A Study of the Use of Immunohistochemical Stains in an Academic Hospital

by

Sharon Hudspeth

Bachelor of Science Industrial Engineering
California Polytechnic State University, San Luis Obispo

Submitted to the Faculty in partial fulfillment of the requirements for the degree of Master of Science in Engineering and Management at Massachusetts Institute of Technology

May 2016

© 2016 Sharon Hudspeth. All Rights Reserved.
The author hereby grants to MIT permission to reproduce and to distribute publicly paper and electronic copies of this thesis document in whole or in part in any medium now known or hereafter created.

Signature redacted

Author: ..........................................................
Sharon Hudspeth
System Design and Management Program

Certified by: ..........................................................
Gregory Y. Lauwers, M.D.
Vice Chairman, Department of Pathology
Director, Gastrointestinal Pathology Service
Massachusetts General Hospital
Professor of Pathology
Harvard Medical School

Accepted by: ..........................................................
Patrick Hale
Chairman & Senior Lecturer, Engineering Systems Division
Director, System Design and Management Program
Dedicated to the memory of Laurel Hoffman (LGO 2009) who encouraged me to take the first steps on this journey.
A Study of the Use of Immunohistochemical Stains in an Academic Hospital

By

Sharon Hudspeth

Submitted to the System Design and Management Program on May 6, 2016 in Partial fulfillment of the Requirements for the Degree of Master of Science in Engineering and Management.

Abstract

With the passage of the Affordable Care Act (ACA), hospitals are under increased pressure to understand and control cost and quality of care. While there are good metrics for primary care physicians on controlling cost and measuring quality (i.e. tracking glucose levels in a diabetic patient), those measures have not been developed for laboratory medicine. This study examines how the pathology department at Massachusetts General Hospital approached this challenge. Specifically, the study is focused on the use of immunohistochemical (IHC) stains in the pathology department. This paper covers the possible effects of the ACA on laboratory operations, an overview of pathology, and the use of IHC by subspecialty. It will conclude with results of the findings and how they can be leveraged both in and outside the department.

Thesis Supervisor: Patrick Hale
Title: Chairman & Senior Lecturer, Engineering Systems Division
Director, System Design and Management Program
Acknowledgments

Thanks to Massachusetts General Hospital for letting me explore the inner workings of the Pathology department.

Thanks to Dr. Lauwers, Dr. Nosé, Dr. Gudewicz and Nicole Hartford for your time, wisdom and guidance.

Thanks to Pat Hale for all you do.
Table of Contents

Chapter 1: Introduction, Motivation and Goal .............................................................. 6
Chapter 2: Slide preparation ......................................................................................... 8
Chapter 3: Immunohistochemistry Usage and Cost ....................................................... 9
Chapter 4: Hospital Background ................................................................................. 12
Chapter 5: The Pathology Organization .................................................................... 13
Chapter 6: Data Analysis ............................................................................................. 14
Chapter 7: Results ....................................................................................................... 18
Chapter 8: Conclusion .................................................................................................. 24
Appendix A .................................................................................................................. 26
Appendix B .................................................................................................................... 39
Appendix C .................................................................................................................... 52
References ..................................................................................................................... 65

Table of Figures

Figure 1 System Dynamics of ACA and Hospitals......................................................... 7
Figure 2 Specimen Preparation ..................................................................................... 8
Figure 3 IHC Decision Tree ......................................................................................... 10
Figure 4 Sample List of IHC stains and Usage .............................................................. 11
Figure 5 Breast ............................................................................................................. 15
Figure 6 Bone and Soft Tissue .................................................................................... 16
Figure 7 Head and Neck ............................................................................................... 17
Figure 8 Percent of Surgical Cases Requiring IHC Stains ........................................... 18
Figure 9 Average Stain--Dermatopathology ............................................................... 19
Figure 10 Breast Subspecialty Stain Case Ratio ........................................................ 21
Figure 11 Bone & Soft Tissue Subspecialty Stain Case Ratio ..................................... 22
Figure 12 Pulmonary Subspecialty Stain Case Ratio .................................................. 23
Figure 13 Gastrointestinal Subspecialty Stain Case Ratio ........................................ 24
Chapter 1: Introduction, Motivation and Goal

