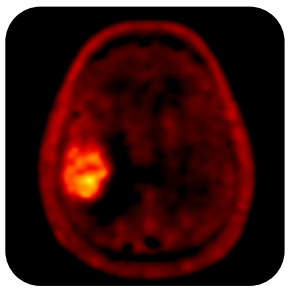
Profiles of Short Chain Fatty Acid Metabolism as Genetic Biomarkers for Primary Brain Gliomas

Marianna Inglese[1,2], Tommaso Boccato[1], Matteo Ferrante[1], Shah Islam[2], Matthew Williams[3,4], Adam D Waldman[5], Kevin O'Neill[6], Eric O Aboagye[2], Nicola Toschi[1,7]

[1] Department of Biomedicine and Prevention, University of Rome Tor Vergata, Italy; [2] Department of Surgery and Cancer, Imperial College London, UK; [3] Computational Oncology Group, Department of Surgery and Cancer, Imperial College London, UK; [4] Institute for Global Health Innovation, Imperial College London, UK; [5] Centre for Clinical Brain Sciences, University of Edinburgh, UK; [6] Imperial College Healthcare NHS Trust, London, UK; [7]Department of Radiology, Athinoula A. Martinos Center for Biomedical Imaging, Boston, MA, USA

marianna.inglese@uniroma2.it



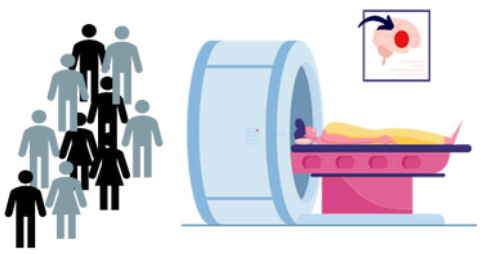
INTRODUCTION

Glioblastoma multiforme (GBM) is the most common malignant primary brain tumor.
The diagnosis, therapy and survival of patients with glioblastoma multiforme is highly affected by the genetic profile of such lesions. The primary GBM biomarker is **isocitrate dehydrogenase** (IDH) and patients with mutant IDH1/2 GBM have a better outcome compared to those with wild-type IDH tumor.

Is the distribution of short chain fatty acids (SCFA) metabolism in primary brain lesions correlated to their genetic profile (patient outcome)?

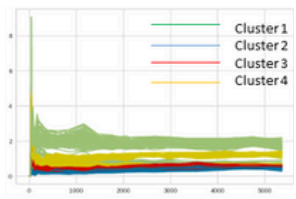
MATERIALS AND METHODS

Ten treatment-naïve patients underwent dynamic [18F]FPIA PET/MRI.
Volumes of interests were manually drawn on the enhancing solid tumour and two reference tissues



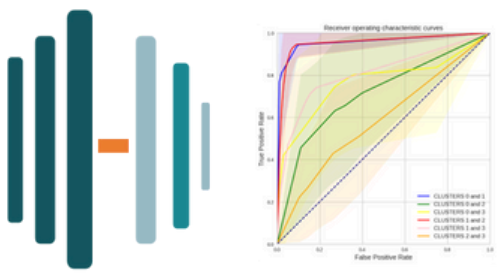
DATA ACQUISITION

25202 (±14337) PET time activity curves (TACs) were extracted voxelwise from the lesion VOIs and clustered with a K-means clustering approach.



METABOLIC CLUSTERING

For the classification of FPIA TACs of IDH mutant vs wild-types GBMs a deep model was used with grouped TACs from the different clusters, alone or concatenated in any possible combination.

