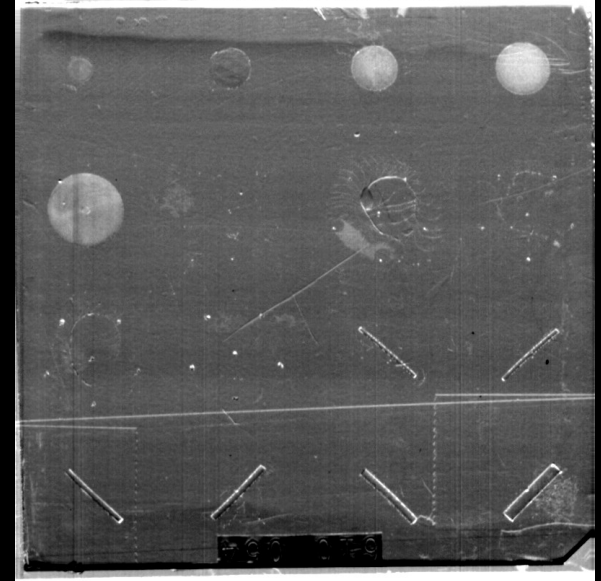
DEI Contrast – Mammography Test Object



Map



Conventional X-ray

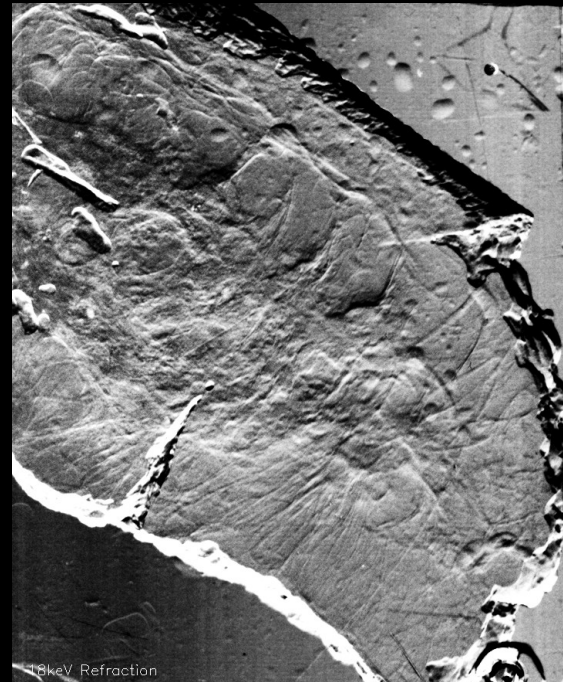


DEI

DEI Benefits in Mammography



Conventional



DEI

What's the OA problem?

- OA is the second leading cause of chronic severe disability in the US
 - ◆ 16-27 Million people afflicted nationwide
 - ◆ 7 Million physician visits per year
 - ◆ Costs the US economy ~35 Billion dollars per year
- OA is a whole joint disease
- OA pain occurs for two primary reasons:
 - ◆ Cartilage has already been degraded, no longer protecting the bone which contains nerves
 - ◆ Inflammation of surrounding tissues
 - ★ This can promote further damage of the cartilage
- Current drugs only mask pain from OA, promoting further damage

