HST.979J/15.123J Spring 2014 Syllabus
Dynamics of Biomedical Technologies

Course Faculty

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Carl Berke, Ph.D.	cberke@partners.org	Tel: 617-954-9358
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Teaching Assistant

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Course Secretary

Candance Weaver	cmweaver@mit.edu	Tel: 617-253 0009

Course Overview

Traditional businesses often start from a novel technology or solution and attempt to shoehorn it into a market. Because the need is neither clear nor compelling, the result is often a fundamentally weak business. In this class, teams of students evaluate a clinical need and learn an effective process for turning this need into a business. Topics in the course include alternative solutions, intellectual property protection, market opportunity, regulatory and reimbursement hurdles, competitive threats and potential return on investment. Students are encouraged to interview key individuals including clinicians, potential customers, other stakeholders, consultants and competitors. Students will also have the opportunity to shadow physicians in a clinical setting. Students will present a series of analyses and solutions to each of the critical issues faced in constructing a business to address the identified need.

Tuesdays 4:00 – 6:30 PM; February 4 – May 13, 2014; Room E25-119/121

Class Schedule

Check Stellar for Homework Assignments Due for Each Class!

02/04/14 Needs Finding

4:05 – 4:20	**Course Introduction**	**Richard Cohen**
4:20 – 6:30	**Needs Finding**	**Richard Anders & Josh Tolkoff**

Reading assignment in Biodesign text to be completed prior to class:

1.1: Strategic Focus
1.2: Observation and Problem Identification
1.3: Need Statement Development
2.1: Disease State Fundamentals

02/11/14 Needs Screening

4:05 – 4:30	**Discussion of Reading and Homework**	
4:30 – 6:30	**Need Screening**	**Richard Anders & Josh Tolkoff**

Reading assignment in Biodesign text to be completed prior to class:

2.2: Treatment Options
3.1: Ideation and Brainstorming
3.2: Concept Screening

2/18/14 7 – 10 PM Brain Storming Session

7:05 – 7:40	**Introduction to Brainstorming**	**Josh Tolkoff, James Rudolph**
7:45 – 9:00	**Brainstorming in Teams**	
9:05 – 10:00	**Team Presentations of Brainstorming Discussions**	

Reading assignment in Biodesign text to be completed prior to class:

2.3 Stakeholder Analysis
2.5: Needs Filtering
4.6 Final Concept Selection

02/25/14 Need Presentations and Market Assessment

4:05 – 5:25	**Need Presentations by Teams**	
5:30 – 6:30	**Market Assessment**	**Bob LaRoche**

Reading assignment in Biodesign text to be completed prior to class:

2.4: Market Analysis
4.4: Business Models
5.7 Marketing and Stakeholder Strategy

03/04/14 Business Plans/Finance

4:05 – 4:30	**Discussion of Reading and Homework**	**Faculty**
4:30 – 5:05	**Business Plans/Story Telling**	**Richard Anders & Josh Tolkoff**
5:10 – 6:30	**Finance**	**Richard Anders, Josh Tolkoff, Carl Berke**

Reading assignment in Biodesign text to be completed prior to class:

6.1 Operating Plan and Financial Model
6.2: Business Plan Development
6.3: Funding Sources
6.4: Licensing and Alternate Pathways

03/11/14 Interim Team Presentations

4:05 – 6:30	**Interim Team Presentations**

Reading assignment in Biodesign text to be completed prior to class:

None

03/18/14 SIP Week

No Class

03/25/14 Spring Break

No Class

04/01/14 IP & Product Development

4:05 – 5:25	**Intellectual Property**	**Carl Berke**
5:30 – 6:30	**Product Development**	**Jeffrey Cerier**

Reading assignment in Biodesign text to be completed prior to class:

4.1 Intellectual Property Basics
4.5 Prototyping
5.1 Intellectual Property Strategy
5.2 Research and Development Strategy

04/08/14 Regulatory/Strategy

4:05 – 4:30	**Discussion of Reading and Homework**	**Faculty**
4:35 – 5:30	**Regulatory**	**Allan Greene**
5:35- 6:30	**Strategy**	**Bill Edelman**

Reading assignment in Biodesign text to be completed prior to class:

4.2: Regulatory Basics

5.3: Clinical Strategy

5.4 Regulatory Strategy

04/15/14 Sales & Marketing

4:05 – 4:30	**Discussion of Reading and Homework**	**Faculty**
4:35 – 5:30	**Sales and Marketing – Devices**	**Tom Burns**
5:35 – 6:30	**Sales and Marketing – Drugs**	**Brad Prosek**

Reading assignment in Biodesign text to be completed prior to class:

5.8: Sales and Distribution Strategy

5.9: Competitive Advantage and Business Strategy

04/22/14 Patriots Day Holiday for MIT Students

No Class

04/29/14 Reimbursement/Insurance

4:05 – 4:30	**Discussion of Reading and Homework**	**Faculty**
4:35 – 5:30	**Reimbursement**	**Ed Berger**
5:35 – 6:30	**Healthcare Insurance**	**Garrett Parker**

Reading assignment in Biodesign text to be completed prior to class:

4.3 Reimbursement Basics

5.5 Quality and Process Management

5.6 Reimbursement Strategy

05/06/14 Corporate Narratives

4:05 – 4:30	**Discussion of Reading and Homework**	**Faculty**
4:30 – 5:30	**Cytyc**	**Stan Lapidus**
5:35 – 6:30	**LumeRx**	**Josh Tolkoff**

Reading assignment in Biodesign text to be completed prior to class:

Acclarent Case Study: pages 51-55, 165-171, 205-206, 378-379, 596-608, 727-733

05/13/14 Final Team Presentations

4:05 – 6:30	**Final Team Presentations**

Reading assignment in Biodesign text to be completed prior to class:

None

Course Notes

Homework

- Homework includes assigned reading, preparation of short (up to 500 words) response papers to assigned questions, weekly individual survey, and preparation of formal in-class presentations (see Student Teams below).
- Readings are mandatory, must be completed prior to class and will serve as the basis for in-class discussion.
- Response paper questions will be posted on Stellar at least one week prior to each class. Response papers should be succinct. Comments may be bulletized as appropriate. Response papers, unless otherwise specified, are individual assignments and collaboration is not permitted.
- Individual survey questions should be answered in a very brief and succinct manner.
- Response papers and weekly individual survey must be submitted by 9 AM on the due date so that faculty has time to review them in preparation for the in-class discussion. Use Google docs form: https://docs.google.com/forms/d/1XfjaMzCVmoaUYOfk-fy_-eV2IlXBNKP3xv14yC9EKE0/viewform Sample completed Google Docs form will be posted on course website.

