Applications of AI/Machine Learning in Gastroenterology & Hepatology

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Associate Professor of Internal Medicine
Goals of the Talk

• Definitions

• How can machine learning help?

• Examples:
  • Medication optimization in ulcerative colitis
  • Identifying benefits of a costly medication
  • Assessing disease progression in Hepatitis C
  • Endoscopic scoring in ulcerative colitis
Development of Maps

42.301265
-83.707957

"Turn right"
Real World Applications

- Large digital datasets
- Known outcomes
- Identify patterns in data to **predict the future**
  - Clicking on an advertisement
  - Purchasing items
  - Signing up for a promotion
  - Switching cell phone providers
Hello, Akbar. We have recommendations for you.
Can you differentiate, Cat vs. Dog?

![Graph showing the relationship between Time spent Sitting in Laps and Time spent Digging Holes, with data points for cats and dogs.]
3 Variables = 3 Dimensions
Approaches to Pattern Recognition

- Artificial Intelligence
- Machine Learning
- Deep Learning
- Support Vector Machine
- Random Forest
What is Random Forest?

- A modern machine learning method

- Computer-based algorithm that uses decision trees to classify outcomes. e.g. Cat or Dog

- Can incorporate many variables and interactions
  - Identifies most important variables for prediction
  - No “pre-conceived notions”
What is Random Forest?

Dataset

Tree #1

Tree #2

Tree #3

DOG

CAT

DOG

Majority vote, i.e. the “Forest” = DOG
How can we improve care for an individual?
Ulcerative Colitis
Treatments for Ulcerative Colitis

• Corticosteroids

• 5-ASA medications

• Immunosuppressants (IS)
  • Thiopurines

• Biologics
Mr. S

• 64 yo male

• Ulcerative Colitis

• Doing well with Imuran (Thiopurine)
Ms. J

• 23 yo female

• Ulcerative Colitis

• She failed a variety of medications and is using corticosteroids to treat this disease
Do you treat them the same?

Individualize Treatment
Example: Medication Optimization

Machine learning algorithms for objective remission and clinical outcomes with thiopurines

Waljee, et al. JCC 2017
Thiopurines and Ulcerative Colitis

• Many IBD patients require thiopurines
Thiopurines and Ulcerative Colitis

• Many IBD patients require thiopurines

• Experts monitor CBC & Chemistry ($60)
Thiopurines and Ulcerative Colitis

• Many IBD patients require thiopurines

• Experts monitor CBC & Chemistry ($60)

• Drug Levels ($300)
Drug Levels

• Low Sensitivity (64%)

• Low Specificity (63%)

• Does not predict:
  • How well they feel (subjective)
  • Healing of bowel (objective)
Hypothesis

Drug Tablets → Metabolite Levels → Effects on Immune System and Body Chemistry → Biologic Response

Pharmacokinetics   Pharmacodynamics
Aims

1. Adequate Immune Suppression
2. Lower Rate of Clinical Events (Steroids, Hospitalization, Surgery)

Patterns

1. Biologic Remission (BR)
2. Lab values and Age
   Blood counts
   Differential Chemistry
3. Objective Inflammation (not BR)
4. Inadequate Immune Suppression
5. Higher Rate of Clinical Events (Steroids, Hospitalization, Surgery)
Methods

• Retrospective analysis

• Random Forest
  • Cross-validation on Out Of Bag (OOB)

• Algorithms were developed for
  • Adequate immune suppression
  • Inadequate immune suppression
Cohort

10,726 Cases (N=1,909)

3,269 Cases (N=1,082)
Excluded all with:
- Missing Values
- Infection
- Not on medication

Biological remission
1,843 Cases (N=731)

Not in Biological remission
1,426 Cases (N=699)

ESR, CRP, FCP - Endoscopy, Histology - CTE, MRE

All normal (30d)

At least 1 abnormal
Performance Characteristics

AuROC
Performance Characteristics

Variable Importance
Performance Characteristics

Partial Dependence Plots

Waljee, et al. JCC 2017
Performance Characteristics

Classification Table

Waljee, et al. JCC 2017
### Biological Response (BR) Drug Levels

<table>
<thead>
<tr>
<th></th>
<th>BR</th>
<th>No BR</th>
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<tbody>
<tr>
<td>Predicted BR</td>
<td>30%</td>
<td>36%</td>
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<tr>
<td>Predicted no BR</td>
<td>70%</td>
<td>64%</td>
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### Biological Response (BR) MLA

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<th>BR</th>
<th>No BR</th>
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<tbody>
<tr>
<td>Predicted BR</td>
<td>69%</td>
<td>25%</td>
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<tr>
<td>Predicted no BR</td>
<td>31%</td>
<td>75%</td>
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</table>

*Predicted BR based on MLA cut-off >57%*
Performance Characteristics

How does this do clinically?
Performance Characteristics

How does this do clinically?

