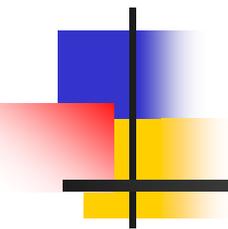
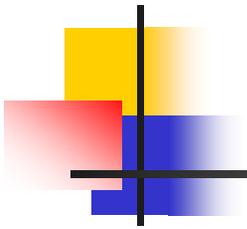


Why Pathology and Lab Medicine Should Merge with Radiology



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Major Concepts to Be Addressed in This Lecture

- Discussion of *early health model* (EHM) & *molecular medicine*; precursors to discussion of specialty merger
- Differentiating diagnostic domain from therapeutic domain; present and future role of prognosis & prognosticians
- Molecular imaging as new technology that places radiology & pathology/lab medicine on a conversion/collision course
- Rationale for merger of pathology/lab medicine & radiology into new entity: “Department of Diagnostic Medicine”
- Possible trajectory for discussions & merger of specialties; critical role of IT and IT vendors in facilitating conversion

Introduction to the Early Health Model: Discussion of Its Component Parts

- *Early health model* represents major shift in healthcare delivery; increased emphasis on preclinical/presymptomatic disease
- EHM comprised of five major components:
 - *Personal health* (environmental, lifestyle, genotype)
 - *Diagnosis* (medical imaging/molecular imaging plus molecular diagnostics)
 - *Prognosis* (see later discussion about this topic)
 - *Treatment* of preclinical/presymptomatic disease
 - *Information technology* (IT); glue for other parts
- Also two divisions of EHM: *applied* and *discovery*; former is clinical practice and latter relates to “early disease research”

Why Is Early Health Model So Disruptive for Established Participants in Healthcare?

- Healthcare payers nervous because EHM adds to cost of healthcare; struggling to pay for clinically diagnosed disease
- Many MDs nervous because have been trained primarily to diagnose symptomatic disease based on signs & symptoms
- Makes “big pharma” nervous; clinical trials for current drugs have historically recruited subjects with symptomatic disease
- Criticality of diagnostic methods in model demands high degree of integration/collaboration across lab/path/radiology
- Happiest group will be pts.; dissatisfied with current approach when told by MDs to come back with symptoms

Why Early Health Model So Important for Pathology and Lab Medicine

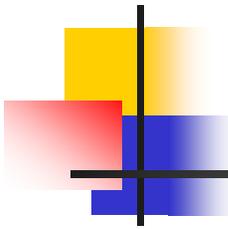
- Essence of EHM is early dx; pathology/lab medicine scientifically easily adaptable to this approach to healthcare
- Molecular diagnostics at epicenter of EHM in terms of *in-vitro* testing & also because of links to molecular imaging
- If develop molecules that bind to *in-situ* biomarkers, can also be used to deliver therapeutic agents to diseased cells
- Theoretically and in long run, EHM *may* reduce cost of healthcare because treating disease in earliest stage
- EHM also important because of inclusion of *personal health*; consumers obligated to take ownership of their own health

Defining Molecular Medicine and Its Interplay with Early Health Model

- As name implies, molecular medicine focuses on the molecular basis of disease and the genesis of tumors
- Necessary to understand this molecular basis to diagnose, to determine prognosis, and to treat various lesions
- Understanding of *molecular medicine* enables and promotes the following advances in healthcare delivery
 - Early detection and treatment of disease
 - More effective monitoring of treatment efficacy, which is important for future drug development
 - Selection of individualized therapy for each patient
 - Expansion of potential for screening programs & determination of genetic predisposition to disease

What's More Important: Patient Diagnosis, Prognosis, or Treatment?