With the passage of the Accountable Care Act (ACA), hospitals have come under pressure to control costs. On October 1, 2013, the Center for Medicare and Medicaid Innovation (CMMI) officially launched the Medicare Bundled Payment for Care Improvement (BPCI) initiative. Under this voluntary pilot program, hospitals, post-acute providers, physician group practices and other organizations assume risk for total spending relative to a target price for up to 48 clinical episodes that begin with an acute-care hospital stay. This means that if the procedure ends up being more costly than the prescribed reimbursement amount the hospital pays the difference, reducing its profits.

The Hospital Readmissions Reduction Program cut payments to hospitals with excessive readmission rates. In 2013 those hospitals saw a 1% reduction in Medicare payments, which rose to 2% in 2014 and will max out at 3% for 2015 and beyond.

The passage of the ACA has had some interesting effect on hospitals. A possible scenario of the system dynamics between the ACA and hospitals could look like this (see Figure 1):

---

1 "Issbrief-Bundledpmt.pdf," http://www.aha.org/content/16/issbrief-bundledpmt.pdf.
Demand on Hospital resources → Quality of care

Newly Insured → ACA roll out

Profit or coverage of cost → Medicare & Medicaid Reimbursement

Amount of internal oversight staffing

Figure 1 System Dynamics of ACA and Hospitals

[Note: Figure 1 shows possible interactions, not forgone conclusions. It is intended to show how changing conditions could interact with each other. Once these interactions are understood, then action can be taken to either increase positive results or mitigate negative ones.] As the figure illustrates, when the ACA is put in place, more insured people enter into the healthcare system which in turn, places more demand on hospital resources. The healthcare industry in the US is facing an acute shortage of expertise. The quality of care has a potential to decrease as a result of the strain on the system. If this happens, the quality score for the hospital decreases, which reduces the amount of reimbursement it gets from Medicare and Medicaid. This in turn limits the amount of money the hospital has to affect control over the situation, which in turn further reduces the quality of care. In the meantime in order to cope with this new reality, hospitals have increased staffing for internal oversight which also takes a toll on the earnings.

Bernstein, Lenny, “U.S. Faces 90,000 Doctor Shortage by 2025, Medical School Association Warns - The Washington Post.”
With the financial pressures being brought to bear, hospitals are needing to understand and control their cost drivers. This study focuses on how one department (pathology) in one hospital (Massachusetts General Hospital, MGH) has faced this challenge.

The goal of this study is to understand variability in use of immunohistochemical (IHC) stains by pathologist by subspecialty. Stains are used by pathologists to provide contrast to the tissue being examined. The use of these stains can be a crucial component in providing additional information that can lead to a more accurate diagnosis. The following chapters will explain how they are used and their associated costs.

Chapter 2: Slide preparation

The following flowchart is a high-level depiction of the steps to prepare a specimen into a slide that a pathologist will examine:

![Flowchart](image)

Figure 2 Specimen Preparation

Specimens are received (accessioned) and entered into the system. Cassettes (a small perforated container) are printed with the case number and a barcode for tracking purposes. From there they are grossed (described by size, appearance, texture, weight, etc.) and a cut section of the specimen is put in the cassette. The cassette is put in formalin solution to be fixed (stop the decay process). Cassettes get gathered up and put in a processor to dehydrate the specimen and prepare it for embedding. Embedding involves the specimen being put in a wax mold in the correct orientation for a representative cut to be obtained. These 'blocks' then are cut to form a ribbon approximately 3-5μm thick. This then is then put on a slide. The slide goes into an oven to dry and melt off the wax. The slide is then stained. The basic nature of histology slide staining is to stain the slide with two or more contrasting dyes that will highlight specific areas or entities with one color, and leave a counterstaining background color. In histology, the standard or "routine stain" is the hematoxylin and eosin stain, better known as the
“H&E” stain. This provides the pathologist/researcher a very detailed view of the tissue. It achieves this by clearly staining cell structures including the cytoplasm, nucleus, and organelles and extra-cellular components. This information is often sufficient to allow a disease diagnosis based on the organization (or disorganization) of the cells and also shows any abnormalities or particular indicators in the actual cells (such as nuclear changes typically seen in cancer).  

