



Research Translation in the digital age: harnessing the power of data and analytical technologies

8th Annual NHMRC Symposium on Research Translation

19 - 20 November 2019, Pullman Albert Park, Melbourne

# Deep PolyOmics: Towards an Integrative Blood+MRI+Omics Al Model for Early Detection and Diagnosis of Prostate Cancers



# Sriganesh Srihari, Lewis Smith, Ray Kwong, Elliot Smith

Maxwell Plus c/o WeWork, 310 Edward Street, Brisbane Queensland 4000, Australia Contact: elliot / sriganesh @ maxwellplus.com

## 1. Introduction **Prostate Cancer (PCa)**

- The prostate gland is part of the male reproductive system.
- Prostate cancer is the second most common cancer among males in Western countries [1].
- Estimated ~165,000 new cases and ~29,500 PCa-related deaths in 2018 alone [2].
- PCa is generally a slow growing disease and the majority of men with low grade PCa live for many years without symptoms and without it spreading and becoming life-threatening. However, high grade disease spreads quickly and can be lethal.
- Appropriate management is key.

#### PCa Diagnosis and Treatment: Current Practice

Prostate screening tests: Prostate-specific antigen (PSA) test from veinal blood sample; Digital Rectal Examination (DRE) to test abnormalities in texture, shape or size of the gland.

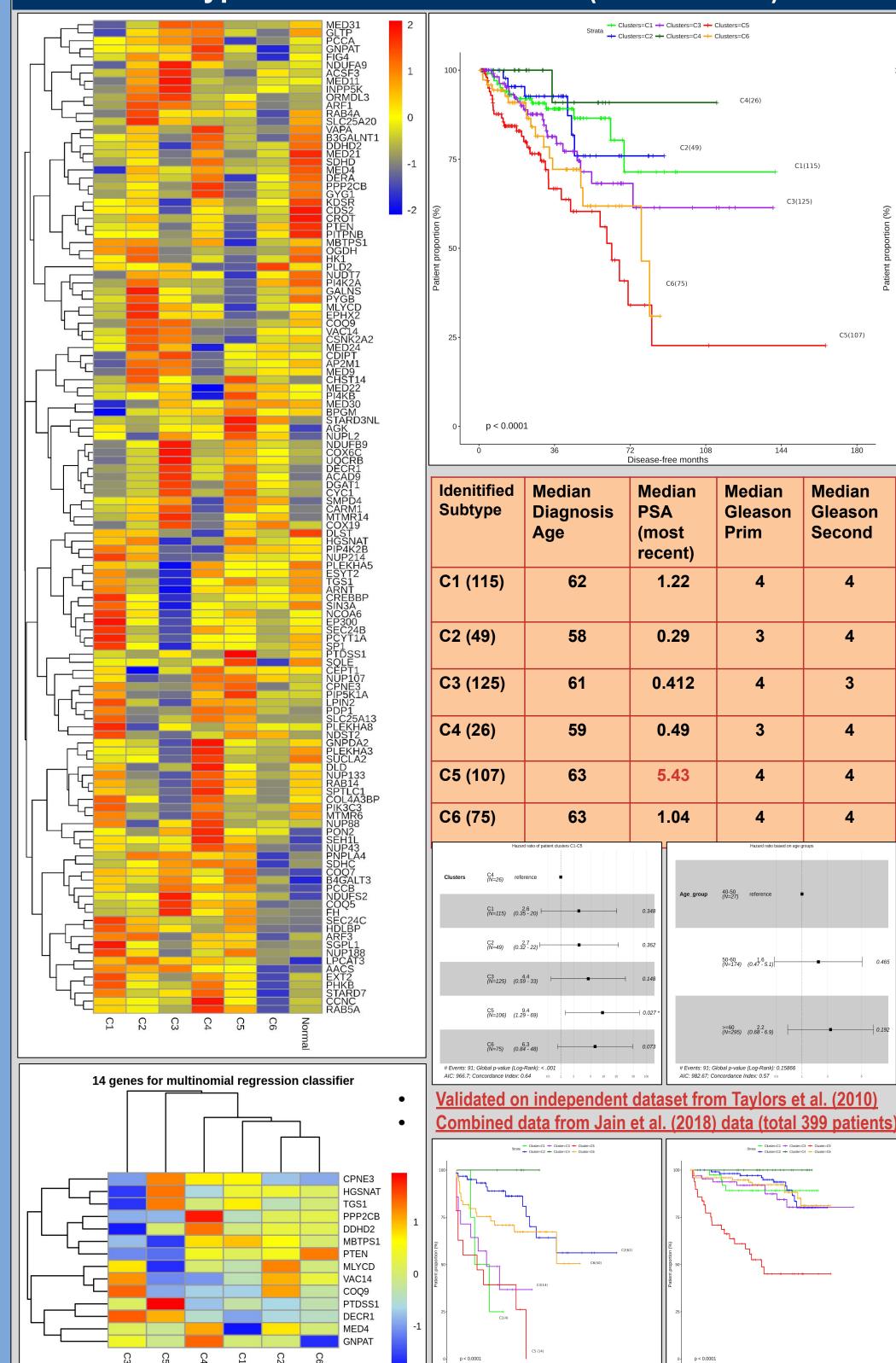
**Diagnosing PCa:** Transrectal ultrasound using a probe; Thin needle biopsy to collect a prostate tissue sample for pathological analysis; MRI fusion combining biopsy and diagnosis; MRI/CT-based diagnosis leading to a PI-RADS score (I-V).

