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.
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
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
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 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.
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.
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.”