- In ancient Greek times, there were two schools of thought in medicine
 - *Knidian* which focused on diagnosis and the *Hippocratic* (or *Koan*) school, which focused on treatment and prognosis
- Hippocratic approach emphasized passive treatment and more generalized diagnosis – became more successful
- Medical practice today focuses on diagnosis & aggressive treatment of disease; prognosis growing in importance
- With genomics/proteomics/new imaging modalities, diagnosis will become more routine – beginning of process
- Prognostics and therapeutics will be considered “higher art” in healthcare delivery because much more integrative



Rationale for the Inclusion of Prognosis in the Early Health Model

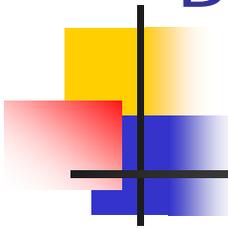
- Prognosis involves predicting likely outcome of a disease based on condition of the patient & action of the disease
- In past, prognostic statements like five-year survival by tumor based on tables using tumor score & type of therapy
- Now IVDMA tests for breast ca like *Oncotype DX* and *MammaPrint* predict prognosis based on tissue microarray data
- Prognosis takes advantage of genomic/proteomic science & deeper understanding of biology of each tumor studied
- Evolution of new type of specialist with new skill set called a prognostician working collaboratively with diagnosticians

\$25 Billion Bet Placed by Siemens and GE on Convergence of Imaging with IVD

- GE Medical purchased Amersham (\$9.5B) in 10/2003 & portion of Abbott Dx (\$8.1B) in 1/2007; pursuit of *EHM*
- Siemens Medical Dx purchased DPC (\$1.9B) and Bayer Diagnostics (\$5.4B) in 2006; pursuit of *molecular medicine*
- We thus have two global corporations betting \$25 billion on the convergence of imaging with molecular diagnostics
- Pressure will be great from these companies for MDs to deliver “integrated” diagnostic reports/services to patients
- In remainder of lecture, will discuss to what extent healthcare delivery system will react to these initiatives

Details About Molecular Imaging; How Differs from Other Imaging Modalities

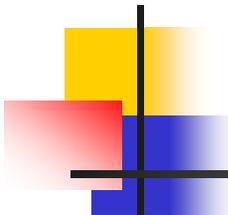
- Molecular imaging involves use of probes (biomarkers) that are used to image various targets, particularly in-vivo.
- Biomarkers interact chemically with various tissues & alter medical image according to the molecular changes in tissue
- Markedly different from previous imaging modalities that created image based on tissue densities or water content.
- Molecular imaging also allows for quantitative analysis such as precise tumor shrinkage, which adds objectivity to treatment
- Research currently focusing on pre-disease states defined as molecular states that occur before onset of symptoms



Biomarkers Discovery as Common Goal for Both Pathology and Molecular Imaging

- Both applied and research pathology/lab medicine have major focus on *in-vitro/in-vivo* biomarkers and predisease
- Molecular imaging based discovery on *in-situ* biomarkers; molecular diagnostics focuses on *in-vitro* biomarkers
- All of the new molecular imaging research centers around the world have a major focus on new biomarker discovery
- Complex imaging studies too expensive and capital-intensive for use in pre-disease discovery and wellness testing
- More cost-effective to monitor serum for expression of abnormal or excessive proteins as means to guide imaging

Ten Reasons Why Pathology/Lab Medicine Should Discuss Convergence or Merger



- Given this background, will now list ten reasons why I think this particular convergence/merger should occur
- Mindful of fact that medical specialty boundaries are relatively rigid; few precedents exist for such a merger
- Ambiguity around some specialty boundaries such as orthopedic surgery, physical medicine, & sports medicine
- Some older disciplines imaging disciplines such as nuclear medicine have been largely absorbed by radiology
- Clinical hematology/oncology has morphed into oncology; much of cellular morphology ceded to hematopathologists

#1: Substantial Overlap Between Disciplines Already Exists; Common Basis for Practice

- Radiology and pathology practices already very similar; both create diagnostic reports using sophisticated IT
- Previously discussed how biomarkers are key to the evolution of molecular imaging; common basis for research
- Some IT vendors already considering or producing common viewer; review data/images from both the LIS and RIS
- Radiologists more advanced re: image storage & accession with their PACS; pathologists embraced image storage later
- Both groups use cutting edge science & technology to render diagnoses, some of which is now converging