Student Teams

All students will be assigned to teams. Each team will be assigned a clinical need from the list provided below in this document. Students may request which team they would like to join, but course staff will make the ultimate assignments to ensure team balance. If a team would like to work on a need not on the list, the team may propose the need which will be reviewed by the course staff. It is expected that teams will work throughout the semester on their team projects to specify the clinical need, propose a product or service that addresses that need, and develop a business plan to develop and commercialize that product or service. Proposed products or services may be speculative but should be at least plausible. The emphasis in this course is how one might build a business around a proposed product or service. Teaching assistant and course faculty are available to assist students. Students should also consult with their physician subject experts and reimbursement, regulatory and IP consultants listed below. Students should identify and contact other individuals who may assist them with their project and also access the scientific and business literature (see Information Sources below).

Students will present their findings formally in several in-class presentations. Presentation slides must be posted on the course Stellar website by NOON on the due date. This is particularly important so that all slides can be preloaded for presentation prior to class. Time limits will be enforced with comments and questions held until after presentation. All team members must participate approximately equally in each presentation. Presentations represent a team effort and collaboration is required. Adherence to time limits is a team responsibility.

Weekly student surveys will include questions about individual contributions to the team effort. In addition, a team survey will allow each team to report periodically overall team progress.

Physician Shadowing

We will attempt to make available opportunities for physician shadowing for interested students. There are a number of forms and medical clearances that must be completed. Please sign up only if willing to make a significant time commitment.

Course Grading

- Homework (response papers) 25%
- Class Participation 25%
- Interim Class Presentations: 25%
- Final Presentation: 25%

Course Enrollment

This course is limited to 24 students. Sloan students who have successfully bid for the course will be guaranteed a spot.

Information Sources

Students are encouraged to pursue all relevant sources of information for their analyses. This may normally involve discussion with physicians and specialty consultants and any other sources that those individuals can provide. Scientific literature, patent literature, clinical literature, and marketing materials are fair game. Interviews with experts in the field, users, payers, potential competitors, and course faculty are also all appropriate.

Class Attendance

It is expected that every student will attend every class. If a student must miss a class for any reason, that student must submit a 500 word paper related to one of the topics covered in class that day. All submissions are due one week after the missed class. If a student must miss more than one class for any reason, please speak to Professor Cohen within the first week of class for advance permission.

It is expected that no student will miss the opportunity to participate in the team presentations. If you anticipate a conflict, please let the teaching assistant and Professor Cohen know well ahead of time.

Sloan Professional Standards

We subscribe to the MIT Sloan professional standards and MIT's standards of Academic Integrity. Please arrive on time for class with uninterrupted attendance for the duration of the class. Furthermore, please maintain a professional atmosphere. This includes, but is not limited to, silencing and not using computers or mobile electronic devices during class.

Course Text (Required) – free access to text book PDF's through stellar site

Biodesign: The Process of Innovating Medical Technologies by Stefanos Zenios, Josh Makower, Paul Yock, Todd J. Brinton, Uday N. Kumar, Lyn Denend ,Thomas M. Krummel. Cambridge University Press, 2010.

Website

Course materials available in electronic format will be posted on the course's website located on the MIT Stellar Course Management System.

Needs Statement Team #1

Team 1: A better way to alleviate lower back pain

In the US, lower back pain is one of the most common conditions and one of the leading causes of physician visits. In fact, at least four out of five adults will experience it at some point in their lives.

Ironically, the severity of the pain is often unrelated to the extent of physical damage. For example, lower back spasms from a simple back strain can cause excruciating lower back pain that can make it difficult to walk or even stand, whereas a large herniated disk or completely degenerated disk can actually be completely painless.

There are conservative treatments for back pain, such as chiropractic, cortisone injections or acupuncture. Although people may report short-term relief from such treatments, there is no evidence that ongoing use of such treatments is effective. Surgery may be indicated when conservative treatment or rest is not effective in reducing pain or when the patient develops progressive and functionally limiting neurologic symptoms such as leg weakness, bladder or bowel incontinence, which can be seen with severe central lumbar disk herniation. The most common types of low back surgery include diskectomy (and microdiskectomy), laminectomy, foraminotomy, or spinal fusion.

However, while surgery for those with neurologic symptoms is often effective in reducing those symptoms, there is ongoing controversy as to whether spinal fusion or other surgery actually improves outcomes in simple chronic low back pain.

There are several difficulties for the surgeon dealing with back pain. First, merely identifying the underlying cause of the pain can be quite challenging. Scans of a patient can show a number of potentially painful problems (e.g. ruptured disks) which in fact do not cause problems. Without properly identifying the pain, it is very difficult to treat. Second, many of the back surgeries now used for patients present their own problems. For example, spinal fusions (in which one or more disks are removed and the adjacent vertebrae 'fused' through such things as bone chips) are known to create stresses that over time weaken adjacent disks. Finally, back pain is believed to be a long-term process that may start with a [relatively painless and self-limiting] disk rupture and years later lead to severe arthritis in the facet joints. For most patients there is no easy way to determine that they have had a serious acute event that will eventually lead to problems.

To illustrate the problems, consider diskectomy surgery:

Diskectomy Surgery
- The most common spinal surgery, with over two hundred thousand diskectomies for pain annually;
- Rationale: Disk material leaks through the annulus, potentially causing leg and back pain;
- Forty percent failure rate one year after surgery;
- Seventy-five percent have ongoing back pain after surgery;
- Two billion dollars annually in re-operation costs;
- Eight hundred million dollars annually in ongoing disability;

These ongoing issues in diskectomy and other surgeries lead to our proposed need:

Proposed need: A more effective and less costly means to treat or prevent lower back pain.