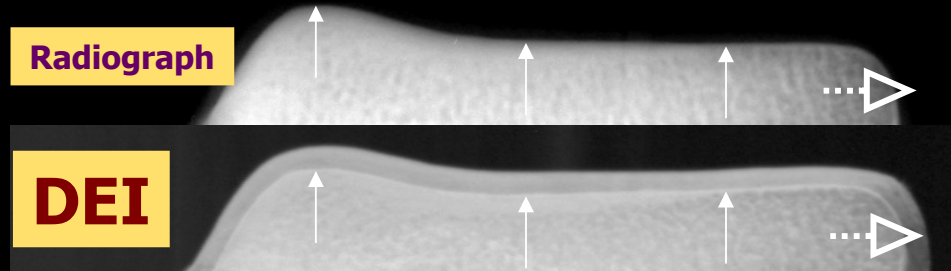
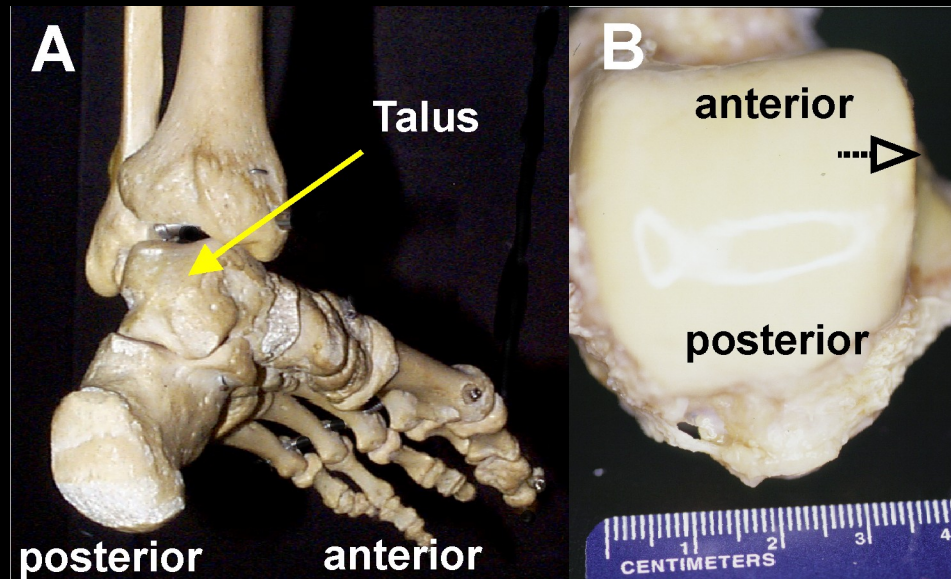
What's the OA drug development problem?

- Current methods inefficient, costly, and ineffective
 - ◆ Numerous animal and human studies
 - ★ Linear vs. statistical studies
 - ★ Human studies subjective
- Ideal - measure the disease state of cartilage over time in a single subject
- Current imaging techniques are costly or cannot visualize the state of the cartilage *in vivo*

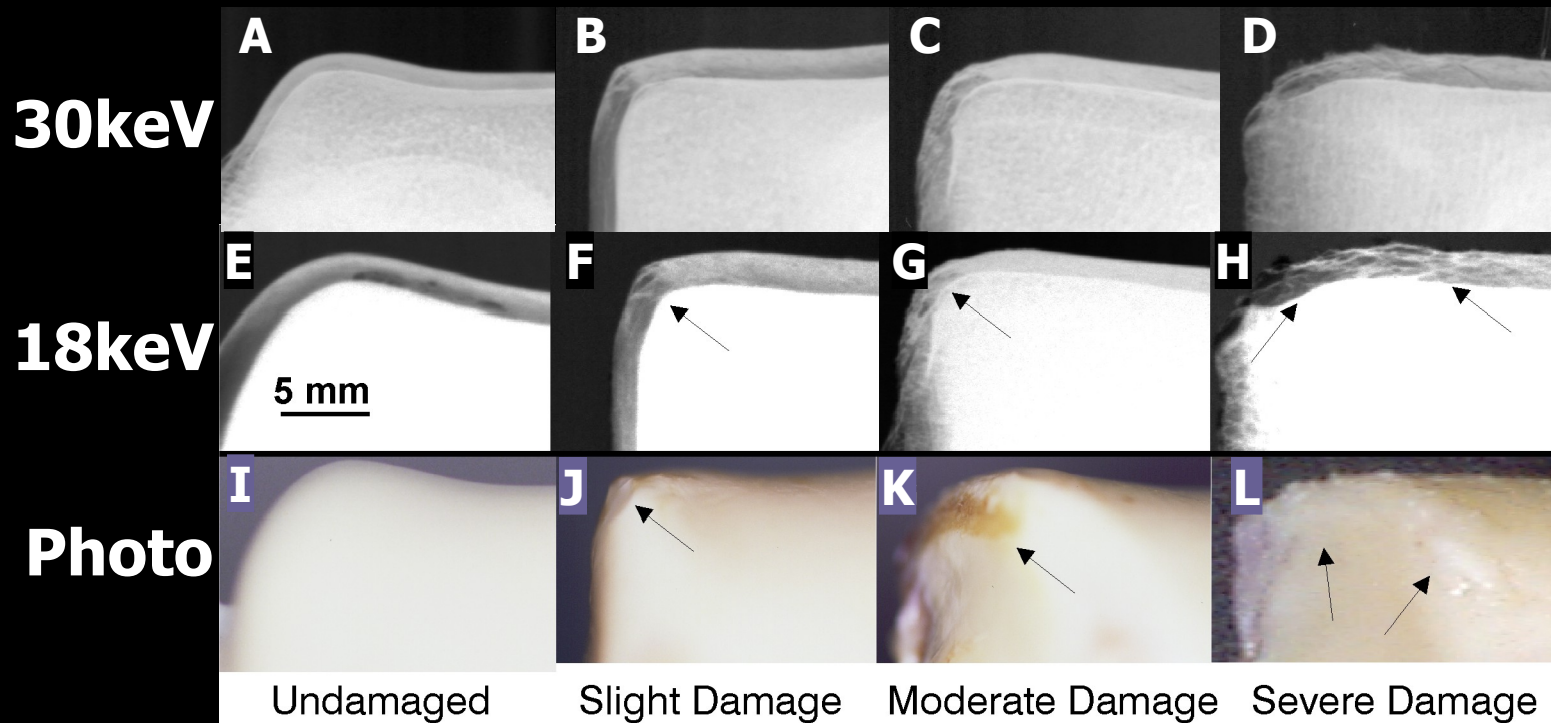
What's the solution?

