Title: Developing a risk calculator for cancer staging for blood cancer by IIIT-Delhi and AIIMS, New Delhi

Multiple Myeloma (MM) is a type of blood cancer that is owing to the malignancy of plasma cells. The overall survival of patients after being diagnosed with MM ranges from 6 months to more than 10 years. The variability in the outcome is an implication of the underlying biological heterogeneity. The current risk predictors of MM have been established on western populations and do not integrate ethnicity-specific information, the impact of which on disease biology cannot be overlooked.

India is ethnically diverse and has wide disparity in its healthcare infrastructure. A large number of cancer patients are initially diagnosed at peripheral hospitals and then seek specialized cancer care at advanced cancer centres. Staging of cancer is important in assessing the risks of progression, morbidity, mortality and to decide the appropriate treatment. The investigations done at the initial presentation of the disease are crucial in staging of the cancers. It is, therefore, important to develop staging systems that are based on simple tests that are widely available and yet have strong impact on disease so as to be informative of the cancer stage.

In this context, a team of researchers led by was led by Dr. Ritu Gupta, Professor, Laboratory Oncology Unit, Dr. B.R.A. IRCH, AIIMS, New Delhi and Prof. Anubha Gupta, Deptt. of ECE and member, Centre of Excellence in Healthcare (CoEHe) IIIT-Delhi, did a systematic evaluation of more than 1000 Indian patients of MM. The team established the impact of ethnicity on MM risk prediction and developed two efficient and robust Artificial Intelligence (AI)-enabled risk-staging systems, namely, 1) Modified risk staging (MRS) system for patients in whom high-risk cytogenetic aberrations (HRCA) based on genomic data is not available and 2) Consensus based risk-staging system (CRSS) to establish the biological relevance of the risk predictions in patients for whom the genomic data is available. The team identified disease-specific parameters and assigned them weightage using AI and incorporated them into the risk stage prediction based on their ability to contribute to the risk of the disease.

The MRS is based on patient and disease-specific parameters of age, serum levels of albumin, creatinine, beta 2 microglobulin, calcium, and haemoglobin. All of these six parameters are tested on blood and are widely available at the level of district hospitals. The simplicity of the method allows for staging of the disease for almost all the patients diagnosed with multiple myeloma in our country. The CRSS is an advanced model which includes additional three genetic parameters and can be used in patients in whom cancer genetic testing is available.

Both these MRS and CRSS works have been published in renowned peer-reviewed international journals and were compared with the current international staging system, i.e., the revised International Staging System (R-ISS). Full details are available for MRS work in the publication in the journal of Translational Oncology, Elsevier, Link: https://www.sciencedirect.com/science/article/pii/S1936523321001492?via%3Dihub, and for CRSS work in the publication in the journal of in Frontiers in Oncology, Link: https://www.frontiersin.org/articles/10.3389/fonc.2021.720932/full. We used curated dataset of more than 1000 patients of multiple myeloma collected over a period of five years and another dataset of 900 patients from the American population curated by the Multiple Myeloma Research Foundation (MMRF), USA. Both the risk prediction and staging systems

developed by us performed better than RISS in Indian cohort and also improved risk stratification in the American dataset.

We have designed simple online tools to allow automated calculation of MRS and CRSS. One can find out the stage of the disease by feeding the values of the laboratory test results and age of the patient; and generates predictions for survival for the particular patient case. These tools are freely accessible via the following links:
MRS calculator: http://sbilab.iiitd.edu.in/pub_files/MRScalculator_DecisionTree.html
CRSS calculator: http://sbilab.iiitd.edu.in/pub_files/CRRScalculator_edit.html

Our CRSS work discovers changes in cut-offs in Indian patients from the established cut-offs of prognostic features and highlights the need for focused research to identify the differences and unique features of Indian patients with cancers for better risk stratification to decide on appropriate treatments. This work establishes novel robust risk-staging models that can be widely employed in India with its existing diversity and disparity in the health care infrastructure. As of now, the proposed calculators are validated for Indian population. In future, this concept can be used to develop risk stratification models for specific ethnic groups across the globe.