Needs Statement Team #2

Team 2: Reducing post-procedure bleeding

- Bleeding is a common problem after a wide variety of surgical procedures (e.g. vascular, GI, orthopedic) and is a major cause of surgical morbidity and mortality. For example, in observational studies 5.6% of patients were found to have bleeding within an 8 hour window after kidney biopsy, tonsillectomy morbidity from post-procedure bleeding is 2-5%, etc.

- Improved pre-operative and post-operative patient management (e.g. measurement and management of clotting function and avoidance of drugs that reduce clotting or irritate the GI tract) may reduce post-procedure bleeding.

- Improved closure technologies may reduce post-procedure bleeding.

- More careful surgery may reduce inadvertent injuries that cause bleeding.

- Better detection of bleeding may lead to earlier intervention to reduce the bleeding.

- Post-procedure bleeding remains a major problem.

Proposed need: Better early detection of bleeding to guide intervention and/or better ways of preventing bleeding.

Needs Statement Team #3

Team 3: Outpatient Management of Heart Failure

- Approximately 5 million patients in the United States suffer from congestive heart failure (CHF).
- Patients with CHF are managed with medical therapy and some also with device therapy.
- Decompensation symptoms include fluid retention and shortness of breath that can lead to emergency hospitalizations.
- 3.5 million annual hospitalizations for CHF account for ~$10Bn in health care spending
- Current clinical means of monitoring heart failure status in order to adjust therapy are inadequate to prevent recurrent decompensation in many patients.

Proposed need: A practical way of improving management of CHF patients to reduce hospitalizations for decompensation of their heart failure.

Needs Statement Team #4

Team 4: Management of Advanced Parkinson's Disease

- Prevalence of Parkinson's Disease is about 0.3% globally in industrialized countries. That figure rises to about 1% in people over 60, and 4% in people over 80.

- "Parkinson's disease (PD) belongs to a group of conditions called motor system disorders, which are the result of the loss of dopamine-producing brain cells. The four primary symptoms of PD are tremor, or trembling in hands, arms, legs, jaw, and face; rigidity, or stiffness of the limbs and trunk; bradykinesia, or slowness of movement; and postural instability, or impaired balance and coordination. As these symptoms become more pronounced, patients may have difficulty walking, talking, or completing other simple tasks. PD usually affects people over the age of 50. Early symptoms of PD are subtle and occur gradually. In some people the disease progresses more quickly than in others. As the disease progresses, the shaking, or tremor, which affects the majority of PD patients may begin to interfere with daily activities. Other symptoms may include depression and other emotional changes; difficulty in swallowing, chewing, and speaking; urinary problems or constipation; skin problems; and sleep disruptions."

(http://www.ninds.nih.gov/disorders/parkinsons_disease/parkinsons_disease.htm) (PDF available on course site)

- Many patients eventually suffer from dementia.

- Currently, the mainstay of the management of Parkinson's disease is pharmacologic therapy with dopaminergic agents as well other drugs. The pharmacologic management of these patients becomes more challenging as the disease progresses involving multiple medications and frequent dosing. The therapeutic window narrows as the disease progresses making it difficult to titrate the medications and also the patient's response to the medications continually fluctuates. Under these circumstances, periodic visits to a neurologist are inadequate to achieve the optimal titration of the medications. Adverse consequences may include falls leading to hip fracture or the patient being restricted to chair or bed in an institution.

Proposed need: An improved means of managing medical therapy of patients with advanced Parkinson's disease to reduce falls and institutionalization while maintaining maximum possible mobility.

Needs Statement Team #5

Team 5: Better management of breast cancer

- **Breast Cancer is a common cancer:** About 1 in 8 women in the US will develop invasive breast cancer at some point in their lives. 30% of cancers in women are breast cancer. In 2011, there were more than 2.6 million breast cancer survivors in the US. (http://www.breastcancer.org)
- **Early detection/treatment of breast cancer:**
  - The current clinical paradigm for the reduction of breast cancer morbidity and mortality is early diagnosis and treatment.
  - The current standard for early diagnosis of breast cancer is Xray mammography followed by needle or open surgical biopsy of suspicious areas.
  - Xray mammography suffers from a false negative rate of approximately 20% and a false positive rate of approximately 65%.
  - Recently, there has been controversy over mammogram guidelines. The American Cancer Society recommends yearly mammograms starting at age 40, clinical breast exam about every 3 years for women in their 20s and 30s and every year for women 40 and over. Women should self-examine their breasts starting in their 20s. However, the U.S. Preventive Services Task Force (USPSTF) (a group of independent health experts convened by the Department of Health and Human Services), reviewed and commissioned research and recently proposed alternative guidelines: starting routine screening at age 50, ending it at age 74, having mammograms every two years (instead of yearly), and that self-exams have little value.
  - According to the Cochrane Collaboration,"(F)or every 2000 women invited for screening throughout 10 years, one will have her life prolonged. In addition, 10 healthy women, who would not have been diagnosed if there had not been screening, will be diagnosed as breast cancer patients and will be treated unnecessarily. It is thus not clear whether screening does more good than harm." http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD001877.pub4/abstract;jsessionid=EC07EED77A8610696E10B83EE6B8C6F3.d02t01 (PDF on course website of brochure for the layman)
  - A recent article in the New England Journal of Medicine found that "Despite substantial increases in the number of cases of early-stage breast cancer detected, screening mammography has only marginally reduced the rate at which women present with advanced cancer." The authors conclude that mammography largely detects tumors that would not have progressed or could have been successfully treated when detected at a later stage. N Engl J Med 2012;367:1998-2005.
- **Breast Cancer Treatment**
- Breast cancer treatment often involves surgical removal of the tumor, local radiation therapy and chemotherapy.
- The standard procedure today is to remove tissue during surgery that is sent to a pathology lab to examine for cancer cells, either during or after surgery. If the margins are not clear, the physician may have to re-operate. This is a laborious and not fully accurate procedure to determine whether the margins are clear of tumor cells.
- There are needs to improve diagnostic methods to detect and monitor the presence of breast cancer (local and metastatic) during treatment as well as for improved chemotherapy.

