

A Survey of the Myriad Forces Changing Anatomic Pathology & Some of the Consequences

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Major Concepts to Be Addressed in This Lecture

- As the lead-off speaker for this conference, my goal is to sketch out the forces that are changing anatomic pathology
- Will define anatomic pathology as surgical pathology, cytopathology, and autopsy, although latter is “dying art”
- Some of my points will be relevant for hematopathology -- hybrid of a CP subspecialty plus morphologic observations
- May make passing reference to some of the consequences of these forces, but this will not be the major goal of talk
- Will list ten major forces but no magic associated with this number – just a way to launch subsequent presentations



Surgical Pathology as Subjective Discipline Supported by Aging Technologies

- Histopathology remains largely a subjective skill based on experience of practitioners in pattern matching of other cases
- Many of the underlying technologies (e.g., tissue stains, paraffin embedding) have been in use for many decades in pathology
- This notion of histopathologic diagnosis as a qualitative and subjective skill set reinforced by our training methods
 - Residents and fellow sit next to an “artful practitioner” who declares a lesion to be closest to another “known” lesion
- For the most complex lesions, there may be wide variation among national experts about which diagnosis to assign to it



Histopathology Remains the Gold Standard for Tissue Diagnoses

- Irrefutable that histopathology & cytopathology reign as gold standard for rapid generation of definitive diagnoses
- This despite fact that much of the practice is highly subjective and highly dependent on skill of observer
- Histopathologic diagnosis provides relatively inexpensive and rapid TAT; frozen sections can provide dx in minutes
- Even new medical imaging modalities can rarely generate definitive diagnoses; molecular imaging only in early phase
- Because histopathology is gold standard, will serve as tool for validation of new imaging modalities like “molecular”



Listing the “Top Ten” Forces for Change of Anatomic Pathology

- Will now proceed to list “top ten” forces for change in pathology & lab medicine; my personal idiosyncratic high level forces
- Hope that many of you will disagree with my list; incentive for you to select your personal list -- grapple with “futurescape”
- Many of these high-level forces are beyond the control of practitioners in the field; others are amenable to “local” action
- I take some comfort from two quotations attributed to the great hockey player Wayne Gretski:
 - *It has been proven beyond a shadow of a doubt that you miss 100% of the shots you do not take*
 - *The secret to my success in hockey has been getting to where the puck is going to be*



#1: Growing Interest in Defining and Executing the Early Health Model

- *Early health model*, popularized by GE Healthcare, characterized by pre-clinical/pre-symptomatic diagnosis
- Fueled by new biology & also constitutes a paradigm-shift in manner in which healthcare services will be delivered
- Will be opposed by major power blocks within healthcare industry because of radical nature of change evoked
 - *Health insurance executives*: increases cost of care in short-term but may possibly result in long-term savings
 - *Clinicians and healthcare professionals*; not trained to diagnose and treat pre-symptomatic diseases
 - *Pharmaceutical companies*: controlled clinical trials for all current drugs based on subjects with symptomatic disease



#2: Molecular Medicine Become a Major Driver in Healthcare

- Process involves: (1) studying molecules as they relate to health and disease and (2) manipulating those molecules to improve the diagnosis, prevention, and treatment of disease.
 - Enables early detection and treatment; this concept thus encompasses early health model just presented
 - Enables monitoring of treatment efficacy using biomarkers and medical imaging; extends their utility into rx domain
 - Enables selection of best individual therapy for each patient; often referred to as *personalized medicine*
 - Expands potential for screening programs & assessment of genetic predisposition; creation of new “wellness” industry
- Key question is how anatomic pathology can be converted from a morphology-driven to molecule-driven medical discipline



#3: Clinicians Seek Key Indicators of Prognostic & Therapeutic Efficacy

- Major shift underway from emphasis on diagnosis to prognosis assessment & monitoring effectiveness of rx
- Shift spawned by more sophisticated medical imaging & molecular diagnostics; dx becoming fast and accurate
- Cancer prognosis in past was simply matter of staging lesion and then reading five-year survival from a chart
- With personalized medicine & targeted chemotherapy, will change drugs midstream if no observed beneficial effects
- Bottom line for pathologists: opportunity exists to change emphasis of reports and better respond to clinicians' needs



