A Decision Support System for the treatment of esophageal cancer

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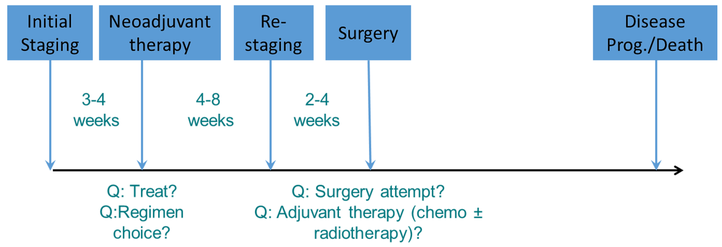
Introduction

In oncology deciding which treatment(s) to use and when can be challenging. Currently there are no global and accessible approaches available to optimise treatment strategies on an individual patient basis. Focusing on cancer of the esophagus and gastro-esophageal junctional, we have developed a prototype of a model-based Decision Support System (DSS). It integrates a novel range of drug, tumour and patient data to better plan clinical treatment, optimise the patient care path, and ultimately deliver improved cancer care.



Time from initial staging to disease progression/death.

Methods

This tool was developed using data from an historical cohort of patients with operable esophageal cancer. This cohort comprised 465 patients who were treated at Oxford University Hospitals NHS Foundation Trust, UK between 2007 and 2014. Of these 465, 277 had complete imaging data with serial 18F-FDG PET-CT before and after neoadjuvant chemotherapy (NAC) were taken forward into the development of the image based DSS.

An initial data analysis using un-supervised learning methods, K-means and Principal Component Analysis (PCA), were used to identify key variables that differentiated groups of patients. These variables were then used to analyse their correlation to survival and key decision points using parametric statistical models. The final models were then used to create a web-based DSS prototype.

Data Set

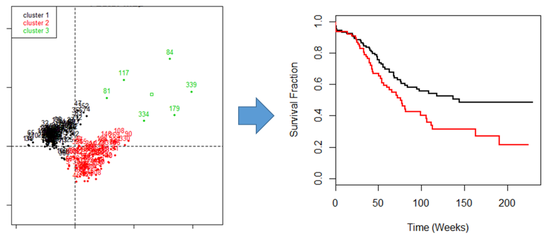
Table below shows a subset of the baseline characteristics of the patients.

Treatment	Neoadjuvant chemotherapy + Surgery	277
Gender	Male Female	74% 26%
Age	Median (IQR)	65 (57-71)
Impassable tumour at endoscopic ultrasound	Yes	65
TNM Stage	II III	100 177
Cell type	Adenocarcinoma Small Cell Carcinoma Adenosquamous	221 49 3
Avid Tumour Length (cm)	Median (IQR)	5.3 (3.7-6.8)
Avid Nodes	Yes	116
Chemotherapy	Double (CF or OF)[1] Triple (ECX or ECF)[2]	210 67
Blood Glucose (mg/dL)	Median (IQR)	5.8 (5.3-6.3)

[1] Two cycles. Key:C=cisplatin; F=5-FU; O=oxaliplatin.
[2] Three cycles. Key:C=cisplatin; F=5-FU; E=epirubicin; X=capecitabine (5-FU metabolite).

Statistical Analysis - Pre-Chemo Prognosis

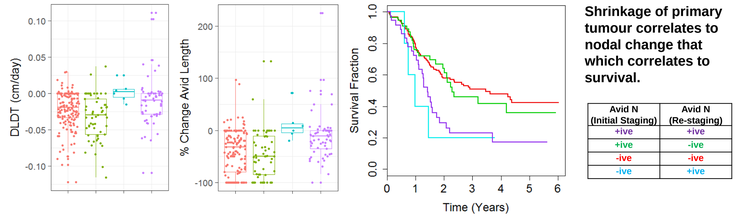
- Using K-means/PCA clustering on all pre-treatment variables
  - Identified 3 clusters – green cluster has low numbers so focus on red v black
- Generated clusters: differing prognosis
  - Top ranking covariates: **Impassable Disease & Avid Nodes (Yes/No)**



Left panel: PCA analysis. Right panel: Survival prognosis for the two main clusters identified by PCA analysis.