Proposed need: Improved methods for the screening, diagnosis and treatment of breast cancer.

Needs Statement Team #6

Team 6: Drug Compliance

A 2007 Report from the National Council on Patient Information and Education (http://www.intelecare.com/downloads/ncpie-adherence-report.pdf) made the following observations:

- According to the World Health Organization (WHO), only about 50 percent of patients typically take their medicines as prescribed. For this reason, WHO calls poor adherence rates "a worldwide problem of striking magnitude" and has published an evidence-based guide for health care providers, health care managers, and policymakers to improve strategies of medication adherence.
- In the US, a survey commissioned by the National Community Pharmacists Association (NCPA) reported that nearly three out of every four American consumers report not always taking their prescription medicine as directed. This survey found that:
    - Almost half of those polled (49 percent) said they had forgotten to take a prescribed medicine;
    - Nearly one-third (31percent) had not filled a prescription they were given;
    - Nearly three out of 10 (29 percent) had stopped taking a medicine before the supply ran out; and
    - Almost one-quarter (24percent) had taken less than the recommended dosage.
- Lack of adherence affects Americans of all ages and both genders, but is of particular concern among those aged 65 and over who, because they have more long-term, chronic illnesses, now buy 30 percent of all prescription medicines and often combine multiple medications over the course of a day.
- Poor medication adherence is also just as likely to involve higher-income, well-educated people as those at lower socioeconomic levels.
- Poor medication adherence has been estimated to cost approximately $177 billion annually (2007) in total direct and indirect health care costs.

Proposed need: A means of improving patient compliance in taking prescribed medications.

Needs Statement Team #7

Team 7: Sleep Apnea

A recent scholarly review article on Common Sleep Disorders published by the American Academy of Family Physicians (http://ehis.ebscohost.com/ehost/pdfviewer/pdfviewer?sid=859f24b8-094b-41e6-bdb4-a8aabf2db778%40sessionmgr114&vid=2&hid=105) made the following observations:

- Experts suggest that adults sleep 7-9 hours each night. However, despite these recommendations, studies have shown that the American adults only sleep on average 6.9 hours of sleep. Sleep deprivation can have adverse health affects ranging from impaired immune function, to an increased risk of diabetes, cardiovascular disease, and cancer.
- Obstructive Sleep Apnea (OSA) results from the partial (hypopnea) or full (apnea) closure of a patient's upper airway. Sources often report that OSA affects 4% of men and 2% of women, however these measurements were taken when the diagnosis definition required both elevated apnea index and sleepiness. Many patients do not report sleepiness and over time the definition was modified to remove that requirement. The current prevalence is likely as high as 16% men and 9% women because of the definition change and because often patients go undiagnosed.
- Common signs and symptoms of Sleep Apnea include: snoring, witnessed apnea, gasping, choking, excessive daytime sleepiness.
- If a patient is suspected of having OSA, a sleep study (polysomnography) can be ordered by his/her physician to observe the patient while sleeping. During the test, the number of apneas or hypopneas per hour are recorded.
    - >5+ events per hour establishes a diagnosis of OSA
    - 5-15 per hour -> mild disease
    - 15-30 per hour -> moderate disease
    - >30 per hour -> severe disease
- Portable home monitoring devices can also be used for diagnosis. These devices are cheaper than the polysomnography studies but they have lower accuracy and therefore may not be used for all patients, particularly those with comorbidities.
- Treatment of OSA is commonly continuous positive airway pressure (CPAP). Other treatment may include weight loss, positional therapy, surgery (palate reduction, tongue reduction, stiffening implants, jaw advancement), or other devices (dental appliance, tongue retention device, Provent nasal valves) designed for the mouth or nose.
- Compliance with treatment is often a real problem for patients. 20-50% of patients do not tolerate CPAP treatment. Simply said, patients generally hate the CPAP machines! They are noisy, uncomfortable, unattractive…. Etc!

Proposed need: A cost effective way to improve the diagnosis and/or treatment of patients with Obstructive Sleep Apnea

Needs Statement Team #8

Team 8: Prostate Cancer

A recent scholarly review article on Prostate Cancer published by the Scientific World Journal highlighted key difficulties with current Prostate Cancer diagnostics and treatment: http://dx.doi.org/10.1155/2013/347263

- Prostate Cancer (PCa) is currently the 2nd leading cause of death for men. But despite this fact, the cancer tends to be very slow-growing and the overwhelming majority of PCa-positive men die "with the disease, not from it."
- Most men diagnosed with PCa are above the age of 60. Typically, men are diagnosed after receiving a PSA (prostate-specific antigen) blood test ordered by their PCP.
- Screening is typically followed by an uncomfortable transrectal ultrasound guided biopsy procedure (TRUS-bx), to diagnose PCa. Cancerous lesions in the gland are often diffuse and hard to image. As a result, the biopsy procedure is known to have low predictive accuracy with the needles often missing cancerous lesions.
- Biopsy samples are graded and given a Gleason score to measure how invasive the cancer is believed to be. Scores above 7 are typically treated more aggressively.
- The current screening test (serum prostate-specific antigen - PSA) is highly controversial as it has a high false positive rate which can lead to an excessive number of biopsies which are invasive, expensive and uncomfortable. And some studies have also shown that early diagnosis and treatment of even PCa-positive patients may not improve overall survival rates.
- There is an evolving controversy over whether to screen using PSA. The American Cancer Society (ACS) recommends that men over 50 years old who are expected to live more than 10 years have a conversation with their physician to understand the current benefits and risks of the PSA screening.
- Current treatment options for PCa include active surveillance (i.e. watching), surgery to remove the prostate (which is generally curative in early stage cancers, but with morbidities that include incontinence and loss of sexual function), external beam radiation therapy, and interstitial radiation therapy (both types of radiation make follow-up surgery much more difficult).