Chapter 3: Immunohistochemistry Usage and Cost

While the H&E stain is the standard stain, it is not the only option for pathologists to use to give a diagnosis. When a tissue sample is passed to a lab to be examined for disease, there are several details that cannot be determined easily. Several diseases or disease sub-types may look alike or appear to have similar size cells under a microscope but have different behaviors and necessary treatments. The best way to differentiate them is to detect specific molecules on these cells that act as markers. IHC is the process whereby antibodies are used to detect proteins (antigens) in cells within a tissue section (for instance liver, pancreas or the heart).

Immunohistochemistry has found numerous applications in medicine, especially in cancer diagnosis. Lymphomas are among the cancers most dependent on IHC for correct diagnosis and treatment decisions. 

---

4 “HEMATOXYLIN & EOSIN’ (The Routine Stain).”
5 Anderson, “An Introduction to Routine and Special Staining.”
6 “What Is Immunohistochemistry.”
Depending on what presents on the slide, a variety of stains may be ordered. Many stains are grouped together, by potential diagnosis, in a panel. The pathologist usually follows some kind of decision tree. Here is an example of how a pathologist may try to work through which stains to order to distinguish what type of tumor exists:

**IMMUNOHISTOCHEMICAL ALGORITHM FOR SMALL-CELL MALIGNANT TUMORS**

*Figure 3 IHC Decision Tree*[^7]

[^7]: Wick, "Immunohistochemical Approaches to the Diagnosis of Undifferentiated Malignant Tumors."
See Figure 4 for a sample list of the stains available and what corresponding diagnosis (primary site) they stain for. As one can see there are many choices.

