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?

30keV

18keV

Photo

- **A**
- **B**
- **C**
- **D**
- **E**
- **F**
- **G**
- **H**
- **I**
- **J**
- **K**
- **L**

**Undamaged**  **Slight Damage**  **Moderate Damage**  **Severe Damage**

5 mm
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:
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- Business Team:
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  - 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***