Statistical Analysis - Post-Chemo Prognosis

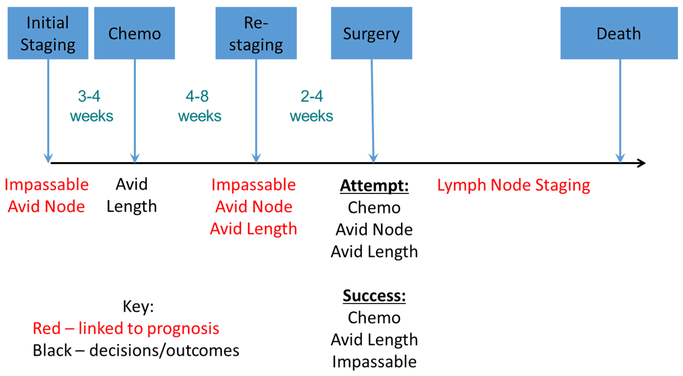
Change in Avid Length and Change in Nodal Status.



Shrinkage of primary tumour correlates to nodal change that which correlates to survival.

Avid N (Initial Staging)	Avid N (Re-staging)
+ive	+ive
+ive	-ive
-ive	-ive
-ive	+ive

Statistical Analysis - Result Summary

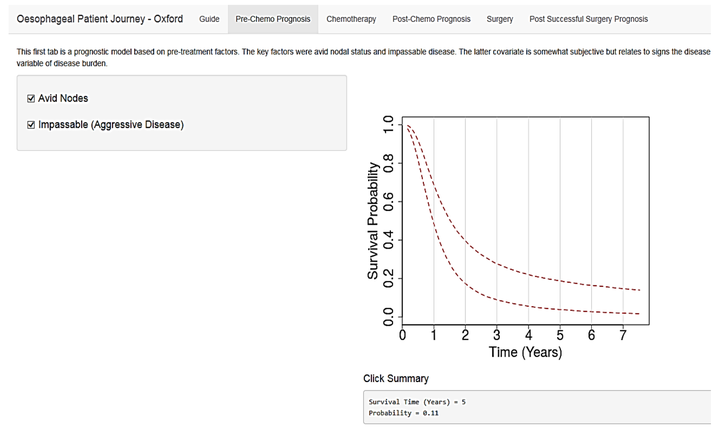


Key Results:

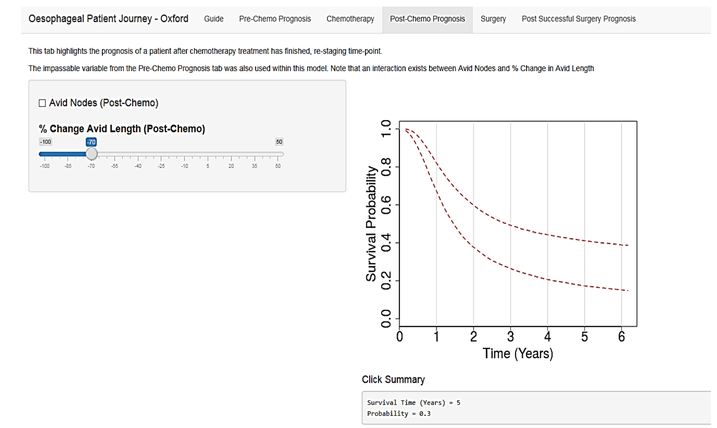
- Change in avid nodal status (metabolic nodal response) due to chemotherapy independently predicts survival
- Change in avid length of the primary tumour (metabolic tumour response) correlates with metabolic nodal response
- Choice of chemotherapy doesn't seem to influence either
- Impassable disease predicts unresectable disease

Decision Support System screen shots

Representative illustrations showing how the DSS could be used to explore a patients treatment journey. Top panel below shows a poor prognosis at staging due to positive nodal status and impassable disease. Bottom panel below shows how the prognosis improves if chemotherapy reduces the size of the tumour and results in a complete metabolic nodal response.



Prognosis at staging, i.e. before neo-adjuvant chemotherapy. Survival at five year for 95% of the patients is comprised between 4 and 20 %.



Prognosis at restaging, i.e. after neo-adjuvant chemotherapy. Survival at five year for 95% of the patients is comprised between 18 and 42 %.

Conclusions

We have created a DSS tool using historical data to support Cancer Multidisciplinary Teams in understanding how key variables affect treatment choices and how these in turn relate to disease outcomes. The tool has the potential to be used to support the optimisation of treatment for individual patients based on the characteristics of their disease. Thus the DSS tool developed is a first step to personalised treatment of cancer.