- We will offer the drug industry an analytical method that tracks the effect of OA on cartilage in animals and humans
 - ◆ DEI offers a more effective and faster route to development of drugs with the potential to reverse OA
 - ★ Reduced number of animal and human studies
 - ★ Provides objective data for improvement of cartilage
 - ◆ Avoids ethical issues

DEI visualizes state of cartilage



What do we deliver?



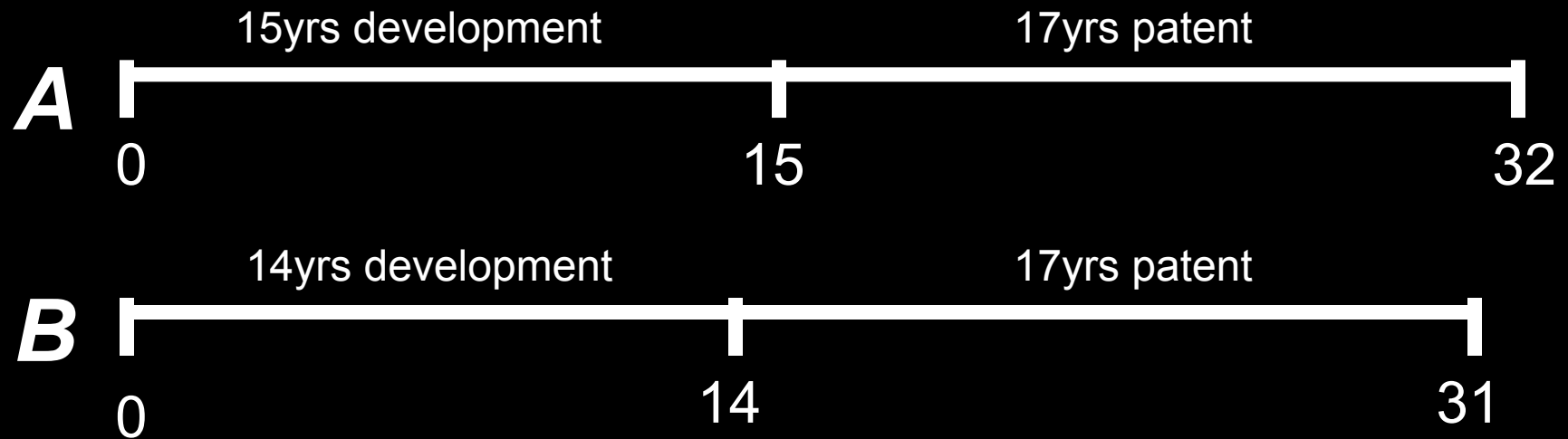
Why are we the A-Team?

- 130 Person-years of synchrotron radiation research experience at APS
- Development of intellectual property in DEI
- Experience at human imaging facilities at synchrotrons
- Successful experience in building and operating an industrial research consortium at the APS
- 14 Ph.D.'s in OA research at Rush
 - ◆ Largest academic OA research group in the world
- Glaxo-SmithKline (GSK)
 - ◆ Major player in OA drug research / development

What are the unique benefits of DEI?

- Only cost-effective imaging technology that can visualize tissue in its diseased state
- Supports the development of arthritis-reversing drugs
 - ◆ Current drug therapies simply reduce inflammation and pain
- Reduction of time to drug discovery significantly improves net present value

Why would a drug company care?