<table>
<thead>
<tr>
<th>Primary Site</th>
<th>Markers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenal cortical neoplasm</td>
<td>Mart-1, inhibin-α, calretinin, SF-1</td>
</tr>
<tr>
<td>Alveolar soft part sarcoma</td>
<td>TFE3</td>
</tr>
<tr>
<td>Angiomylolipoma</td>
<td>HMB-45, SMA</td>
</tr>
<tr>
<td>Atypical lipomatous tumor</td>
<td>MDM2 (MDM2 by FISH is a more sensitive and specific test), CDK4</td>
</tr>
<tr>
<td>Breast carcinoma</td>
<td>GATA3, ER, GCDFP-15, TFF1, MGB</td>
</tr>
<tr>
<td>Chordoma</td>
<td>Cytokeratin, SI00</td>
</tr>
<tr>
<td>Choriocarcinoma</td>
<td>β-HCG, CD10</td>
</tr>
<tr>
<td>Desmoplastic small round cell tumor</td>
<td>Cytokeratin, CD99, desmin, WT1 (N-terminus)</td>
</tr>
<tr>
<td>Embryonal carcinoma</td>
<td>SALL4, LIN28, OCT4, NANOG, CD30, SOX2</td>
</tr>
<tr>
<td>Endocrineonal adenocarcinoma</td>
<td>PAIX8, p16, CEA, HPV 18, loss of PAX2</td>
</tr>
<tr>
<td>Endometrial adenocarcinoma</td>
<td>PAIX8/PAIX2, ER, vimentin</td>
</tr>
<tr>
<td>Endometrial stromal sarcoma</td>
<td>CD10, ER</td>
</tr>
<tr>
<td>Epitheloid sarcoma</td>
<td>CD14, loss of INI1</td>
</tr>
<tr>
<td>Esophage sarcoma/PE/ET</td>
<td>CD99, HXK2-2</td>
</tr>
<tr>
<td>Follicular dendritic cell tumor</td>
<td>CD21, CD35</td>
</tr>
<tr>
<td>Gastrointestinal stromal tumor</td>
<td>CD117, DOG1</td>
</tr>
<tr>
<td>GI tract, lower</td>
<td>CDH17, SATB2, CDX2, CK20</td>
</tr>
<tr>
<td>GI tract, upper</td>
<td>CDH17, CDX2, CK20</td>
</tr>
<tr>
<td>Hepatocellular carcinoma</td>
<td>ARG1, glycopen-3, HepPar-1, AFP</td>
</tr>
<tr>
<td>Histiocytosis X</td>
<td>CD1a, SI00</td>
</tr>
<tr>
<td>Hyalinizing trabecular adenoma of the thyroid</td>
<td>MIB-1 (unique membranous staining pattern)</td>
</tr>
<tr>
<td>Intrahepatic cholangiocarcinoma</td>
<td>pVHL, CAIX</td>
</tr>
<tr>
<td>Low-grade fibromyxoid sarcoma</td>
<td>mUC4</td>
</tr>
<tr>
<td>Lung adenocarcinoma</td>
<td>TTF1, napsin A</td>
</tr>
<tr>
<td>Mast cell tumor</td>
<td>CD117, tryptase</td>
</tr>
<tr>
<td>Melanoma</td>
<td>ST00, mart-1, HMB-45, MITF, SOX10, PNL2</td>
</tr>
<tr>
<td>Merkel cell carcinoma</td>
<td>CK20 (perinuclear dot staining), MCPV</td>
</tr>
<tr>
<td>Mesothelial origin</td>
<td>Calretinin, WT1, D2-40, CK5/6, mesothelin</td>
</tr>
<tr>
<td>Myeloid sarcoma</td>
<td>CD43, CD34, MPO</td>
</tr>
<tr>
<td>Myoepithelial carcinoma</td>
<td>Cytokeratin and myoepithelial markers. May lose INI1</td>
</tr>
<tr>
<td>Myxoid and round cell liposarcoma</td>
<td>NV-550-1</td>
</tr>
<tr>
<td>Neuroendocrine origin</td>
<td>Chromogranin, synaptophysin, CD56</td>
</tr>
<tr>
<td>Ovarian clear cell carcinoma</td>
<td>pVHL, HNF-1B, KIM-1, PAIX8</td>
</tr>
<tr>
<td>Ovarian serous carcinoma</td>
<td>PAIX8, ER, WT1</td>
</tr>
<tr>
<td>Pancreas, acinar cell carcinoma</td>
<td>Glycopen-3, antitryptin</td>
</tr>
<tr>
<td>Pancreas, ductal adenocarcinoma</td>
<td>mUC5AC, CK17, maspin, SI00P, IMP3</td>
</tr>
<tr>
<td>Pancreas, neuroendocrine tumor</td>
<td>PR, PAIX8, PDIX1, CDH17, islet-1</td>
</tr>
<tr>
<td>Pancreas, solid pseudopapillary tumor</td>
<td>Nuclear β-catenin, loss of E-cadherin, PR, CD10, vimentin</td>
</tr>
<tr>
<td>Papillary RCC</td>
<td>PDS05, RCCma, pVHL, CD10, PAIX8, KIM-1</td>
</tr>
<tr>
<td>Prostate adenocarcinoma</td>
<td>PSA, PSAP, ERG, KIM-1</td>
</tr>
<tr>
<td>RCC, clear cell type</td>
<td>PAIX8/PAIX2, RCCma, pVHL, CD10, KIM-1</td>
</tr>
<tr>
<td>Rhabdomyosarcoma</td>
<td>Myogenin, desmin, MyoD1</td>
</tr>
<tr>
<td>Salivary duct carcinoma</td>
<td>GATA3, AR, GCDFP-15, Her-2/neu</td>
</tr>
<tr>
<td>Seminoma</td>
<td>SALL4, LIN28, OCT4, CD117, D2-40</td>
</tr>
<tr>
<td>Sex cord stromal tumors</td>
<td>SF-1, inhibin-α, calretinin, FOXL2</td>
</tr>
<tr>
<td>Smooth muscle tumor</td>
<td>SMA, MSA, desmin, calponin</td>
</tr>
<tr>
<td>Solitary fibrous tumor</td>
<td>CD34, BCL2, CD99</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>p40, CK5/6, p63, SOX2, desmocollin-3</td>
</tr>
<tr>
<td>Synovial sarcoma</td>
<td>TLE1, cytokeratin</td>
</tr>
<tr>
<td>Thymic origin</td>
<td>PAIX8, p63, CD5</td>
</tr>
<tr>
<td>Thyroid follicular cell origin</td>
<td>TTF1, PAIX8, thyroglobulin</td>
</tr>
<tr>
<td>Thyroid medullary carcinoma</td>
<td>Calcitonin, TTF1, CEA</td>
</tr>
<tr>
<td>Transiational RCC</td>
<td>TTF3</td>
</tr>
<tr>
<td>Urothelial carcinoma</td>
<td>GATA3, UPiA/UPH, SI00P, CK5/6, CK903, p63, CK20</td>
</tr>
<tr>
<td>Vascular tumor</td>
<td>ERG, CD31, CD34, HI-1</td>
</tr>
<tr>
<td>Yolk sac tumor</td>
<td>SALL4, LIN28, glycopan-3, AFP</td>
</tr>
</tbody>
</table>