Waljee, et al. JCC 2017
Clinical Event Rate with Sustained Predicted Immune Suppression vs. Non-Immune Suppression

<table>
<thead>
<tr>
<th>Clinical Event</th>
<th>SPIS</th>
<th>NIS</th>
<th>SPIS</th>
<th>NIS</th>
<th>SPIS</th>
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<td>Steroid</td>
<td>0.76</td>
<td>2.39</td>
<td>0.26</td>
<td>1.31</td>
<td>0.06</td>
<td>0.25</td>
<td>1.08</td>
<td>3.95</td>
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<td>Hospital</td>
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<td></td>
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<tr>
<td>Total</td>
<td></td>
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<td></td>
<td></td>
<td></td>
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</tbody>
</table>

N=274
N=235

p=0.00000000004
Validation

External Validation of a Thiopurine Monitoring Algorithm on the SONIC Clinical Trial Dataset

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‡Department of Veterans Affairs Center for Clinical Management Research, Ann Arbor, Michigan;
§Department of Statistics, University of Michigan, Ann Arbor, Michigan
MiCHART View

Thiopurine Monitoring Test
Status: Final result  Visible to patient: MyUofMHealth.org  Next appt: 11/05/2015 at 09:45 AM in Gastroenterology

Newest results are available. Click to view them now.

- Immunosuppression Score
  - Ref Range: 100.0-160.0 %
  - 106.1
Example: Benefit of Medication

Machine learning models at week 6 can predict benefit of a biologic drug at week 52

Waljee, et al. APT 2018
Waljee, et al. IBD 2018
Background

Vedolizumab:

- is effective, but....

Background

Vedolizumab:

• is effective, but....

• Slow to work

Background

Vedolizumab:

- is effective, but....
- Slow to work
- Expensive

Decisions

It can be difficult to decide what to do with a patient who shows limited early response

- Keep using?
- Shorten Interval?
- Change to another drug?

83.1 %
Methods

• Data acquired from phase 3 study of vedolizumab in IBD
  https://clinicalstudydatarequest.com/

  • Be sick at entry

  • Week 52 have healthy bowel and no corticosteroids

Week 6 Model

- **AuROC**: 0.73
- **95% CI**: [0.65, 0.82]
Results

Variable Importance at Week 6
Predicting Success with Week 6 Model (Ulcerative Colitis)

UC subjects in testing set N=148

Model predicts 47.3% as likely to Succeed
59% Healed

Model predicts 52.7% as likely to Fail

Only 21% Healed
Disease Progression

Evaluation of Hepatitis C Disease Progression
Hepatitis C

170 Million

250,000 Veterans in 2016

3 Million
Progression

- Normal Liver
- HCV Infection
Longitudinal data

leverage longitudinal available data

Enrollment

Time Zero
(2 years after enrollment)

Person 1: Cirrhosis

Time-to-event

Person 2: Censored
## Results

<table>
<thead>
<tr>
<th>Time</th>
<th>N</th>
<th>% Events</th>
<th>Model</th>
<th>AuROC</th>
<th>SN</th>
<th>SP</th>
<th>PPV</th>
<th>NPV</th>
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<td>1 year</td>
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<td>CS Cox</td>
<td>0.807</td>
<td>0.79</td>
<td>0.71</td>
<td>0.11</td>
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<td>CS Boosting</td>
<td>0.817</td>
<td>0.77</td>
<td>0.73</td>
<td>0.11</td>
<td>0.99</td>
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<tr>
<td></td>
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<td></td>
<td>LGT Cox</td>
<td>0.828</td>
<td>0.75</td>
<td>0.76</td>
<td>0.10</td>
<td>0.99</td>
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<td>LGT Boosting</td>
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<td>0.76</td>
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<td>3 years</td>
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<td>0.72</td>
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<tr>
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<td>CS Boosting</td>
<td>0.799</td>
<td>0.76</td>
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<td>0.76</td>
<td>0.73</td>
<td>0.28</td>
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<td>5 years</td>
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<td>CS Cox</td>
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<td>0.74</td>
<td>0.70</td>
<td>0.41</td>
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<td>CS Boosting</td>
<td>0.790</td>
<td>0.75</td>
<td>0.70</td>
<td>0.42</td>
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<td>0.794</td>
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<td>0.73</td>
<td>0.74</td>
<td>0.41</td>
<td>0.92</td>
</tr>
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</table>
Example: AI in endoscopic scoring

Automated Grading of Endoscopic Disease Severity in Ulcerative Colitis
Deep Learning

Mayo 0
No Friability or Granularity
Intact Vascular Pattern

Mayo 1
Erythema
Decreased Vascular Pattern
Mild Friability

Mayo 2
Marked Erythema
Absent Vascular Pattern
Friability
Erosions

Mayo 3
Marked Erythema
Absent Vascular Pattern
Friability
Granularity
Spontaneous Bleeding
Ulcerations
The Team

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- @UM_MICHAMP