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TEXAS MEDICAL CENTER NASA/JOHNSON SPACE CENTER

COOPERATIVE AGREEMENT PROGRAM NCC-9-38, ROUND

COVER SHEET FOR FINAL REPORT

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Title:	A Comparison of NASA Induction Tools for the Creation of Decision Rules Regarding Treatment for Clinically Localized Prostate Cancer
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ARTICLES

Kattan MW, Hess KR, Beck JR. Experiments to determine whether recursive partitioning (CART) or an artificial neural network overcome theoretical limitations of Cox proportional hazards regression. *Computers & Biomed Res* 1998; 31(5):363-373.

BOOK CHAPTERS

Kattan MW, Ishida H, Scardino PT, Beck JR. Applying a neural network to prostate cancer survival data. In: Intelligent Data Analysis in Medicine and Pharmacology. Edited by N Lavra, E Karavnou and B Zupan. Boston: Kluwer Academic, 1997: 295-306.

PROJECT SUMMARY

NASA has developed computationally intensive tools which can be used for medical classification problems. These tools include recursive partitioning (also called CART) and artificial neural networks. However, most medical decision making problems are not those of classification but those which contain time-until-event (also called survival) data. The challenges are (1) how to extend these computational tools to survival-type data, (2) how to tell when the computationally-intensive tool will perform better than a standard statistical method, and (3) to test these tools on a clinically challenging problem, the prognosis of patients with clinically localized prostate cancer who are treated with surgery.

In the beginning of this project, work was directed at the methodology for extending these tools to the context of survival data. We did this by extending some of the previous work by others who have developed a similar tool. We tested our extensions and found that the were feasible.

With the tools in place, we began to experiment with performance issues. Theoretically these tools overcome limitations of the traditional survival technique, the Cox proportional hazards regression model. Experiments were designed to test whether the new tools would, in practice, overcome these limitations. Two datasets were selected where theory suggests CART and the neural network should outperform the Cox model. The first was a published leukemia dataset manipulated to have a strong interaction that CART should detect. The second was a published cirrhosis dataset with pronounced nonlinear effects that a neural network should fit. Repeated sampling of 50 training and testing subsets were supplied to each technique. The concordance index C was calculated as a measure of predictive accuracy by each technique on the testing dataset. In the interaction dataset, CART outperformed Cox ($p<0.05$) with a C improvement of 0.1 (95% CI: 0.08 to 0.12). In

the nonlinear dataset, the neural network outperformed the Cox model ($p<0.05$) but by a very slight amount (0.015). As predicted by theory, CART and the neural network were able to overcome limitations of the Cox model. Experiments like these are important to increase our understanding of when one of these new techniques will outperform the standard Cox model. Further research is necessary to predict which technique will do best *a priori* and to assess the magnitude of superiority.

Prediction of treatment efficacy for prostate cancer therapies has proven difficult and requires modeling of survival-type data. One reason for the difficulty may be infrequent use of flexible modeling techniques, such as artificial neural networks. The purpose of this part of the project was to illustrate the use of an artificial neural network to model prostate cancer survival data and compare the neural network to the traditional statistical method, Cox proportional hazards regression.

Clinical data and disease follow-up for 983 men were modeled by both an ANN and a Cox model. Repeated sampling of 200 training and testing subsets were supplied to each technique. The concordance index was calculated for each testing dataset. As further validation, neural network and Cox models were applied to a totally separate dataset.

The neural network outperformed the Cox model in the 200-fold cross-validation (neural network c=0.76, Cox c=0.74) and on the validation dataset (neural network c=0.77, Cox c=0.74). Neural networks were more discriminating than Cox models for predicting cancer recurrence. Calibration of the neural network remains a problem. Once solved, it is expected that a neural network will make the most accurate predictions of prostate cancer recurrence and improve treatment decision making.