Mathematically Predicting Treatment Response of Hepatocellular Carcinoma Patients

Team Live and Let Liver
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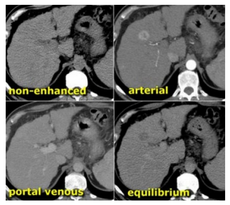
Motivation

- Hepatocellular Carcinoma (HCC) is one of the most lethal forms of cancer, with most patients not surviving more than 20 months [1]
- Treatment options, such as transcatheter arterial chemoembolization (TACE) are invasive, expensive, and often ineffective in extending the lives of patients [2]
- Oncologist methodology for deciding which treatment to use are subjective and based on experience
- We seek a **mathematical model that predicts the responsiveness of HCC patients to TACE**

Background: Hepatocellular Carcinoma (HCC)

Hepatocellular Carcinoma (HCC)
- Third most lethal variety of cancer, often associated with cirrhosis of the liver and hepatitis [3]
- Life expectancy is 6-20 months [1]
- HCC causes more than 660,000 deaths per year
- Common treatment is TACE, which is quite invasive, but not all patients respond to it [2]

Patient Imaging
- Patients are imaged using computerized tomography (CT)
- Four images are taken at different times
- Contrast agent is injected into patient's arm and flows through circulatory system, illuminating the tumor first



Description of Data

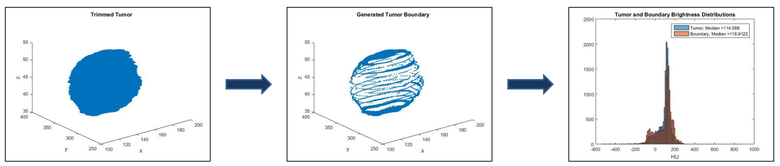
Our patient feature data comes from three sources:

1. CT Scan Feature Data
   - Each patient's 4 CT scans were processed with software called Atropos
   - This generates ~450 features per patient

2. Patient Medical Data
   - Mentor provided anonymized patient medical records
   - Includes ~ 15 features including age, hepatitis, cirrhosis, etc.

3. Self-Generated Data
   - Some features were expected to be predictive, but were not in dataset
   - We generated tumor encapsulation and vascularity features in MATLAB

Tumor Encapsulation Feature:
Measures whether the tumor contains a dense boundary of connective tissue



Regression-Based Feature Selection

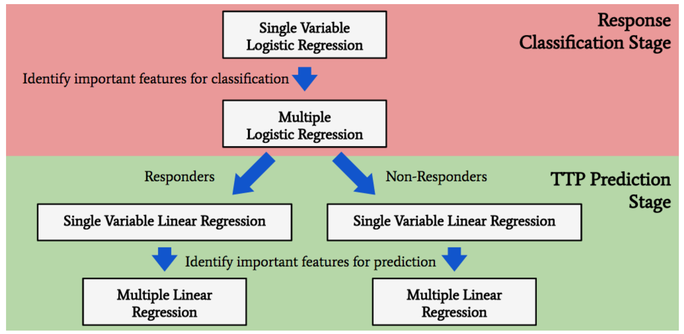
- With a dataset that contains 500 features but only 20 patients, it was important to select only important features to include in the model
- We used a single-variable regression-based method for selecting important features to include in our model

Method:
- For each feature, perform a regression of that feature compared to a response variable:
  - Categorical variable – logistic regression – binary response variable
  - Continuous variable – linear regression – TTP is response variable
- Compare R^2 or deviance values to determine predictive features

Model Overview

- The model was split into two stages:

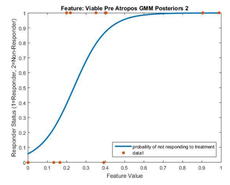
1. Response-Classification Stage:
   - Select features for R/NR classification with logistic feature selection
   - Use multiple logistic regression to classify patients
2. TTP Prediction Stage
   - Select features for TTP prediction with linear feature selection
   - Use multiple linear regression to predict TTP for each group



Response Classification Stage

- Generate a multiple logistic regression model using three most important features identified by single logistic regression:
  1. Del_Atropos_GMM_Posteriors3
  2. viable_Pre_Atropos_GMM_Posteriors2
  3. viable_Pre_Atropos_GMM_Posteriors3

$$Response = 2 - \frac{1}{1 + e^{-(16.7 - 9.0x_1 - 23.4x_2 - 287.9x_3)}}$$



Average classification accuracy of 92% using cross-validation

- Next step: improve classification accuracy with multilayer neural network

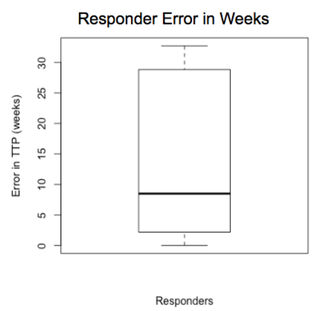
TTP Prediction Stage

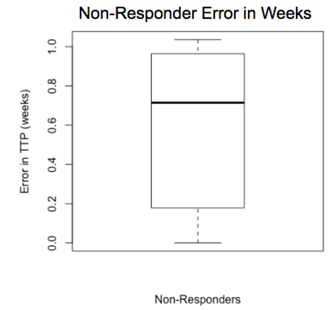
- After patients are classified as responders or non-responders, a multiple linear regression model is used to fit to each group
- Different features are significant for each case:
- Important responders features:
  1. Mean.Del_ATROPOS_GMM_POSTERIORS2
  2. Mean.Del_ATROPOS_GMM_POSTERIORS1
  3. Mean.Del_SKEWNESS_RADIUS_3
  4. hep_b
- Important non-responders features:
  1. Mean.Pre_SKEWNESS_RADIUS_5
  2. Metastasis
- Responders: Mult. R-squared: 0.87, Adj. R-squared: 0.77

$$TTP = 1.76 * 10^2 - 1.011 * 10^2 x_1 + 4.906 x_2 + 9.6 * 10 x_3 - 1.12 * 10^7 x_4$$

- Non-Responders: Mult. R-squared: 0.80, Adj. R-squared: 0.75

$$TTP = 5.04 - 7.21 * 10^{-5} x_5 + 0.96 x_6$$





Conclusion and Future Plans

Results:
- ***92% classification accuracy for Responders vs. Non-Responders***
- Median TTP prediction errors for split models:
  - Responders: 8 weeks
  - Non-responders: 0.7 weeks

Next steps:
1. Improve classification error using multilayer perceptron neural network
2. Obtain more data and further test model
3. Hand over to MD Anderson to continue work

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References

[1] Forner et al. "Hepatocellular Carcinoma." *Lancet (London, England)* 379, no. 9822 (March 31, 2012): 1245–55.
[2] Altekruse er al. "Hepatocellular Carcinoma Incidence, Mortality, and Survival Trends in the United States From 1975 to 2005." *Journal of Clinical Oncology* 27, no. 9 (March 20, 2009): 1485–91.
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