The Importance of Medical Imaging

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The Evolution of Clinical Imaging

- Technical advances-improving the technical quality of the images
- Improving the ability to review and interpret the images-digital age

Trends

- Structure-function (anatomy-physiology/metabolism)
- Diagnostic accuracy (sensitivity-specificity)
The Continued Evolution of Clinical Imaging

- Extracting the maximum amount of diagnostic information from the images
- Relating imaging features to pathology, physiology, and biology

Contrast Enhanced MRI of the Breast Has Diagnostic Value
Behavior of Contrast Agent in Body

- Depends on:
  - Cellular density or “Extracellular Volume Fraction”
  - Blood vessel permeability “Microvascular Permeability”
Dynamic Contrast Enhanced MRI (DCEMRI)

Components

- "High-field" MRI machine (1.0 tesla or greater)
- Standard breast coil
- Gadolinium contrast agent (GdDTPA)
- Images taken at several time points (spatial vs temporal resolution)
- Software algorithm processes data for either parametric maps or semi-quantitative plots

Radiology 1999; 211:101-110

Dynamic Breast MR Imaging: Are Signal Intensity Time Course Data Useful for Differential Diagnosis of Enhancing Lesions?
**Color Coding by the 3TP Algorithm**

**Time Points**
- $t_0 = 0$ minutes
- $t_1 = 2$ minutes

**Wash-in rate**
- color intensity
- (256 shades)

**Wash-out pattern**
- determines color
- (3 shades)

**Breast Cases: Cancer**

**MRI Images – Same Slice**

<table>
<thead>
<tr>
<th>pre – t0</th>
<th>post – t1</th>
<th>post – t2</th>
<th>3TP</th>
</tr>
</thead>
</table>

**Additional Slices**
Breast Cases: Fibroadenoma

VEGF Mediated Angiogenesis

MRI Images – Same Slice

Individual Slices

Brain Tumors-GBM’s
Paradoxical improvement in imaging parameters followed by clinical progression or worsening of Imaging parameters with no tumor progression
Beyond “Radiologic-Pathologic Correlation”

Cardiomyocytes (red) and fibroblasts (green) isolated from chicken embryo heart.

Radiogenomics in Diagnosis
Decoding global gene expression programs in liver cancer by noninvasive imaging

Eran Segal¹, Claude B Sirlin², Clara Ooi³, Adam S Adler⁴, Jeremy Gollub⁶, Xin Chen⁸, Bryan K Chan², George R Matcul⁷, Christopher T Barry⁵, Howard Y Chang⁵ & Michael D Kuo²

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Fig. 2. Knowledge of imaging traits allows approximate reconstruction of a given HCC sample's gene expression pattern, as reported by Segal et al. [8]. The authors created a global “association map” between imaging features and gene expression. Expression variation of 6732 genes, as measured by microarray data and captured by 116 gene expression “modules”, was sufficiently reconstructed by a combination of only 28 imaging traits. The decision tree of imaging trait expression patterns is used to predict variation of expression in a given gene expression module. Each split in the tree is determined by variation of an imaging trait, while each terminus identifies a group of samples that share a similar expression pattern of genes in a particular gene expression module.
Otto Warburg, 1931

Cancer cells will undergo glycolysis even in the presence of oxygen

Opposite of the Pasteur effect

Figure 1. Molecular underpinnings of the Warburg effect

Good News

We can image glycolysis with FDG PET

Glucose and FDG metabolism.

Hoffman J M, Gambhir S S Radiology 2007;244:39-47
Glucose and FDG metabolism.

Hoffman J M, Gambhir S S Radiology 2007;244:39-47

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Glycolysis is common trait of metastatic cancers

Table 4. Sensitivity and Specificity of FDG PET for detection of metastases (data culled from reference (39))

<table>
<thead>
<tr>
<th>Cancer metastasis</th>
<th>Sens</th>
<th>Spec</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSCLC - mediastinal</td>
<td>67-100</td>
<td>94</td>
</tr>
<tr>
<td>CRC - LN &amp; hepatic</td>
<td>73-100</td>
<td>95</td>
</tr>
<tr>
<td>Melanoma</td>
<td>70-100</td>
<td>100</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>50-100</td>
<td>80</td>
</tr>
<tr>
<td>Breast</td>
<td>83-100</td>
<td>97</td>
</tr>
<tr>
<td>Cervical – LN</td>
<td>3-100</td>
<td>72</td>
</tr>
<tr>
<td>Esophageal – distant</td>
<td>69-100</td>
<td>91</td>
</tr>
<tr>
<td>Prostate – LN &amp; bone</td>
<td>40-75</td>
<td>65</td>
</tr>
</tbody>
</table>
Time Series Analysis: Can “Chronobiopsy” of individual lesions predict pathological stage and disease progression?
Timing and Sequence of Pathological Processes

**Inflammation**
- Blood Brain Barrier breakdown
- Edema
- Cellular Infiltration

~ days - weeks

**Degeneration**
- Demyelination
- Axonal/Neuronal Damage

~ weeks-months

**Repair**
- Macrophage activity
- Astrocytosis
- Remyelination
- Axonal Repair?

~ months-years?
T1-Gd+  PDw  T2w Examples (patient 2)

**T2w Examples**

- Propagation
- Residual damage T2w
- Residual damage PDw

**MRI Intensity**

- Y1: Inflammation
- Y2: Resorption

**Features / Parameters**

- F1 = Level of hyperintensity
- F2 = Level or recovery
- F3 = Duration

**Model Fit**

- $\hat{y} = \sum_{i=1}^{N} \frac{\alpha_i}{1 + e^{\beta_i (\delta_i - y)}}$

**Y1 + Y2**

- Complete recovery
- Partial recovery
- No recovery

- T2 intensity
- R² = 0.943
- R² = 0.943
- R² = 0.670
• reduced short-term lesion recovery was associated with greater atrophy rates and disability.

• smaller lesions disproportionally more damaging: leaving more residual, associated with greater disability.

Spatial Analysis: Does normal cerebral perfusion predict lesion prevalence at different locations?

Fact: Repair Does Occur in MS

1. When?
2. Under what Conditions?

Does perfusion modulate brain repair?

Voxel Based Morphometry (VBM)
Context Based Morphometry (CBM)

Healthy Perfusion Atlas
Tc-99m SPECT
N = 47

Context Based Morphometry (CBM)
Early MS (N=89)
Context Based Morphometry (CBM)
MS (N=1249)