**Determining aggressiveness:** Pathological examination of biopsied tissue sample to determine how much cancer cells differ from normal cells, leading to a Gleason score (2-10).

#### **Prostate Cancer Risk Factors**

- Age: PCa is an age-dependent disease with risk 1:7 (by age 75) and 1:5 (by age 85).
- Family history: First-degree male relative with PCa, then higher risk of early PCa.
- Genetics: Inherited/familial genetic alterations in BRCA1, BRCA2 and HOXB13.
- Genes associated with PCa onset: ATM, BRCA1, BRCA2, FANCA, HOXB13, PALB2, PTEN. Diet and Lifestyle: Processed meat or food high in fat; Obesity: PCa risk is 9-50% higher per
- 5-unit of body-mass index (BMI) likelihood of higher-BMI men diagnosed at advanced stage.

## 2. Six Metabolic Subtypes of Prostate Cancer **Subtypes identified from TCGA (498 Patients)**

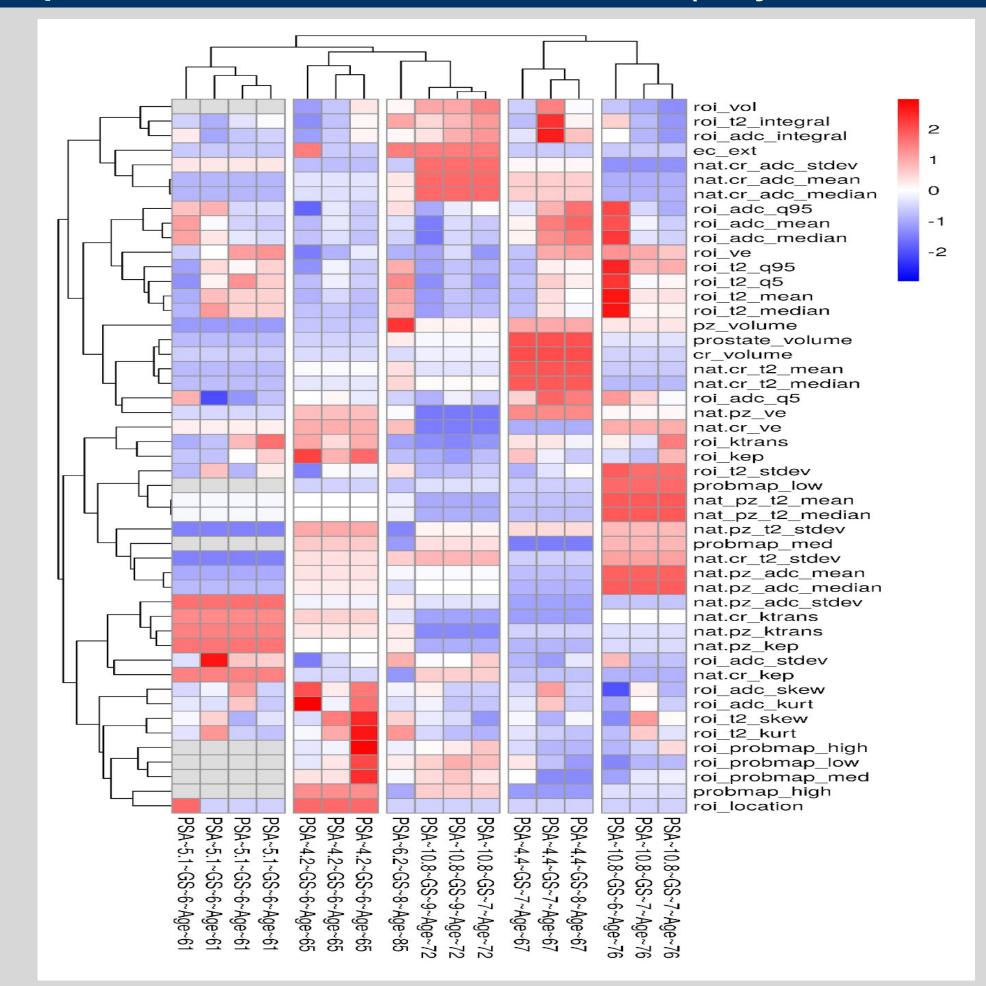