#4: Constant Pressure for More Cost Effective Healthcare Delivery

- Key question for pathology & lab medicine: how lower cost of healthcare delivery as dx/rx more sophisticated?
- One possible answer: multiplexed biomarker testing for dx and monitoring may be less expensive than imaging
- For neoplasms, earlier diagnosis and targeted therapy may avoid expensive surgery and prolonged hospital stays
- Wellness monitoring and healthy lifestyles may avoid complications of chronic diseases like diabetes and CHF
- Major new healthcare option: walk-in clinics in retail drug stores/discount stores; begin to offer CLIA-waived testing



#5: Early Interest in Merging Pathology & Lab Medicine with Radiology

- Some early models attempted of such a merger (e.g. VA system) resulting in a new discipline of “Diagnostic Medicine”
- Rationale behind idea buttressed by economic, political, strategic, quality, and organizational considerations
- Medical imaging on collision course with AP based on molecular imaging & total body MRI for wellness screening
- Radiology losing control over imaging procedures & revenue to clinical specialties like cardiology & emergency medicine
- For me, most important rationale for this new idea are quality advantages of two groups merging & interoperating



#6: Multiplexed Biomarker Panels

Deliver Diagnoses & Wellness Monitoring

- Large panels of biomarkers will become cost-effective method of choice for monitoring wellness/disease status
- More comprehensive & sensitive than current methods such as yearly cursory physical exam + small set of routine labs
- More cost-effective and less morbidity than medical imaging; periodic venipunctures to obtain serum samples
- Approach predicated on knowledge that diseased & neoplastic cells communicate by their protein secretions
- Research challenge is to develop algorithms to more accurately interpret the significance of serum protein shifts



#7: Digital Pathology Begins to Emerge as Fully Mature Discipline

- Major disconnect for decades; CP totally digital & AP generating “analog” images & non-integrated and unstructured reports
- Grapple with implications of two disciplines now totally digital; all information totally accessible, integrated, & transportable
- Microscopic dx delinked from specimen grossing and histopathology labs; second opinions available in minutes
- Given that lab data & medical imaging form basis for ~80% of diagnoses, medical consultation will be available globally
- Look at *Nighthawk Radiology* as example of companies that may evolve inside pathology; mimic experience in radiology



#8: Direct Searching of Image Databases Becomes Practical and Commonplace

- Real-time differential diagnoses based on region of interest; increased chance of recognizing low-incidence lesions
- Rapid whole-slide image scans for features of interest (e.g., micro-metastases or local invasion) with increased success
- For rare diseases, faster recognition that a cohort of distinct cases exists; yields improved rare disease discovery
- Simplified consensus generation; cases with similar morphology can be “queried” for grade or extent of certain features
- Ability to search for cohort cases across geographically diverse repositories; option of creating larger sets of cases for study
- Real-time correlation of whole slide quantitative morphology with historic prognosis/rx response using matched cases



#9: Hyperspectral Imaging

Supplements Brightfield Microscopy

- Ability to leverage existing “low-cost” conventional histochemical stains to add significant diagnostic power
- Ability to discern disparate and diagnostically important cell populations that are currently difficult to distinguish (e.g. κ, λ)
- Apply multiplex staining to brightfield microscopy using five to eight immunostains in a section; approaches cell cytometry.
- Ability to detect spectrographic signatures of distinct disease processes currently missed by conventional brightfield.
- Quantitatively assess prognostic value of multispectral data elements; similar to multi-parametric gene expression



#10: Need for Strategy to Counteract Commoditization of Lab Medicine

- Commoditization of CP has occurred because of highly automated lines & competition by national reference labs
- Antidote will be genomic/proteomic testing; labs will be able to differentiate themselves by unique test offerings
- Further product differentiation on basis of lab consultations and correlation with medical imaging
- Secret will be staying ahead of competition and creating unique and useful diagnostic products faster than others can copy them
- One of major threats to this approach currently is the FDA seeking to regulate the algorithms used to interpret IVDMIAs



Summary and Take-Home Points from Lecture

- Anatomic pathology has been “protected” from disruptions because of inherent efficiency/effectiveness of histopathology
- Major forces bearing down on discipline that will disrupt the franchise & practitioners; need to adapt or become irrelevant
- First reform will be closer integration with clinical pathology; critical because genomics/proteomics basis for new biology
- Second reform will be closer integration with radiology, resulting in more powerful specialty of Diagnostic Medicine
- This new approach/specialty will be better able to respond to clinicians’ interest in prognosis/rx and “early health model”



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