*Figure 4 Sample List of IHC stains and Usage*

---

8 Lin and Liu, "Immunohistochemistry in Undifferentiated Neoplasm/tumor of Uncertain Origin."
Each time a stain is ordered, there are costs associated with it. Some of the elements that affect costs are:

- Price of reagents
- Lab labor cost
- Cost per hour of a pathologist’s time to interpret an IHC stained slide

Specific cost data associated with this study will be discussed in further detail in Chapter 6.

Chapter 4: Hospital Background

MGH is a not-for-profit hospital located in Boston. It is the original and largest teaching hospital of Harvard Medical School, where nearly all of the staff physicians serve on the faculty. MGH offers sophisticated diagnostic and therapeutic care in virtually every specialty and subspecialty of medicine and surgery. Mass General also conducts the largest hospital-based research program in the United States.9

MGH has a rich history of contributing to the advances of medicine. Here are some of the individuals involved:

John Collins Warren
- One of the two founders of the MGH
- Publications on gross pathology
- First public demonstration of ether anesthesia
- Began the collection that became the Warren Anatomical Museum

John Barnard Swett Jackson
- First professor of Pathology in the United States
- Developed Warren Anatomical Museum, serving as first curator

Oliver Wendell Holmes
- Popularized the use of the microscope at HMS
- May have influenced the purchase of the first microscope at the MGH
- Drew attention to the contagious nature of puerperal fever

John Bacon Jr.
- First Microscopist and Chemist at MGH

Calvin Ellis
- First MGH physician to use the microscope to evaluate anatomical specimens

Reginald Heber Fitz
- First officially designated ‘Pathologist’ at the MGH

9 "Hospitals, Affiliates & Medical Centers | Hospitals & Services | Partners HealthCare."
- Characterized and named ‘appendicitis’ and encouraged its surgical treatment
- Wrote seminal paper on acute pancreatitis

J Collins Warren
- Began recording of microscopic diagnoses in patient records at MGH
- Demonstrated use of biopsy needle and biopsies for patient management
- Use of the term ‘surgical pathology’ (in the title of a textbook)
- Early work with frozen sections
- Considered one of the 5 most significant contributors to the growth of clinical microscopy in the US in the 19th century.

William Fiske Whitney
- First officially designated ‘Surgical Pathologist’ at the MGH
- First full-time anatomical pathologist
- Active in intraoperative pathology consultation

Lyn McDivitt Duncan
- Led the largest US study of pregnancy associated melanoma

Ruth Graham
- Established the Gynecological Cytology Laboratory – the 2nd organized cytology lab in the US

Chapter 5: The Pathology Organization
Because MGH is a large research oriented teaching hospital, it treats many patients, which in turn provides the pathology department steady work; approximately 1500 slides are produced per day. Specimens are received from a variety of sources internally from the hospital as well as from other local clinics.