Proposed need: An improved, cost effective way to diagnose and manage patients with prostate cancer.

Primary contacts for Each Team

Below are the primary consultants for each team. Each team should attempt to contact their primary consultants first for advice. However, other consultants, lecturers and faculty are also available to be contacted.

Team 1: Back pain

Subject Expert: Dr. Paul Glazer
Primary Consultants
Regulatory: Howie Golub
Reimbursement: Charles Mathews
Patent: Tom Meyer

Team 2: Post-procedure bleeding

Subject Expert: Dr. Ali Tavakkolizadeh
Primary Consultants
Regulatory: Vicki Anastasi
Reimbursement: Jim Coccia
Patent: DeAnn Smith

Team 3: Heart Failure

Subject Expert: Dr. Lynne Stevenson
Primary Consultants
Regulatory: Bill Morton
Reimbursement: Randel Richner
Patent: Richard Gervase

Team 4: Parkinson's Disease

Subject Expert: Dr. John Growdon
Primary Consultants
Regulatory: Bill Edelman
Reimbursement: Charles Mathews
Patent: Ron Cahill

Team 5: Breast Cancer

Subject Experts: Dr. Harold Burstein, & Dr. Kevin Hughes
Primary Consultants
Regulatory: Howie Golub
Reimbursement: Jim Coccia
Patent: Tom Meyer

Team 6: Drug Compliance

Subject Expert: Mr. David Rose
Primary Consultants
Regulatory: Bill Morton
Reimbursement: Randel Richner
Patent: DeAnn Smith
Additional resources: JD Haldeman & Susan Hogue

Team 7: Sleep Apnea

Subject Expert: Dr. Matt T. Bianchi, MD, PhD
Primary Consultants
Regulatory: Howie Golub
Reimbursement: Charles Matthews
Patent: Richard Gervase

Team 8: Prostate Cancer

Subject Expert: Dr. Chris Cutie
Primary Consultants
Regulatory: Bill Edelman
Reimbursement: Jim Coccia
Patent: Ron Cahill

Subject Experts

Dr. Paul Glazer, MD, surgeon, BIDMC – #1 Back Pain

paulglazer@comcast.com or Assistant: Janet Sterling at (617) 667-2223

Dr. Paul A. Glazer is a board-certified fellowship-trained Orthopaedic Spine Surgeon at Beth Israel Deaconess Medical Center (BIDMC) and Assistant Professor of Orthopaedic Surgery at Harvard Medical School, Boston, MA. He completed an internship in general surgery at St Luke's-Roosevelt Hospital Center and residency in orthopaedic surgery at Orthopaedic Hospital, Columbia University both in New York, NY. His residency included Shriners Hospital for Crippled Children in Springfield, MA. He completed fellowships in research at the New York Orthopaedic Hospital Research Laboratory, New York, NY and in spinal surgery at the University of California at San Francisco, CA.

Dr. Glazer is an active member of several spine societies, including the International Society for the Study of the Lumbar Spine, North American Spine Society, Scoliosis Research Society, and American Academy of Orthopaedic Surgeons. Further, Dr. Glazer's research interests include the evaluation of methods to attain spinal fusion. He has published several articles on the biomechanical stability of instrumentation.

Dr. Ali Tavakkolizadeh, surgeon, BWH - #2 Post-procedure bleeding

atavakkolizadeh@partners.org or (617) 732-6337 general line at BWH

Ali Tavakkolizadeh, MD, is an Associate Surgeon at the Brigham and Women´s Hospital, and an Assistant Professor in Surgery at Harvard Medical School. He specializes in minimally invasive surgery and bariatric surgery. His research focuses on the regulation of the intestinal glucose transporter SGLT1, with the goal of developing less invasive and novel therapeutic approaches for altering intestinal absorptive capacity of glucose in disease states such as obesity and Type II diabetes. Dr. Tavakkolizadeh is a Fellow of the American College of Surgeons, and the Royal College of Surgeons of England. He is a member of many professional societies, including the American Gastroenterological Association (AGA), and the American Society for Metabolic and Bariatric Surgery (ASMBS). He has published peer-reviewed articles and abstracts on the regulation of intestinal SGLT1 expression and function, and serves as an associate editor for "Digestive Disease and Sciences". Dr. Tavakkolizadeh received his medical degree at The London Hospital Medical College in England, and after becoming a Fellow of the Royal College of Surgeons of England (FRCS), completed his surgical and minimally invasive surgery training at the Brigham and Women´s Hospital, Boston.

Dr. Lynne Stevenson, cardiologist, BWH - #3 Heart Failure

lstevenson@partners.org or (617) 732-7406 general line at BWH

Dr. Lynne Stevenson, MD, practices is a Senior Physician, Brigham and Women's Hospital and Professor of Medicine, Harvard Medical School. She specializes in Cardiovascular Medicine. Her research focuses on the elucidation of principles for the therapy of patients with heart failure. She is a member of many professional societies, including the American College of Cardiology (ACC), and the International Society for Heart Transplantation (*ISHT*).

Dr. John Growdon, neurologist, MGH - #4 Parkinson's disease

jgrowdon@partners.org; growdon@helix.mgh.harvard.edu or (617) 726-1728 general line

John Growdon is Professor of Neurology at the Harvard Medical School and attending neurologist at the Massachusetts General Hospital. He graduated from Northwestern University in 1960 with a BA in English Literature and obtained the MD degree from the University of Pennsylvania in 1965. His post-graduate training was in Internal Medicine at the University of Chicago Hospitals (1965-69), in Neurology at the Massachusetts General Hospital (1971-74) and in Neurochemistry at the Massachusetts Institute of Technology (1975-1977). Since 1982, he has directed the Memory and Movement Disorders Units at the Massachusetts General Hospital, which provide diagnostic services and continuing care for individuals with Parkinson disease and related movement disorders, and for individuals with cognitive impairments and dementia, including Alzheimer disease.