- Assumptions for B:
 - ◆ \$30 million initial investment
 - ◆ \$2 million per year operations cost
- B takes one year out of the drug development time
 - ◆ @ 15% discount rate, NPV = \$39 million
 - ◆ @ 10% discount rate, NPV = \$100 million

Who's interested?

- Drug companies interested in development of OA drugs
 - ◆ Commercial discussions in progress with GSK
- Why they should be interested:
 - ◆ Access and experience with synchrotron technology
 - ◆ Patented technology in DEI and the application to cartilage imaging
 - ◆ Collaboration with medical experts at Rush Medical College
 - ◆ Provide objective proof of drug efficacy that speeds up the regulatory process
 - ◆ Impractical to develop internally

How big is the market?

- At least 7 drug companies who presently offer products in this market space
- Total Market Size - 16-27 Million patients who suffer from OA
- Current Drug Sales: > \$10 Billion
 - ◆ Celebrex sales increased from \$1.5 billion in 1999 to \$2.6 billion in 2000
- We estimate sufficient value to persuade GSK to make a one-time payment of \$30 million and ongoing payments of \$2 million per year

What's our marketing strategy?

- In the long run, offer better patient-monitoring technology useful in other drug development studies
- Also in the long run, develop clinical version of DEI
- OA is initial target
 - ◆ GSK is early adopter of technology
- Pricing based on:
 - ◆ Cost savings in the drug discovery process sets the maximum
 - ◆ Supporting facility costs and contribution to ongoing academic research sets the minimum
- Will invite GSK to participate in the demonstration of the effectiveness of DEI

Who might compete with us?

- Experts at Rush state MRI is the only alternative to DEI
 - ◆ MRI can visualize state of cartilage as well as DEI
 - ◆ Significant disadvantages:
 - ★ Time consuming
 - ★ Complete immobilization necessary for some images
 - ★ Costly
- Conventional X-ray:
 - ◆ Cartilage damage is inferred by joint space narrowing
 - ◆ Good spatial resolution, but cannot see cartilage
- Other Synchrotrons:
 - ◆ Would lack partnership / expertise of APS, CSRRI-IIT, Rush, and GSK

What commercialization options did we consider?

- License patents to drug companies
- Operate a non-profit university / national laboratory / medical school / drug company consortium
 - ◆ Academic Model
- Start a for-profit business

What are the economics of our choice?

- Start-up Cost: \$30 Million over 2 years
 - ◆ To be requested from GSK
- On-going Operating Cost: \$2 Million / year
- Projected revenue

What comes next?

- Need capital for:
 - ◆ Building animal and human imaging facility
 - ◆ Commissioning, shake down, and demonstration
- Staffing (12)
- Product and business development plan:
 - ◆ Sales literature
 - ◆ Agreements / Contracts
 - ◆ Presentations
- Planar / CT development
- Negotiate final agreement with GSK

What could cause us to fail?

- Lack of regulatory approval
 - ◆ IACUC (Animals) & HSRC (Humans)
 - ◆ Analogous synchrotron radiation exposure has been approved in both the US and Europe
- Drug testing for arthritis-reversal fails
 - ◆ Other applications may appeal to drug companies
- Significant initial capital investment may be refused by drug company partner
 - ◆ Offer DEI to other companies
 - ◆ Create a consortium of drug companies
- Cheaper and faster MRI
- Unanticipated new technology may arise

Summary and Conclusions

- Many people suffer from OA
- Many drug companies are pursuing drugs that may reverse debilitating effects of OA
- We have an attractive value proposition
- Technology is developed and demonstrated
- This technology may ultimately lead to early detection of OA and intervention in the disease process
- Long term, this new approach in drug discovery has numerous applications beyond OA

The Team

- EnPro Team:

- ◆ Manoj Dalmia
- ◆ Yugenia Hong
- ◆ Padma Sresty
- ◆ Paul Hung
- ◆ Edward Morrison
- ◆ Stephen Johnson
- ◆ Brian McGuire
- ◆ Sarjan Patel
- ◆ Monali Patel
- ◆ Ajay Bhatt

- Business Team:

- ◆ Robert Anderson
- ◆ Dean Chapman / CSRRI - IIT
- ◆ Carol Muehleman / Rush
- ◆ APS
- ◆ GSK

What are the current treatments available?

- Important to remember that OA is an entire joint disease
- Exercise
 - ◆ Swimming - strengthen rest of joint (stabilization)
- Lifestyle changes
- Physical therapies
- ***Must keep repetitive compression of cartilage to avoid further degradation***