MGH in the mid 1990’s decided to switch to subspecialized pathologists. There were a variety of reasons for this:

- Large enough staff to cover all organ systems
- Change in environment—impossible for any one individual to maintain diagnostic competence and familiarity with the literature in all areas of surgical pathology

---

10 Young and Louis, “The Warrens and Other Pioneering Clinician Pathologists of the Massachusetts General Hospital during Its Early Years.” 1287.
11 Louis, Keen Minds to Explore the Dark Continents of Disease: A History of the Pathology Services at Massachusetts General Hospital, 261.
12 Ibid., 267.
13 Young, Robert H. MD and Harris, Nancy L. MD, “Subspecialization of Surgical Pathology at the Massachusetts General Hospital.”
• Pressure from subspecialized clinicians to have an equally subspecialized pathologist
• Decrease turnaround time and increase quality of diagnosis
• Develop greater rapport with clinicians
• Increase the quality of teaching

The sub-specialties within surgical pathology at MGH are:

• Bone & Soft Tissue (BST)
• Breast
• Cardiovascular (CV)
• Dermatopathology (Derm)
• Gastrointestinal (GI)
• Genitourinary (GU)
• Gynecologic (GYN)
• Head & Neck (ENT)
• Hematopathology (Heme)
• Neuropathology (Neuro)
• Obstetrical (OB)
• Pulmonary
• Renal

Chapter 6: Data Analysis
The scope of this study is one academic year, July 2014 to July 2015, in order to include a full year of pathology fellows’ work. The fellows carry a large amount of sign out work during the year, and it was felt important to include their work in that particular subspecialty. The data was pulled from the hospital’s LIS (laboratory information system). The specimens were surgical pathology samples from all clients (not including consults). These IHC stains were either ordered on the initial sections cut at the time of processing or were ordered afterwards. IHC ordering is under the purview of direct control of the pathologist signing out that case.

The expectations at the start of this project were that notable outliers would show up, either in very high or very low usage, due to expertise or experience. If any variance was found, then some analysis would be done to control over-users. Some of the other expectations that were held at the outset were some services such as Heme, BST and HN and the breast would show a fair amount of usage.

It was decided to graph the total number of cases against the ones that had IHC ordered by
pathologist and subspecialty. The following graphs are a sample of the results (Note: Doctors' names have been anonymized):
Figure 6 Bone and Soft Tissue
As stated previously, there are real costs associated with ordering IHC stains. From Figure 8,
one can see that approximately 15% of all surgical pathology cases require IHC stains.

Using very rough estimation of costs of $88.80 per slide per IHC stain (not including the cost of rush orders). This results in the following range of costs for IHC staining for this study:

\[
\begin{align*}
\text{Pessimistic} & : \$37,310,208.00 \\
\text{Realistic} & : \$4,663,776.00 \\
\text{Optimistic} & : \$932,755.20
\end{align*}
\]

The pessimistic number was calculated using the max number of stains ordered (40) for every case. The Realistic number was calculated using an average of five stains per case. The Optimistic number was calculated assuming only one stain per case. These calculations were performed in order to illustrate how decisions can drive cost. It is somewhat obvious the extremes are to be avoided. Ordering unnecessary tests wastes resources, as well as delays patient care. Underutilization of stains runs the risk of misdiagnoses. The ideal situation is to use just the right amount for each case.

Chapter 7: Results
Comparing the different subspecialties to each other, i.e. Breast to GI is not useful due to the intricacies and protocols involved. The focus of this study was to look at each subspecialty individually. In the final data set the average number of stains per case was impressively consistent within a subspecialty See Figure 9.
The small amount of variance that does show up can be attributed to the fact that more experienced pathologists tending to order less IHC than ones in training or who are newer to that service. Due to the varying workload of each subspecialty as well as the need to have at least two pathologists on each service (for coverage for vacation, illness, etc.) at any given time, means that most doctors are assigned to multiple services/subspecialties. This in turn can lead to a familiarity of one service over another. Fellows on the other hand mostly work in one subspecialty (in special cases 2) over the course of the year spent at MGH. Adding to the complexity, most faculty members must juggle signing out cases, teaching, research and administrative duties. There is a fairly complex scheduling activity that must be undertaken to accommodate all the above. Because of this, it is possible that more experienced and senior faculty may have fewer weeks of service and sign out fewer cases than their colleagues. Yet another factor that plays into this study is IHC stains themselves. IHC stains have existed since
the 1930s but in the 1980s became more widely used. As a result, many of the pathologists that are more experienced are used to diagnosing disease without the aid of many of the IHC stains that are available today. On the other hand, many of the more recent graduates of pathology are knowledgeable about the latest developments in IHC stains. This is all to say that there are many factors that are in play when a pathologist orders IHC stains.