Dr. Harold Burstein, oncologist, DF/BWH Cancer Center – #5 Breast Cancer

hal_burstein@dfci.harvard.edu; or (617)-632-3495 office line

Dr. Burstein graduated from Harvard College before earning his MD at Harvard Medical School. He also received a PhD in cellular immunology and a master's degree in the history of science from Harvard. He trained in internal medicine at Massachusetts General Hospital before his oncology fellowship at DFCI. In 1999, he joined the staff of DFCI and Brigham and Women's Hospital, where he is a clinician and clinical investigator in the Breast Oncology Center.

Dr. Kevin Hughes, surgical oncologist, MGH – #5 Breast Cancer

kshughes@partners.org; or (617) 724-4561 office line

Dr. Hughes is the Co-Director, Avon Comprehensive Breast Evaluation Center at Massachusetts General Hospital, and Associate Professor of Surgery, Harvard Medical School. He is a graduate of Dartmouth Medical School, did his surgical residency at the Mercy Hospital of Pittsburgh, and did a fellowship in surgical oncology at the National Cancer Institute. Dr. Hughes is actively involved in research regarding the genetics of breast cancer and is actively involved in the development of Electronic Health Records that decrease clinician workload. He co-authored the HL7, ANSI approved standard for transmitting family health history.

J.D. Haldeman, EVP, Marketing & Sales, Medvantx - #6 Drug Compliance

jd.haldeman@medvantx.com or (858)-964-1497 office line

Jennifer "J.D." Haldeman has served as our Executive Vice President, Marketing, since December 2011, and brings nearly 25 years of commercial experience in strategic planning, new product launches, brand management, sales, managed care, and business development. From 2006 to 2010, Ms. Haldeman served as Chief Commercial Officer of Zogenix, where she developed the commercial strategy and oversaw the tactical implementation of commercial activities for the company's product portfolio of central-nervous system drugs prior to its IPO. Ms. Haldeman has also fulfilled executive leadership roles at other innovation-focused companies including InterMune, Prometheus Laboratories, Tandem Medical, and Shaman Pharmaceuticals in the pharmaceutical, diagnostic, and medical device arenas. She spent the first ten years of her sales and marketing career at Parke-Davis (now Pfizer) where she rose to the level of senior director, Cardiovascular Disease Team, managing a $500 million product portfolio. Ms. Haldeman received a Master's of Management from the J.L. Kellogg Graduate School of Management at Northwestern University and holds a Bachelor of Arts in Philosophy from Brigham Young University.

Dr. Matt Bianchi, M.D., Ph.D, MGH - #7 Sleep Apnea

mtbianchi@mgh.harvard.edu; mtbianchi@partners.org; 855-644-6387

Matt Bianchi MD PhD is in the Sleep Division, Neurology Department, at the Massachusetts General Hospital (MGH). He received his undergraduate degree from Brandeis University (Neuroscience), and his MD and PhD (Neuroscience) degrees from the University of Michigan joint degree program. He also has a Masters in Medical Science from Harvard Medical School. He completed his residency training in Neurology at Partners (combined MGH and Brigham and Women's program), and subsequently completed a fellowship in Sleep Medicine at the Beth Israel Deaconess Medical Center. He is board certified in Neurology and sub-specialty board certified in Sleep Medicine.

Dr Bianchi has an ambulatory clinic in the Sleep Division, and he interprets sleep studies conducted at the nearby Wyndham Hotel Sleep Laboratory. Active research projects focus on sleep disturbances such as insomnia, and the use of home sleep monitoring devices to gather "real world" data about sleep in the home. Dr Bianchi has published in the areas spanning electrophysiology, statistics, decision theory, and sleep.

Christopher Cutie, M.D., MGH - #8 Prostate Cancer

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Dr. Cutie graduated from the University of Pennsylvania with honors, where he majored in anthropology. His thesis project was to study the evolution of concealed ovulation in primates. He then attended medical school at Yale University, where he received the Marguerite Rush Lerner Humanities in Medicine Award. He completed his internship and residency training at Harvard Medical School.

Dr. Cutie spent two years in General Surgery training at the Massachusetts General Hospital. He then completed four years of training in Urology at the Massachusetts General Hospital. This program included training at the Children's Hospital of Boston. He then pursued an oncology fellowship at the Massachusetts General Hospital, where he studied prognostic genomic signatures and their utility in the prediction of prostate cancer recurrence in men who have undergone radical prostatectomy.

Dr. Cutie received a Master's Degree in Business Administration from the Harvard Business School. He is the co-founder of two medical device companies.

Consultants

Regulatory

Vicki Anastasi –Aptiv Solutions

Vicki.Anastasi@aptivsolutions.com or 508-316-7135 direct line

Vicki oversees all business development activities for the company and all activities of the Regulatory Services group, which provides strategic consulting and submission preparation, review and post market compliance support to U.S. and international clients. She has over twenty years of experience in the medical device industry, with over fifteen years specifically focused on device regulation.

Prior to joining MDCI in 2007, Vicki served as director of regulatory affairs at TissueLink, Inc., (now Salient Surgical Technologies) where she was responsible for developing and implementing a U.S. and EU regulatory strategy for medical devices in the electro-surgery market. At Vista Medical Technologies, Inc., an emerging device manufacturer, she served as regulatory affairs manager, responsible for regulatory activities supporting the company's 3-D visualization and information systems to enable minimally invasive surgical solutions in cardiothoracic, head, neck and spine, general surgical and other microsurgical procedures. She is also experienced with in vitro diagnostic products, having held senior positions at ATC Diagnostics, Inc. and bioMerieux Vitek, Inc., where she was responsible for regulatory activities related to infectious disease and genetic-based products. Vicki holds a B.S. in medical technology from the University of Connecticut. She is an active member of AdvaMed and participates in many of the organization's industry working groups.