#2: Blending of Imaging, Molecular Dx, & IT Already Actively Underway in For-Profits

- Siemens and GE have made \$25B bet on molecular imaging; these investments cannot help but shape future
- Companies are developing new vocabulary to describe this convergence with major marketing/education campaigns
- Press releases for molecular imaging discuss search for *in-situ* biomarkers; clinical labs assess *in-vitro* biomarkers
- GE has launched “re-imaging” campaign directed to both physicians and patients; power of consumers in market
- Unknown currently to what extent new business model by for-profits can/will influence medical specialty boundaries

#3: Molecular Imaging Has Potential in Future to Compete with Surgical Pathology

- Most medical imaging (e.g., CT, MRI) seeks to identify the mass/shape of a lesion but does not address the “biology”
- PET scan makes three-dimensional image of functional processes in the body; can be integrated with other studies
- By linking radio-opaque substance to molecule that binds to biomarker(s), can make inferences about function
- Molecular imaging has potential to locate a space-occupying lesion & also provide clues to dx & behavior
- Surgical pathology is current diagnostic gold standard; wise approach at this time is to *collaborate* in order to *validate*

#4: Overarching Benefits Can Be Achieved by Closer Integration of Specialties

- Currently, radiology & pathology/lab operate in two separate diagnostic silos with few interactions between the groups
- Closer integrated approach would yield quality & strategic benefits for both patients and for specialists themselves
- No coding system for radiology reports similar to the SNOMED system in pathology; report retrieval difficult
- Radiology uses DICOM, a standard for handling, storing, printing, and transmitting information in medical imaging
- With closer integration, radiology could adopt SNOMED & pathology a DICOM variant for image storage and retrieval

#5: Enhanced Quality of Reporting with Merged LIS/RIS/PACS Databases

- At earliest stage of technology allowing us to query image databases: find all previous instances of “this” image
- From quality perspective, don’t yet fully comprehend value of integrated radiology, CP, & AP reporting and analysis
- Greater value than simply retrieving past dx’s; with merged databases, can track success of prior treatment
- Advocating analysis/integration of all preoperative *in-vivo* and *in-vitro* studies as part of surgical pathology reports
- Many current pathology residents inadequately trained to even integrate molecular dx results into surg path reports

#6: Radiology Under Threat from Clinicians so Politically Useful to Join Forces

- In large tertiary care centers, budget of a merged department could reach \$100M – formidable leverage
- Current estimate of 70% of dx's based on lab testing; add to this the diagnostic yield of current medical imaging
- Strength of pathology: control over all *in-vitro* testing and surgical pathology/cytology (gold standard for dx)
- Strength of radiology: control over most digital imaging + evolving molecular imaging & interventional radiology
- Some capital acquisitions in radiology may *not* be necessary with enhanced molecular diagnostic screening

#7: New Specialty of Diagnostic Medicine Could Create Critical Mass of Trainees

- Trainees are “shock troops” that serve to expand scope of a specialty & expand its boundaries in healthcare delivery
- Good example is adoption of portable ultrasound as diagnostic tool in emergency medicine; basis for fellowships
- Cardiologists emerge from residency/fellowship program and lobby in hospitals for expanded scope of practice for them
- Problems in current pathology training programs; fewer trainees in CP and many surgical path fellows too specialized
- Residents and fellows trained in imaging, lab medicine, and surgical pathology could serve as salient for new specialty

#8: Core Technologies in Surgical Path Would Benefit from Infusion of New Technology

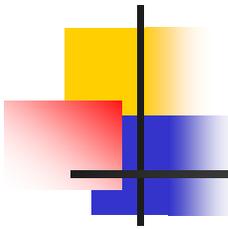
- Surgical pathology stuck in a rut, using some core technologies that have been in place for many decades
- Very few incentives to change because techniques yield highly accurate and very cost-effective diagnoses
- Not suggesting that we abandon stained thin-section histologic specimens with microscopic examination
- Current histopathology techniques will serve as diagnostic gold standard; critical to validate molecular imaging
- Rather, time now ripe to begin to supplement histopathology with some newer & evolving technologies