For example, in the Breast subspecialty (Figure 5), Dr. G7 was a Fellow during this time, while Dr. A53 is a more senior pathologist who carries fewer weeks of service.

As another example in Bone and Soft Tissue, Dr. Z26 was a Fellow during this time frame, signed out 599 cases while Dr. K37 is the subspecialty head with BST as their only subspecialty.

How tightly is the ratio of IHC clustered around the average? Each subspecialty was graphed against the average bounded by 1.5 standard deviations on either side. This is an arbitrary reference point, but raises some interesting questions. The following graphs show little variation around the mean (see figures 9-11):
Figure 10 Breast Subspecialty Stain Case Ratio
Figure 11 Bone & Soft Tissue Subspecialty Stain Case Ratio
There are other subspecialties that show greater variance in the ratios, Gastrointestinal is an example (see figure 13):
As a result of looking at this graph, there is more research that could be done (which is outside the author's knowledge and expertise). What drives Dr. F32 and Dr. I35 to have extreme ratios? Is it due to:

- Specimen type?
- Assignment of cases?
- Expertise in certain diseases?

There is no value judgment looking at the data in this way, merely pointers to areas that might provide insight to how the each subspecialty functions.

Chapter 8: Conclusion
Because the variances are so low, this indicates a uniform approach within each department to IHC staining. This in turn is an indication of the quality of education that the residents receive.
This study provides three benefits to MGH. The first benefit that the hospital has is a baseline for the usage of IHC stains by subspecialty. The study shows that for each subspecialty there are different rates of usage, but within that subspecialty the variance is low. This information was not available before. In the future another study could be conducted to see what changes, if any, have occurred with the passage of time.

Second benefit the hospital receives is data in a form that allows for productive internal analysis of how decisions are made and work distributed among the doctors within a subspecialty. As mentioned above, the subspecialty group may want to have an internal discussion on the findings.

The third benefit is understanding costs, which was a driver for performing this study. Because of the low variability, the hospital can work with CMS (Centers for Medicare & Medicaid Services) to negotiate the amount of reimbursement. For women's health, especially looking at breast cancer, that 62% of cases will require IHC stains. While the Breast subspecialty, uses quite a bit of IHC stains, Head and Neck service uses less, in the 15% range. Because the process is in control the ability of the pathology department as well as the hospital to predict costs is increased.
Appendix A
Graphs of Average IHC Usage by Subspecialty and Pathologist

BREAST
BONE & SOFT TISSUE

Average Max Number of IHC cases

- Average
- Max
- Number of IHC cases

Values:
- 69
- 126
- 72
- 37
- 21
- 26
- 15
- 5
- 5
- 5
- 0
Average S Max -*-Number of IHC cases
HEMATOPATHOLOGY

