FRONTIERS OF ARTIFICIAL INTELLIGENCE (AI) IN IMAGING

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Key points
• Medical imaging is key to many important clinical use cases
• Clinicians who interpret images need assistance to reduce variations in care
• AI methods are promising for decision support and for reducing variations in care
• Deep learning methods are promising, but there are challenges, and best machine learning approach depends on the clinical problem

Outline
• Medical imaging and key clinical use cases motivating AI in imaging
• AI approaches and challenges
• Recent work and potential of AI in imaging

Imaging is key in several medical specialties
• Radiology
• Pathology
• Ophthalmology
• Dermatology
• Micro&Neurobiology

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Many imaging modalities within each specialty

Key clinical uses of medical imaging (and AI)

- Disease detection
- Lesion segmentation
- Diagnosis
- Treatment selection
- Response assessment
- Clinical prediction (of response or future disease)

1) Flood of image data...

Why do we need AI?

- Flood of image data
  - Impacts disease detection
- Variation in clinical practice
  - Impacts diagnosis
- Variation in disease among people
  - Impacts treatment selection

2) Variation in practice

- There are large variations and disparities in care (Institute of Medicine, 2001)
- “Errors and variations in interpretation now represent the weakest aspect of clinical imaging*”

Variable Performance of Radiologists

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3) Variation in disease among people

People (and their diseases) differ...

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Disease in different people varies

- Molecular diversity
  - Heterogeneous genomic aberration landscape of individual tumors
- Phenotypic diversity
  - Variable appearance of lesions on images
- Clinical diversity
  - Patients have different response to treatment
- Ideally we will “profile” disease for personalized medicine

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Data-driven, precision medicine

- Mine biological and medical data to create classifiers of disease and treatment response
- “Profile” disease in patients for personalized / precision medicine

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AI approaches

- Specify and process **pre-defined image features** in large volume to create clinical models
  - “radiomics”
- Process **raw image data** (unsupervised features learning) to directly create clinical models (usually classification)
  - Image patches
  - Deep learning, CNNs, etc.

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Large-scale quantitative image features analysis: "Radiomics"

"High-throughput extraction of quantitative image features with the intent of creating mineable databases from radiological images"

Quantitative Image Features

Shape:

Edge:

Texture features:
(characterize lesion interior)

Quantifying texture: GLCM

• Gray-Level Co-Occurrence Matrix (GLCM)
• Captures heterogeneity in tissues

Structured image data ("image phenotype") represented as feature vector

Feature vector = quantitative features

Describing texture as composition of of elements from Riesz filterbank

$N = 8$

$\sum$ associated texture model
Texture model learning

2-D tissue from interstitial lung diseases in CT

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  — “radiomics”

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  — Image patches
  — Deep learning, CNNs, etc.

Image patch analysis

Image patch analysis: Feature vectors of visual words

Image patch analysis: classifying liver lesions

1. Patch Feature Extraction

• Uniform-sized patches extracted (including entire lesion and its margins)
• Sliding grid
• Normalize patches
  – Subtract mean
  – Divide by SD
• Final result = set of patch feature vectors
2. Dictionary Generation

- Represents all the unique “visual words” derived from all raw patches in all images
- Collect all raw patches
- Dimensionality reduction: PCA on patches to select components (“codewords”) with highest variance
- Cluster patches using K-means
- **Visual Word** = The centroids of each clusters
- **Dictionary** = all visual words

Feature Vector Generation

- Each image is a feature vector based on histogram of visual words
  - Dimensions = visual words in dictionary
  - Value of each dimension = count of patches closest to that visual word
- Normalize by dividing by number of patches
- Get separate feature vectors using interior and boundary dictionaries

Deep learning

- High-level abstractions of image features hierarchical, non-linear transformations
- Inspired by hierarchical visual processing by the brain
- Higher-level features (layers) are defined from lower-level ones, and represent higher levels of abstraction

Deep learning learns **feature hierarchies**

Why not do everything with deep learning?

- Need **lots of data** to train models
- Need **powerful hardware**
- Large amounts of **tagged training data** is in short supply and expensive to produce
- Many **parameters** need to be tuned, requires expertise and labor intensive
- Main applications limited to only **classification** and **segmentation**

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Key clinical uses of medical imaging (and AI)

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2. Lesion segmentation
3. Diagnosis
4. Treatment selection
5. Clinical prediction (of response or future disease)

1) Detection of image abnormalities

AKA “where’s Waldo?”