Bill Edelman – TyRx

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Bill Edelman is a medical device industry executive with over 32 years experience and currently serves as Co- Chairman for ETView, Ltd. (TASE: ETVW) (airway management), Chairman of the Board for PolyTouch, Ltd. (general surgical instrumentation), Medivalve, Ltd. (percutaneous aortic valve placement), and Cardioflow, Ltd. (embolic protection). Mr. Edelman also serves as an Advisor on the Heathcare Board, for Northeast Securities, Inc., a member of the Screening Committee, Medical Devices for Mass Medical Angels, a member of the Advisory Counsel for the Department of Biomedical Engineering at Rensselaer as well as an Advisor to Highland Instruments, Inc., and MindChild Medical, Inc. Mr. Edelman recently served as COB for Stimatix GI, Ltd. (ostomy products).

Mr. Edelman was most recently President & Chief Executive Officer, TYRX, Inc., a commercial stage venture backed medical device company focused in drug/device implant products for general surgery, electrophysiology and cosmetic surgery.

Prior to TYRX, Mr. Edelman held executive level positions at MicroSense International, LLC (bio-sensing), FibraSonics, Inc. (ultrasonic surgical products), NeuroMod, Inc. (neuro-stimulation technologies), St. Jude Medical, Inc. (NYSE: STJ), Pfizer, Inc. (NYSE: PFE), and Baxter International, Inc. (NYSE: BAX). Mr. Edelman graduated with a degree in Biomedical Engineering from Rensselaer Polytechnic Institute. He has been issued 15 U.S. patents and is an applicant on 3 additional pending patent applications.

Howie Golub – Care-Safe

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Dr. Golub is an alum of the H.S.T. - M.D., Ph.D. program (Ph.D. is in Bioelectrical Engineering, and M.D. is class of 1983). He has been a medical device based serial entrepreneur for the first 20 years of his career, and a senior consultant for medical device product development, clinical development, clinical study design and FDA regulatory strategy for the last 15 years.

Bill Morton – Aptiv Solutions

wammdci@comcast.net or 508-878-0200 Cell

Bill has over 30 years of experience in the field of medical device research, development and regulatory science.
Prior to founding MDCI in 1980, he was Director of Regulatory Affairs and Clinical Studies for AVCO Medical Products Division of AVCO Corporation.

Bill has contributed numerous publications to scientific literature, and is a member of the Regulatory Affairs Professionals Society (RAPS), the American Society of Artificial Internal Organs (ASAIO) and the Association for the Advancement of Medical Instrumentation (AAMI). He serves on the editorial advisory boards for Medical Product Outsourcing and Medical Device Technology. He is a past member of the board of directors for RAPS and served as chairman of the regulatory affairs certification board for RAPS from 2003 to 2006. He holds a B.S. in materials science from San Jose State University, is Regulatory Affairs Certified and a Fellow of the Regulatory Affairs Professional Society.

Reimbursement

Charles Mathews – Boston Healthcare

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Mr. Mathews has worked on a variety of reimbursement projects during his 6 years at Boston Healthcare. These projects have involved the analysis of coding, coverage, and payment issues for drugs, diagnostics and medical devices. Mr. Mathews has been the driving force behind the development of both public and private payer strategy and tactical activities for both emerging and established innovators. This includes involvement in the commercialization of over 60 different products in the cancer, diabetes, cardiovascular disease, and infectious disease spaces. Mr. Mathews' prior experience includes several years of working on health policy issues as a legislative aide on Capitol Hill. He also worked for the government affairs office of a biotechnology company and has worked on a National Institutes of Health sponsored clinical trial. Mr. Mathews completed his undergraduate work at Colgate University and received a Masters Degree in Public Policy at Duke University.

Jim Coccia – BioMedical Insights

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Jim Coccia is the Vice President for Commercial Decision Support at Genzyme Corporation. In this role he oversees all commercial analytics and operations for the four business units. These roles include; market analytics, contracting, sales compensation, data and infrastructure, and business process analysis. Prior to this role, Jim led the reimbursement and pricing groups at Genzyme and was instrumental in guiding reimbursement and pricing strategy for their drugs, devices, and biotechnology products both at the local payer and government levels as well as with decisions makers at CMS and specialty societies. Jim has been at Genzyme for 10 years.

Prior to Genzyme, Jim was Director of Reimbursement Strategy for Cambridge Heart (a company that was founded out of MIT work). At Cambridge Heart Jim developed the reimbursement strategy for the Heart Wave technology and successfully implemented the tactics necessary to secure reimbursement, coverage, coding, and high payment for the procedure. Before Cambridge Heart Jim was a senior reimbursement consultant at Health Technology Associates in Washington DC; the leading healthcare reimbursement consulting firm. Jim worked in all areas of economic strategy and consulted on drugs, devices, diagnostics, and biotech products.

Randel Richner – Neocure

richner@neocuregroup.com be persistent with email or call 617-916-2631 office

Randel Richner is the President and Founder of the Neocure Group, a consulting firm specializing in reimbursement, health policy, economics, and government advocacy support for biopharmaceutical and medical technology companies. Randel designed and built the entire government affairs and reimbursement infrastructure for Boston Scientific – both domestically and internationally – in nine years, growing from a single employee to more than 60 worldwide, to drive commercialization success for BSC's diverse product portfolio.

Her extensive experience and long-standing relationships with health care policy-makers in Washington DC, and around the world have allowed her tremendous access to bring visibility to new technologies and to help commercialization.

Patent Attorneys

Tom Meyer – Brown Rudnick

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Tom Meyer is a Partner at Brown Rudnick and a part of their Cleantech Team. Mr. Meyers represents public and private companies, investors, and academic institutions in the life sciences arena. His portfolio of life science companies spans diagnostics, life science tools and technology platforms, genomics and genetics and therapeutics. He also advises companies in these sectors: medical devices (cardiology, orthopedics, neurology, spine), organic and medicinal chemistry (including synthetic

processes, industrial processes, small molecule synthesis, labeling dyes), and optics (fluorescent detection; microscopy). As part of Brown Rudnick's Cleantech Team, Mr. Meyers is also part of collaborative, cross-disciplinary initiatives to assist clients in this evolving sector.

