Machine Learning for Optimal Detection of Metastatic Prostate Cancer

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Background

Prostate cancer

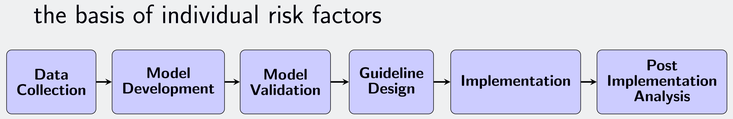
- The most common malignancy diagnosed in men
- Prognosis and survival depends greatly upon whether or not skeletal metastases or spread to lymph nodes can be identified at the time of diagnosis

Staging methods

- During staging, the urologist may order a bone scan (BS) and/or a CT scan, which are the most frequently used noninvasive imaging methods
- There are harms associated with both over-imaging and missing a patient with undetected metastases

Problem Statement

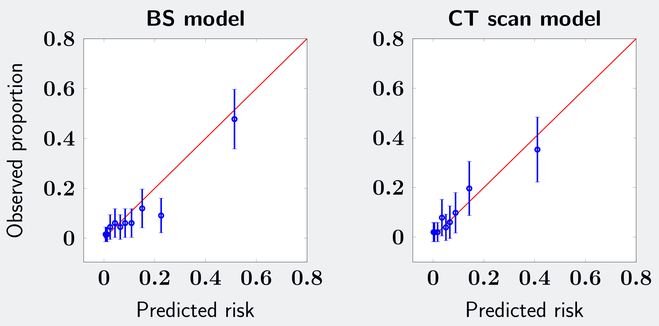
- Standard clinical guidelines indicate the need for BS and CT scan only in patients with certain unfavorable characteristics; however, the guidelines vary in their recommendations
- The goal was to determine which patients should receive a BS and/or a CT scan and which patients can safely avoid imaging on the basis of individual risk factors



- The proposed approaches were evaluated in a population-based sample of newly-diagnosed men in the Michigan Urological Surgery Improvement Collaborative (MUSIC) — a physician-led, statewide collaborative including 90% of the urologists in the state

Risk Prediction Models

- **Multivariate logistic regression models** were fit to determine the probability of a positive imaging test as a function of all routinely available clinical variables in a sample of patients who received an imaging test



Classification Modeling

- Two important challenges: learning from unlabeled data and learning from imbalanced data
  - In practice not all patients receive a staging BS or CT scan at diagnosis
  - A minority of patients has metastatic cancer
- We propose **Cost-sensitive Laplacian Kernel Logistic Regressions (Cos-LapKLR)**, a spectral clustering based semi-supervised learning approach that accounts for missing labels and class imbalance:

$$f^* = \underset{f\in\mathcal{H}}{\operatorname{argmin}} \frac{1}{l}\sum_{i=1}^{l}\left[\delta \mathbb{1}_{\{y_i=1\}}\log\left(1+e^{-f(\mathbf{x}_i)}\right)+(1-\delta)\mathbb{1}_{\{y_i=-1\}}\log\left(1+e^{f(\mathbf{x}_i)}\right)\right] + \gamma_{\mathcal{H}}\|f\|^2_{\mathcal{H}} + \gamma_{\mathcal{M}}\mathbf{f}^{\mathbf{T}}\mathbf{L}\mathbf{f}$$

where f is the decision function, $f^*(\mathbf{x}) = \sum_{i=1}^{l+u}\alpha_i^*\mathbf{K}(\mathbf{x}_i,\mathbf{x})$, u the number of unimaged patients, $\mathbf{K}$ the positive definite kernel function and $\mathbf{L}$ the Laplacian matrix

- In addition to Cos-LapKLR, several other classification models adapted for imbalance data learning were implemented:
  - Cost-sensitive logistic regression and support vector machines
  - Random forests and AdaBoost combined with advanced sampling techniques

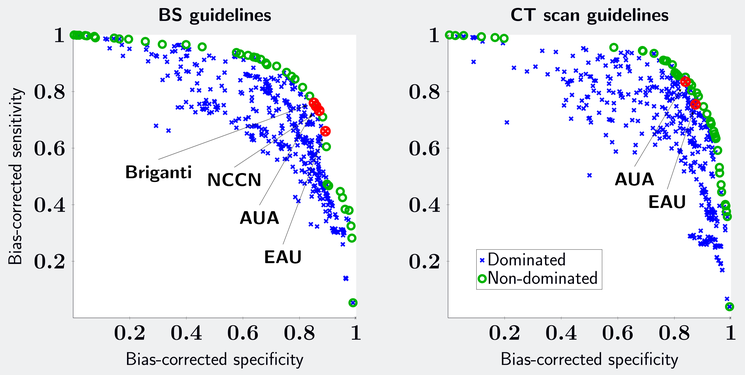
Bias-Corrected Guidelines

- The diagnostic accuracy of alternative classification models are systemically biased since they are based on only the imaged patients
- We used an established method to correct for verification bias proposed by Begg and Greenes (Stat Med., 1987 6(4):411) to evaluate the performance of the guidelines