#9: Imaging Studies Yield High Profit Margins; Lab Studies Are Commodity

- Can't ignore the economics of healthcare delivery; imaging studies yield profits margins for hospitals of about 40%
- Lab testing often viewed as commodity by hospital administrators; difficult to advocate for capital investment
- Part of attitude flows from the technology deployed in labs; automated assembly lines with low cost-per-test
- Because radiology viewed as profit center, little hesitation by administrators to invest in new imaging modalities
- With an integrated diagnostic departmental hub, some of "magic" will rub off on lab, particularly for molecular dx

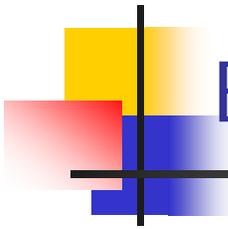
#10: Pathology Would Benefit from Research Capital Invested in Imaging

- One of major advantages of the “imaging” industry is that global companies making huge capital investments in R&D
- Have already discussed Siemens and GE Healthcare in this context; Phillips (Dutch company) is not far behind
- Molecular imaging research centers being established around the world; major focus on biomarkers research
- Recall that both Siemens and GE are both now major participants in IVD and particularly molecular diagnostics
- With a merged specialty, some of these research capital investments will flow into nexus between imaging and IVD



Spark That Will Ignite Closer Collaboration Between Two Specialties

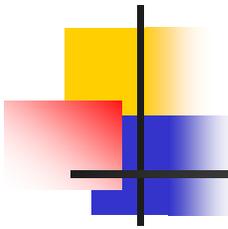
- Agreement that surgical path is gold standard for tissue dx; will retain this title for probably a decade or more in future
- Surgical pathologists not looking at cells *in-vivo*; we fix, dehydrate, & stain tissue to create system of “our” artifacts
- We have learned to schematize our artifacts to create surgical pathology reports that predict biologic behavior of disease
- Radiologists work with “their” artifacts to detect tissue abnormalities that are also very useful in diagnosing disease
- What is now critical is for these specialists to directly collaborate to enhance quality of dx’s & learn from each other



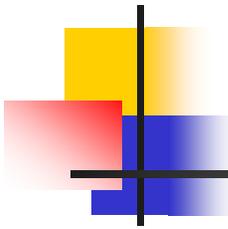
Possible Trajectory for Discussions & Eventual Convergence of Two Departments

- I believe that the first step for early discussions will be bench research collaboration relating to biomarkers
- Second step for discussion will be IT convergence; examples include common viewers & integrated image databases
- Third step will be integrated reporting functions
 - When necessary and appropriate, all radiology/lab/pathology reports will comment on both diagnosis and prognosis
 - Cadre of “Dx. Specialists” will adopt multi-disciplinary approach with review & analysis of all *in-vitro/in-vivo* data for pts.
- While this is taking place, pathology training programs need to internally emphasize criticality of molecular diagnostics

IT Issues as They Related to a Merged Department of Dx/Px Medicine



- Aspyra already proposing integrated CIMS (clinical image management system) for all clinical images in health system
 - This would capture images from radiology, pathology, clinical labs, ophthy, GI, cardiology, dermatology, etc.
- Availability in the market of such CIMSs may provide a stimulus for some degree of convergence between depts.
- Perspective of “EHR vendors” is that all of the integration should take place at the level of their central clinical system
- I support the view of a “federated architecture” with deployment of “best of breed” systems across enterprise



Summary and Take-Home Points from This Lecture

- New vocabulary now being hatched to encompass diagnostic/prognostic/therapeutic continuum
 - *Early health model* and *molecular medicine* covers medical imaging, molecular imaging, molecular dx, & surgical path.
- With new biology (genomics + proteomics), diagnosis will be rendered quickly; art of medicine in prognosis + therapy
- Molecular imaging evolving quickly; amalgam of sophisticated imaging technologists + *in-situ* biomarkers
- Merger/convergence between pathology/lab medicine/radiology make political, economic, and quality sense
- First step will be research collaboration with IT support; next will be integrated reports across care continuum