## 3. Prostate Cancer Datasets Used in the Study

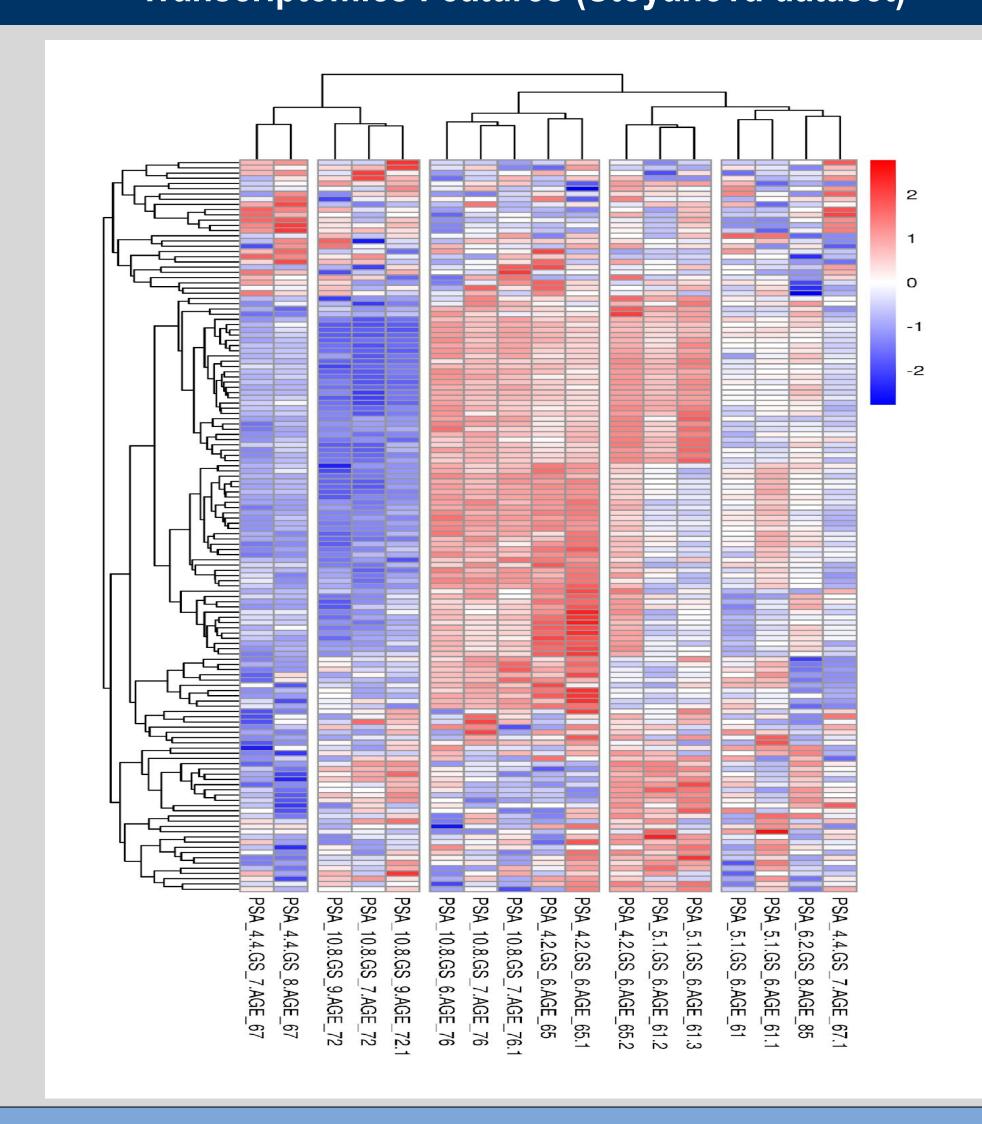
- Stoyanova et al. (2016, 2017, 2018): MRI T2 and ADC and transcriptomics data from a total 44 PCa patients.
- Li et al. (2018): MRI T2 and transcriptomics data from 17 patients including information on whether MRI-detectable/visible or MRI-undetectable/invisible.
- The Cancer Imaging Archive (TCIA) dataset including 498 patients with transcriptomics data of which 14 patients have MRI T2 and ADC images.
- Radiomics features extraction: Using the IBEX radiomics platform (2015) References: Stoyanova et al.: Prostate cancer radiomics and the promise of radiogenomics. Transl Canc Res 2016, 5(4):432-447.
- Li et al.: Genes involved in prostate cancer progression determine MRI visibility. Theranostics 2018, 8(7):1752-1765.
- TCIA PRAD: https://www.cancerimagingarchive.net/