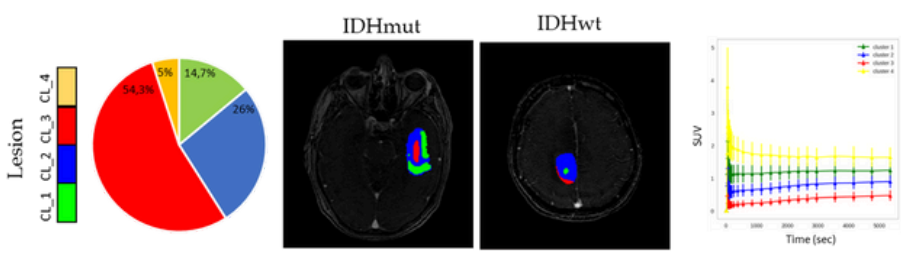


GENOTYPE CHARACTERISATION

RESULTS

- Functional profiles of SCFA metabolism were found in GBMs

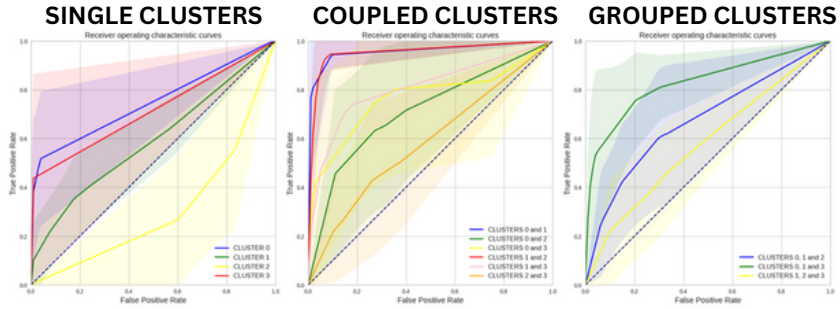
K-Means algorithm found **4 different profiles of SCFA metabolism** in the lesion with a more heterogeneous distribution as compared to healthy tissue and vessel.



- Clusters 1 and 2 metabolic profiles define IDH mutation

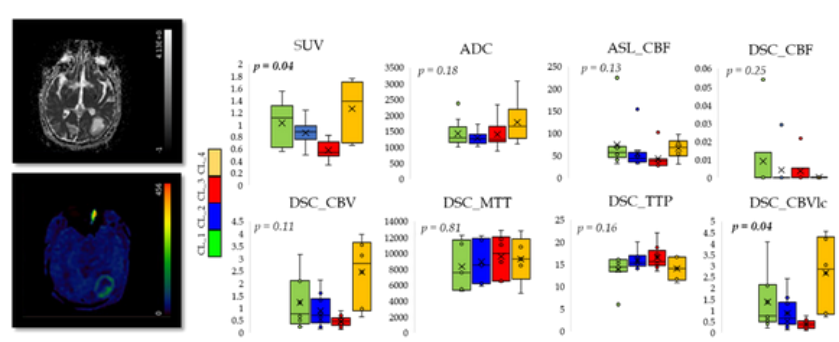
Mutant GBMs are classified with **96.15% (± 3.24) accuracy and 0.96 (± 0.04) AUC** by clusters 1 and 2's FPIA TACs. The worst performance was obtained by Cluster 3 with 23.67% (± 16.83) accuracy (0.31 (± 0.17) AUC). Static and unclustered PET also failed in the classification.

SINGLE CLUSTERS **COUPLED CLUSTERS** **GROUPED CLUSTERS**



- A multiparametric analysis revealed a trend in diffusion and perfusion MRI parameters

Over imposing the FPIA-PET-cluster-defined subregions over the multiparametric MRI maps revealed subregions with a high FPIA uptake are also characterised by **restricted diffusion** (as defined by ADC maps).



DISCUSSION AND CONCLUSION

- Four distinct SCFA metabolic profiles within GBMs underscores their metabolic heterogeneity crucial for the challenges faced in their diagnosis and treatment.
- Disregarding heterogeneity within the lesion and using non-clustered TACs lead to the lowest model performances in the genotypic characterisation of the lesion suggesting a specific SCFA mechanism in mutant GBMs.

Ackowledgements: #NEXTGENERATIONEU (MUR); MNESYS (PNRR); MUR-PNRR M4C2I1.3 PE6 project PE00000019 Heal Italia; the NATIONAL CENTRE FORHPC, BIG DATA AND QUANTUM COMPUTINGthe European Innovation Council with the projects CROSSBRAIN (Grant Agreement n. 101070908) and BRAINSTORM (Grant Agreement 101099355). EOA acknowledges UK Medical Research Council award MR/N020782/1.