Biomarkers and the Future of Radiology

John R. Votaw
CBIS 5th Year Anniversary Celebration/Look to the future
February 8, 2013
Statistics/Radiology Collaboration

• The utility of Radiologic procedures must be demonstrated as we move towards an accountable care model for funding healthcare in this country.
• Determination of relevant biomarkers must be followed with demonstrations that they improve patient outcomes.
• Technology is producing imaging data sets that are too vast for any one person to completely explore.
• In 5 years data sets will contain over 100,000 images.
• Efficient methods for extracting the relevant (or discarding the irrelevant) information are needed.
Risk of not performing imaging

- FDG in Non-Small-Cell Lung Cancer
  - Conventional: 81% thoracotomy (78/97), 41% futile (39/78) (Van Tinteren et al. 2002)
  - With FDG: 65% thoracotomy (60/92), 21% futile (19/60)
  - Surgical-related mortality: 6.5%
  - 175k new lung cancer/yr
  - Surgery deaths without FDG: 3766
  - Surgery deaths with FDG: 1574
  - LNT radiation dose: 61 deaths ???
  - Net benefit with PET: 2131
New/Better Biomarkers

• With FDG: 65% thoracotomy (60/92), 21% futile (19/60)
• Current: Physician examine data with crude machine support (MIP)
• Future: Machine/human partnership
  – Integration of multiple data sets from multiple modalities and multiple sources
PET CT
Projection images
(source images = 273)
Breast Cancer Missed by Mammography

44 y/o female complained of right breast fullness and slight discomfort from an axillary nodule for several months.

An initial mammogram was performed and called negative. Over the course of the next 6 months, another 2 mammograms were performed. Both were negative.

A fine needle biopsy of the axillary node was finally performed which demonstrated poorly differentiated adenocarcinoma. An ultrasound guided biopsy of an 8mm breast nodule was negative.

The PET scan demonstrates the primary breast cancer and multiple metastatic tumors.
Source images
(88 images)
MIP Abdominal Angiogram
1792 slices... or 1 volume?
Moore's Law
History of Radiology

- Planar x-ray 1896
- Multiple views (film)
- 1960 tomography
- Ultrasound 1960
- 1970 CT
- 1980 MRI
- 1974 - 1 plane
- 1985 - 5 planes
- 1993 - 31 planes
- 2000 - 207 planes
- Current - 10,000+

- 1 radiologist
- Subspecialization
- Convenience combined modalities (PET/CT)
- Wide-spread data integration
Increasing Size and Complexity of Datasets

• Standard exams performed with faster acquisitions at higher resolution = more data
• Increasing variety of techniques:
  – Perfusion
  – Diffusion
  – Arterial spin labeling
  – Spectroscopy
  – Elastography
  – Blood volume
  – Mean transit time
  – ...

Vulnerable plaque – A clinical challenge (I)

State-of-the-art dual energy CT in the clinic is capable of material decomposition, but needs higher spatial resolution.

DECT: 70 kVp

DECT: 120 kVp

Courtesy: Dutta, PhD, GE Healthcare
X-ray differential phase contrast CT (DPC-CT)

Preclinical: Pathophysiologic, pharmacologic and therapeutic research in cancer, athroscerosis, ...

Clinical: Breast imaging ...

Phase contrast coming soon

Projection image

Attenuation contrast

Prototype phase/attenuation contrast (2-in-1) micro-CT

Xiangyang Tang Lab
MRI – Large Datasets

Whole Body MRI

Comprehensive Internal Medical Exam and “The Virtual Biopsy”
MRI Sequences ≈ Histology Stains
The most common clinical applications of CT

- Cardiovascular: stenosis, plaque, stent ...
- Body: chest, abdomen, pelvis
- Head & Neck: trauma, stroke, brain, carotids ...
- Misc: extremities, interventional, ...
Quantitation

• Radiology
  – Calculate values for parameters known to be physiologically important

• Statistics
  – When are these parameters abnormal?
  – Do the data sets contain other parameters or combination of parameters that are specific for disease?
DWI vs Gleason Score

- Hambrock et al Radiology 2011
  - n=51 PZ cancer
  - Difference between median ADCs of LG and IG larger than that between IG and HG.
  - $A_z$ of 0.90 for median ADC to differentiate LG from combined IG and HG
Elastography

Tumors are 5-28 times stiffer than normal soft tissue.

Fibrosis score and elasticity are correlated.

*Developed by Richard Ehman, Mayo Clinic*
**Circumscribed ROI’s on cortical-medullary phase image just prior to contrast excretion into the pelvis**

Relative signal values = \( \frac{S_t - S_0}{S_0} \)
Gd concentration in the aorta and kidneys over time are derived from circumscribed ROIs.

Fitting the model to the kidney data gives estimates of GFR and RBF.
## Eigenvalue Concept

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"Important Information"

(Biomarkers)

Noise
Summary

• Information content exploding
  – Finer detail images
  – Multi-modality
  – Many different properties (transmission, stiffness, light speed, density, metabolic rates, ...)
• Find relevant information
• Find unexpected information
• Need Human-Machine (decision making) interaction
  – Point out “high probability” areas
  – Remove “low probability” areas
• Transmit information to users