- Average
- Max
- Number of IHC cases
Appendix B

Graphs of Average IHC Usage by Subspecialty and Pathologist

BREAST

<table>
<thead>
<tr>
<th>Year</th>
<th># Cases IHC</th>
<th>Total Cases</th>
<th>Max Stain</th>
<th>Stain Case Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>02</td>
<td>320</td>
<td>313</td>
<td>0.62</td>
<td>0.62</td>
</tr>
<tr>
<td>03</td>
<td>147</td>
<td>35</td>
<td>0.57</td>
<td>0.57</td>
</tr>
<tr>
<td>04</td>
<td>259</td>
<td>35</td>
<td>0.53</td>
<td>0.53</td>
</tr>
<tr>
<td>05</td>
<td>245</td>
<td>35</td>
<td>0.51</td>
<td>0.51</td>
</tr>
<tr>
<td>06</td>
<td>291</td>
<td>35</td>
<td>0.56</td>
<td>0.56</td>
</tr>
<tr>
<td>07</td>
<td>192</td>
<td>30</td>
<td>0.54</td>
<td>0.54</td>
</tr>
<tr>
<td>08</td>
<td>135</td>
<td>21</td>
<td>0.51</td>
<td>0.51</td>
</tr>
<tr>
<td>09</td>
<td>121</td>
<td>34</td>
<td>0.51</td>
<td>0.51</td>
</tr>
</tbody>
</table>

# Cases IHC | Total Cases | Max Stain | Stain Case Ratio
### Appendix C
<table>
<thead>
<tr>
<th>Cases</th>
<th>IHC</th>
<th>Total Cases</th>
<th>Max Stain</th>
<th>Stain Case Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>583</td>
<td>0.15</td>
<td>583</td>
<td>0.15</td>
<td>0.15</td>
</tr>
<tr>
<td>217</td>
<td>0.13</td>
<td>217</td>
<td>0.13</td>
<td>0.13</td>
</tr>
<tr>
<td>222</td>
<td>0.11</td>
<td>222</td>
<td>0.11</td>
<td>0.11</td>
</tr>
<tr>
<td>138</td>
<td>0.12</td>
<td>138</td>
<td>0.12</td>
<td>0.12</td>
</tr>
<tr>
<td>136</td>
<td>0.11</td>
<td>136</td>
<td>0.11</td>
<td>0.11</td>
</tr>
<tr>
<td>84</td>
<td>0.10</td>
<td>84</td>
<td>0.10</td>
<td>0.10</td>
</tr>
<tr>
<td>255</td>
<td>0.18</td>
<td>255</td>
<td>0.18</td>
<td>0.18</td>
</tr>
<tr>
<td>225</td>
<td>0.15</td>
<td>225</td>
<td>0.15</td>
<td>0.15</td>
</tr>
<tr>
<td>328</td>
<td>0.22</td>
<td>328</td>
<td>0.22</td>
<td>0.22</td>
</tr>
<tr>
<td>101</td>
<td>0.05</td>
<td>101</td>
<td>0.05</td>
<td>0.05</td>
</tr>
<tr>
<td>96</td>
<td>0.05</td>
<td>96</td>
<td>0.05</td>
<td>0.05</td>
</tr>
<tr>
<td>135</td>
<td>0.05</td>
<td>135</td>
<td>0.05</td>
<td>0.05</td>
</tr>
<tr>
<td>290</td>
<td>0.10</td>
<td>290</td>
<td>0.10</td>
<td>0.10</td>
</tr>
<tr>
<td>2219</td>
<td>0.50</td>
<td>2219</td>
<td>0.50</td>
<td>0.50</td>
</tr>
</tbody>
</table>

GASTROINTESTINAL
Appendix C
Graphs By Subspecialty Of Ratio Of Usage Against The Average And ± 1.5 Standard Deviations

BREAST

G7  C3  D4  N14  Y25  C29  T46  A53

Stain Case Ratio  Average  UCL  LCL
References


Anna Plourde, MD; Alden Gross, PhD; Zhong Jiang, MD; Christopher L. Owens, MD, Alden Gross; Zhong Jiang Zhong Jiang, MD; MD;, and Christopher L. Owens Christopher L. Owens, MD MD. “Patterns in Immunohistochemical Usage in Extended Core Prostate Biopsies--Comparisons Among Genitourinary Pathologists and Nongenitourinary Pathologists.” *Archives of Pathology & Laboratory Medicine* 137 (November 2013): 1630–35.


Brown, Skip H. “‘HEMATOXYLIN & EOSIN’ (The Routine Stain).” Sigma-Aldrich Corporation, 2002.


http://www.immunohistochemistry.us/what-is-immunohistochemistry.html.