# 4. Feature Extraction from Multiple Modalities

mpMRI T2 and ADC Radiomics Features (Stoyanova dataset)

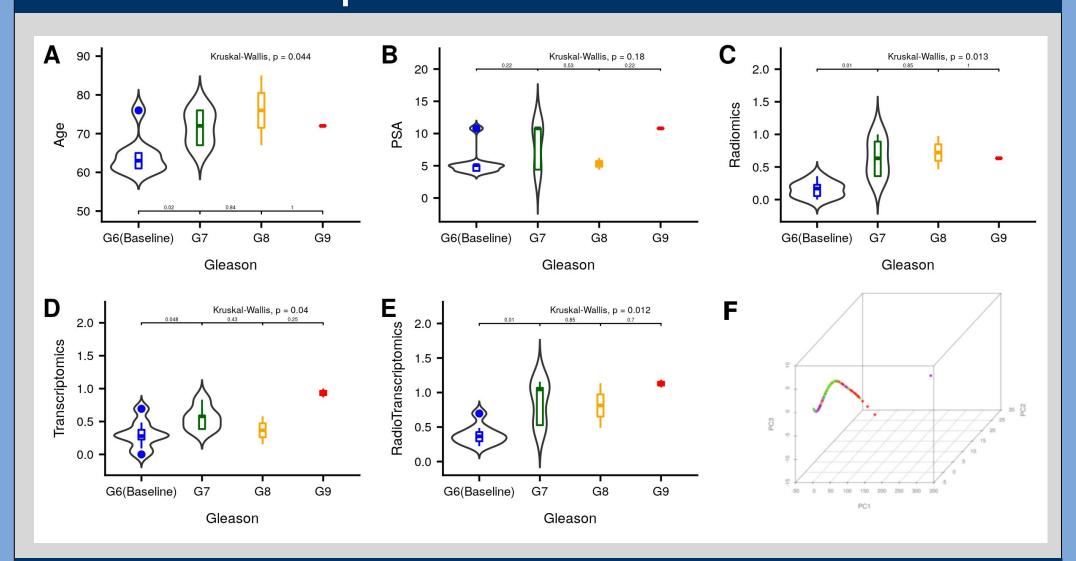


## Transcriptomics Features (Stoyanova