Detection of breast masses with deep learning

- Digital Database for Screening Mammography (DDSM)
- 2420 mass ROIs
- 80%/10%/10% training/test evaluation sets
- 256x256 patches, labeled as “mass” or “non-mass”
- Data augmentation: cropping, translation, rotation, flipping and scaling of image tiles
- Probability classification map of location (fully connected CNN)

Performance:

<table>
<thead>
<tr>
<th>Method</th>
<th>No. of Images</th>
<th>No. of Parameters</th>
<th>Validation Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNN-L (Deep)</td>
<td>1473</td>
<td>10,000</td>
<td>88%</td>
</tr>
<tr>
<td>CNN-II (Fully)</td>
<td>225</td>
<td>1,000</td>
<td>87%</td>
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</tbody>
</table>

Examples

Detecting retinal hemorrhages
Sliding window detection of small features compared to physician manual detection

![Image of sliding window detection](image1)

Single 224x224x3 input CNN sliding window:
Detecting any abnormal feature
Red = P ~ 0.99  Green = P ~ 0.5  Blue = ~ 0.01

2) Segmentation of image regions

- Division of image into non-overlapping, homogeneous regions
- Segmented regions often input to other processing (e.g., feature extraction, image classification)

![Image of segmentation](image2)

Segmentation of brain tumors using deep learning

- **BRAIn Tumor Segmentation (BRATS)**
  - Glioblastoma Segmentation
  - 257 Patients
  - 4 Modalities of Co-registered MR Data
  - Expert Segmentations
- Algorithm: 3-Dimensional 4-Channel Fully Convolutional Neural Network (AlexNet)
- Dice Score Accuracy: 0.89
- Inter-radiologist Dice Score: 0.89

![Image of brain tumor segmentation](image3)

3) Diagnosis: Classification of images

**AKA “is it Waldo?”**

- Benign Lymph Node
- Infiltrating Cancer

Diagnosis of liver lesions with image patches

![Image of liver lesion diagnosis](image4)

Pathology classification using quantitative image feature analysis

**Goal:** Automated classification of high- and low-grade glioma

<table>
<thead>
<tr>
<th>Actual</th>
<th>LGGGBM</th>
<th>GBM LGG</th>
</tr>
</thead>
<tbody>
<tr>
<td>GBM</td>
<td>LGGGBM</td>
<td>GBM LGG</td>
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</table>

![Image of pathology classification](image5)

<table>
<thead>
<tr>
<th>Type of Dictionary</th>
<th>Only Boundary Dict</th>
<th>Only Interior Dict</th>
<th>Both Boundary and Interior Dict</th>
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<tbody>
<tr>
<td># of Errors: 16</td>
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- **Confusion Matrix**

<table>
<thead>
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<th>Both Boundary and Interior Dict</th>
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<tbody>
<tr>
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<td>0</td>
</tr>
</tbody>
</table>

Barker, J., Hoogi, A., Depeursinge, A., Rubin, D. Medical Image Analysis 30(80-71, 2016)
Deep learning: Diagnosis of masses on mammography

- Classify breast masses as benign vs. malignant
- Branching structure of CNN to account for two views of breast
- Predictive accuracy ~ 0.8

Confocal Endomicroscopy

- Enables clinicians to obtain real time microscopic images
- “Optical biopsy”
  - based on confocal microscopy
- High resolution, dynamic, sub-surface imaging
- Used in GI and pulmonary applications
  - Barrett’s esophagus, colonic dysplasia

Bladder pathology

| Normal | Low Grade | High Grade | CIS | Inflammation |

Normal Bladder Tissue

Bladder Cancer

4) Treatment selection

Goal: Identify which GBM patients will respond to anti-angiogenic drugs

Magnetic resonance perfusion image features uncover a subgroup of GBM patients with poor survival and better response to drug treatment.
5) Clinical prediction

• Will disease respond to the treatment?
• Will the disease progress?
• Will disease recur?

Prediction: Predicting survival from quantitative analysis of histopathology images

Summary: Key points

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Thank you.

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