	Uncorrected		Bias-Corrected	
Clinical guidelines	**Sensitivity**	**Specificity**	**Sensitivity**	**Specificity**
Bone scan				
EAU	100.0	31.5	84.5	75.9
AUA	97.9	43.5	81.3	82.0
NCCN	97.9	40.8	82.3	80.9
Briganti's CART	89.6	45.4	79.4	83.3
CT scan				
EAU	98.4	36.7	90.2	74.7
AUA	96.8	49.2	87.3	82.6

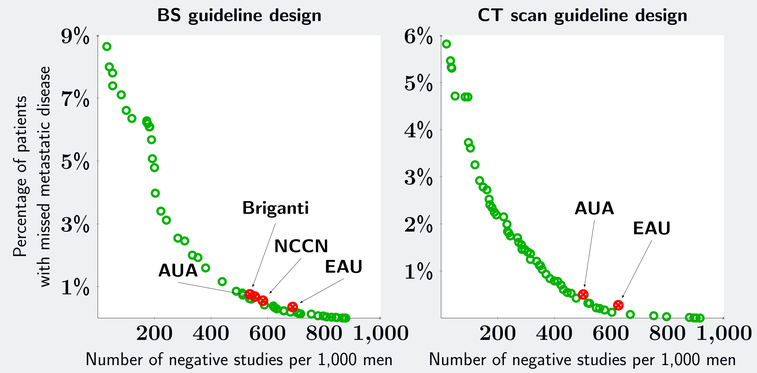
The numbers are the percentages. EAU: European Urological Association; AUA: American Urological Association; NCCN: National Comprehensive Cancer Network; CART: classification and regression tree.

- Trade-off curves were created to determine Pareto optimal models based on sensitivity and specificity
  - A model is considered *dominated* if there is another model that has a higher sensitivity and a higher specificity



Patient Centered Criteria

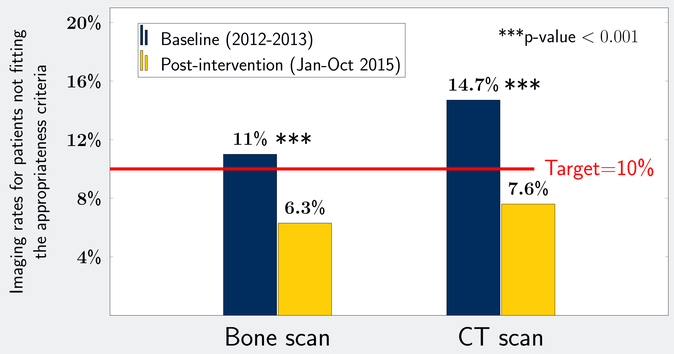
- Two important criteria were considered: expected number of positive outcomes missed and expected number of negative studies



- The published guidelines are very close to the efficient frontier for BS and CT scan while also achieving a missed metastasis rate $< 1\%$

Implementation

- The MUSIC consortium instituted statewide criteria for BS and CT scan, known as the **MUSIC Imaging Appropriateness Criteria**
- MUSIC set a statewide goal of performing imaging in $\geq 95\%$ of patients that meet the criteria and in $< 10\%$ of those that do not



- This work has had a significant societal impact by decreasing the chance of missing a case of metastatic cancer and reducing the harm from unnecessary imaging tests
- Our publications were cited in the 2016 NCCN guidelines

Selin Merdan, Christine Barnett, David C. Miller, James E. Montie, Brian T. Denton. Data Analytics for Optimal Detection of Metastatic Prostate Cancer, submitted to Operations Research (preprint available on `http://www-personal.umich.edu/~smerdan/`).

Selin Merdan, Paul R. Womble, David C. Miller, Christine Barnett, Zhu Ye, Susan M. Linsell, James E. Montie, Brian T. Denton. Toward better use of bone scans among men with early-stage prostate cancer. Urology, `DOI: 10.1016/j.urology.2014.06.010`.

Rachel Risko, Selin Merdan, Paul R. Womble, Christine Barnett, Zhu Ye, Susan M. Linsell, James E. Montie, David C. Miller, Brian T. Denton. Clinical predictors and recommendations for staging computed tomography scan among men with prostate cancer. Urology, `DOI: 10.1016/j.urology.2014.07.051`.

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