dataset)

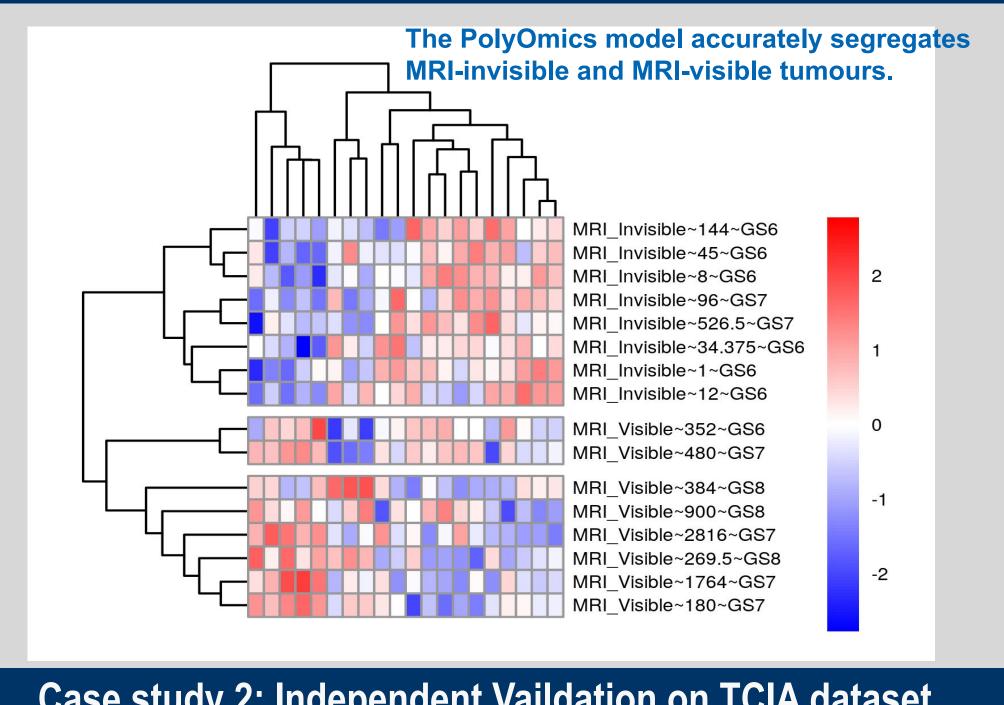


## 5. PolyOmics Machine Learning Model

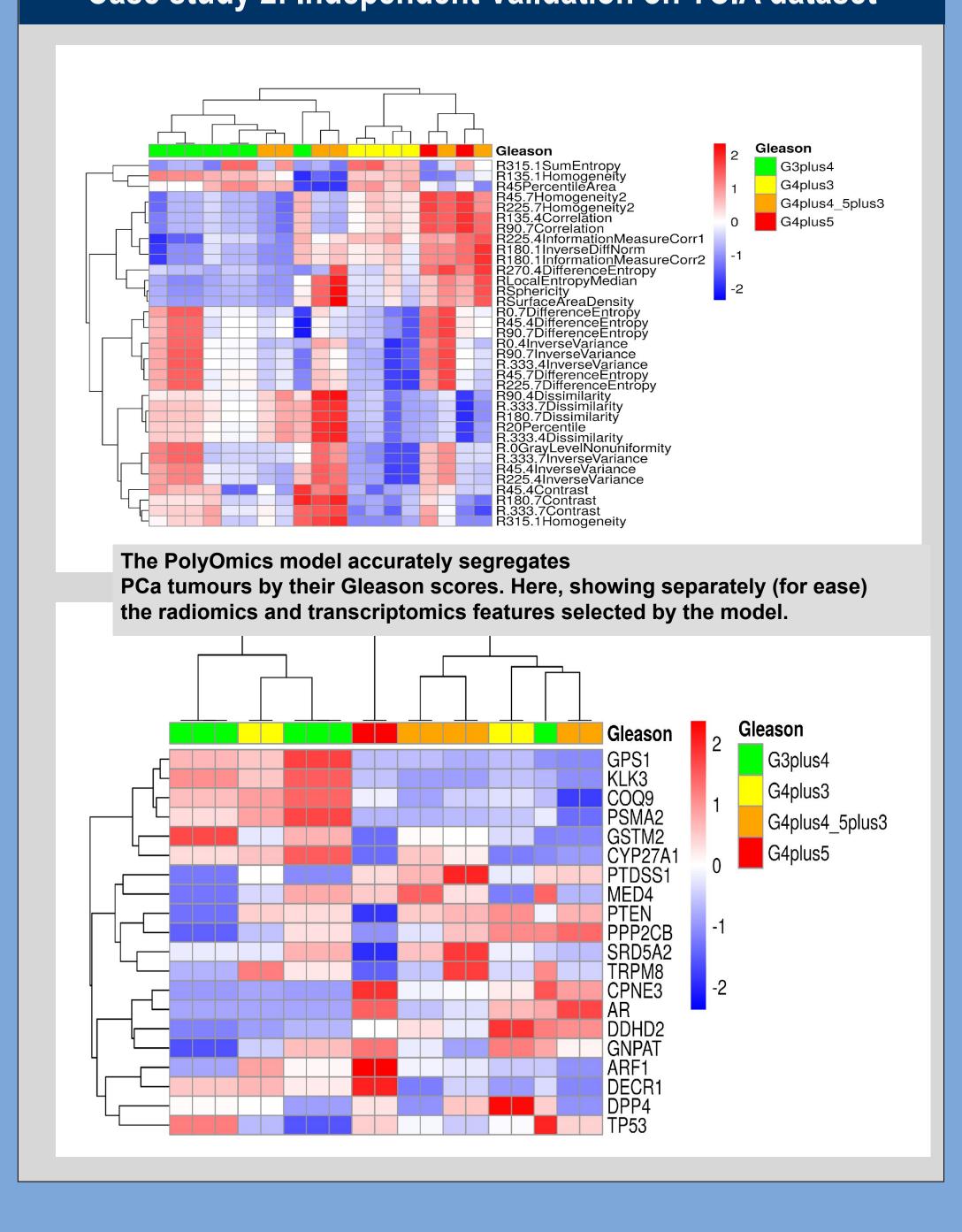
## RadioTranscriptomics Model to Combine Modalities