DeAnn Smith – Foley Hoag

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DeAnn Smith is a registered U.S. patent attorney with over 20 years of experience in obtaining worldwide patent protection for clients and advising on matters relating to intellectual property portfolio strategy, including development, implementation and management of intellectual assets. DeAnn's areas of technology expertise include immunology, genomics, proteomics, bio-markers and drug development. She understands the business implications of establishing and implementing intellectual property strategy, having served as in-house counsel for a pharmacogenomic/diagnostic biotechnology client.

Richard Gervase – Mintz, Levin, Cohn, Ferris, Glovsky & Popeo, PC

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A registered patent attorney, Richard regularly counsels companies in the development and protection of their intellectual property portfolios, with a particular emphasis on computer software, medical devices and diagnostics, and he provides advice on intellectual property strategy in general. He also provides patentability, non-infringement, and invalidity opinions in a variety of technology areas and serves on Mintz Levin's Opinion Committee.

Richard has extensive experience performing intellectual property audits and due diligence for high tech and life sciences companies and investors in connection with various commercial transactions, including mergers and acquisitions, private placements and underwritten public offerings. He advises clients in structuring and negotiating a wide variety of technology transactions, including patent, trademark, and copyright licenses, software and database licenses, stock and asset acquisition agreements, strategic alliances, joint ventures, collaboration agreements, sponsored research agreements, and materials transfer agreements. Richard also has substantial experience in the valuation, monetization and securitization of royalty streams and other intellectual property assets.

Ron Cahill – Nutter

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Ronald E. Cahill is a partner in the Intellectual Property Department. He co-chairs the Intellectual Property Litigation practice group and is a member of the Emerging Companies practice group. He concentrates his practice in patent portfolio development, patent litigation in federal courts and related counseling.

Ron also takes lead roles in patent infringement and patent validity opinions, re-examination and re-issue proceedings, patent interferences, corporate intellectual property due diligence undertakings and advising clients in foreign patent opposition proceedings. Ron's practice covers a broad range of technologies. His patent prosecution practice focuses primarily upon software inventions and medical technology.

Guidelines for Hiring a Patent Attorney

General notes on hiring patent attorneys: Legal issues can grind on endlessly, taking up your time and budget. There's a stark difference between attorneys who can manage this effectively by focusing on key business issues and those who will be budget-busting legal perfectionists, spending time and money you do not have.

I. Typical Deliverables
   a. Full search for existing patents and determination of freedom to operate
   b. Where to file patents and timeline of filing-> expiration worldwide
   c. Patent writing, claims crafting, and any subsequent discussion with USPTO
   d. Cost saving strategies, if applicable
   e. Potential licensing negotiations if needed

II. Cost
   a. Range of rates
   b. Types of billing plans (fixed fee for service, deferred costs, ongoing contract, etc)
   c. Typical cost of engagement
   d. What costs are associated with the actual filing

III. Expertise and experiences
   a. Does the attorney have enough experience in similar devices?
   b. Does the attorney have experience in this particular medical area?
   c. Does the attorney have (or need) international experience?
   d. Does the attorney have other resources to draw upon if needed?
   e. Are there any potential conflicts-of-interest with that law firm's other clients?

IV. Mitigation Strategies
   a. What will happen if the attorney doesn't come through or the relationship falters?
   b. How can they ensure a smooth transition in case of a change?

Guidelines for Hiring a Regulatory Consultant

I. Cost
   a. Range of rates
   b. Types of billing plans (fixed fee for service, payment on delivery, ongoing contract, etc)
   c. Typical cost of consulting engagement
   d. Typical cost of trial design

II. Expertise and experiences
   a. Does the consultant have enough experience in devices, especially this type of device?
   b. Does the consultant have experience in this particular medical area?
   c. Does the consultant have (or need) international experience?
   d. Does the consultant have sufficient experience with your product's pathway?
   e. Does the consultant have other resources within their firm to draw on if needed?
   f. Have they developed strategies for companies in addition to the regulatory implementation work?
   g. How successful have they been in getting approvals? On time? On budget?

III. Mitigation Strategies
   a. What will happen if they don't come through or the relationship falters?
   b. How can they ensure a smooth transition in case of a change?

IV. Typical Deliverables
   a. Plan for discussions with FDA
   b. Regulatory pathway (is this a 510(k)?
   c. Assistance with FDA meetings and submissions
   d. Ensure compliance to FDA standards
   e. Engagement with EU / CE Marking
   f. Optional: Clinical development planning and execution
   g. Optional: Quality system / quality assurance support

Guidelines for Hiring a Reimbursement Consultant

I. Cost
   a. Range of rates
   b. Ability to break engagement into appropriate phases/components
   c. Types of billing plans (fixed fee for service, payment on delivery, ongoing contract, etc)
   d. Typical cost of consulting engagement
   e. What costs are associated with attaining reimbursement
   f. What level of involvement is expected from the client

II. Expertise and experiences
   a. Does the consultant have enough experience in similar devices?
   b. Does the consultant have experience in this particular medical area?
   c. Does the consultant have (or need) international experience?
   d. Does the consultant have other resources to draw upon if needed?
   e. Have they developed strategies for streamlined reimbursement of products/ services? Have they developed short as well as longer term strategies?
   f. How quickly can the consultant develop a reimbursement strategy?
   g. Get examples where they have helped develop or modify clinical trials to support the reimbursement strategy.

III. Mitigation Strategies
   a. What will happen if the consultant doesn't come through or the relationship falters?
   b. How can they ensure a smooth transition in case of a change?
   c. What happens in the case of timeline slippage?

IV. Typical Deliverables
   a. Reimbursement landscape analysis and needs assessment
   b. Determine expected reimbursement levels for your product (based on precedents, etc)
   c. Locate existing reimbursement mechanisms and develop new ones
   d. Verify generation of required supporting documentation
   e. Determine relevant clinical and economic endpoints needed to support reimbursement strategy.
   f. Describe/implement path to gaining reimbursement from various payers
   g. Develop ongoing pricing strategy
   h. Develop plan for international pricing (individual EU countries, etc)
   i. Timing for attaining reimbursement