#### Case study 1 (Li 2018 dataset): Identifying MRI-invisible Tumours

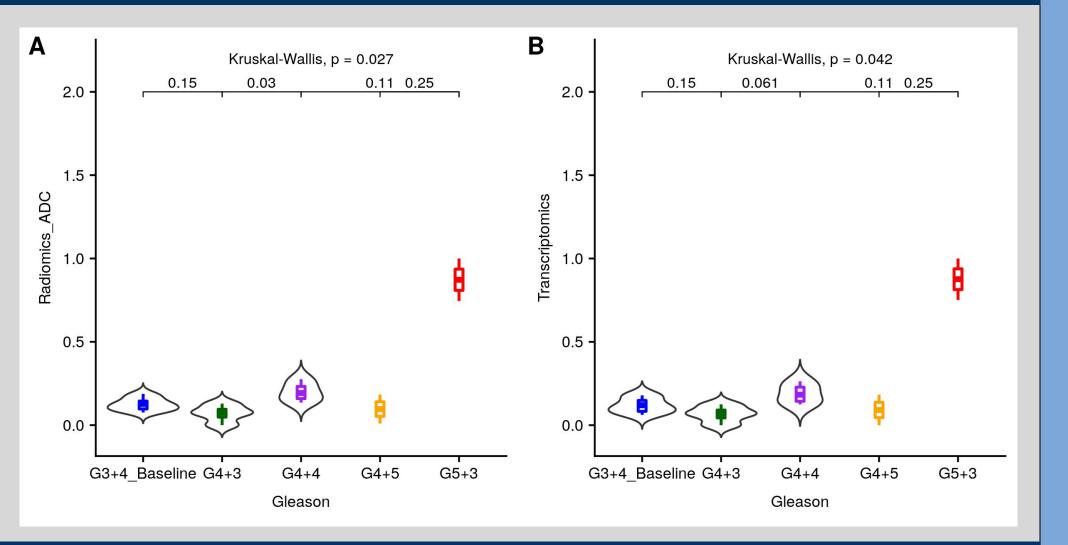


## Case study 2: Independent Vaildation on TCIA dataset



## 6. PolyOmics Machine Learning Model

## RadioTranscriptomics Model



#### **10. Conclusions**

- Early detection and accurate diagnosis of prostate cancers will help accelerate treatments for patients with aggressive tumours and at the same time deescalate treatments including placing on active surveillance for patients with slow-growing or low-risk tumours.
- The commonly used first-line screening PSA test is highly non-specific and in many cases overestimates the tumour aggressiveness while missing out on certain aggressive tumours of the central gland that do not express high levels of PSA/KLK3.
- T2 and ADC mpMRI play an important role in catching aggressive tumours early and add significant prognostic value to the PSA-based first-line screening.
- However, the undetectable/invisible nature of certain PCa tumours, particularly fragmented tumours, makes it hard for radiologists to spot them quickly, thereby making diagnosis harder.
- Here, we are developing a "PolyOmics" model to integrate clinical risk factors, age, PSA, and mMRI-derived radiomics data together with biopsy- or circulating-tumour-cells-derived transcriptomics data for early and precision diagnosis
- Preliminary results albeit on small cohorts shows that the PolyOmics model performs better than individual models (age, PSA, radiomics and transcriptomics alone)

#### The Maxwell Plus Platform

For more information, visit: <a href="https://maxwellplus.com/">https://maxwellplus.com/</a>