Integrating multiparametric MRI with spatial transcriptomics to identify "Radio-Spatial Genomic" features of prostate cancer using artificial intelligence.

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Introduction

A challenge in prostate cancer (PCa) management involves risk stratification, to precisely identify the subgroup of men at highest risk of progressing from localised to metastatic disease. Multiparametric MRI (mpMRI) is key in the PCa diagnostic pathway. By integrating clinical parameters, mpMRI radiomics and spatial transcriptomics (ST), this novel "Radio-Spatial Genomics" platform offers an exciting opportunity to identify mpMRI radiomic features associated with important biological aspects of PCa linked to an aggressive disease phenotype.

Methods

Multi-regional spatial transcriptomics (Visium 10x Genomics) was performed on archived formalin-fixed paraffin-embedded prostatectomy sections. Axial sections were sequenced using ST (8 per patient) from 2 patients with Gleason 4+4 PCa and preoperative mpMRI available was used for this study. Anatomical landmarks on mpMRI were segmented by a Radiologist. Using a proportional size algorithm and a convolutional neural network (ProsRegNet), T2-axial MRI slices were aligned and registered to histopathology sections. An application, SpatialStitcher was developed on Python 3.7.0 to digitally stitch separate ST sections for image registration.

Results

Using the prostatic capsule and urethra as landmarks, histopathology sections from 2 patients were co-registered to corresponding T2-axial MRI slices. In total a median of 114670 sequenced ST barcoded spots were co-registered to 30424 pixels on MRI per patient. A median DICE correlation score of 0.942, 0.738 and 0.756 was achieved for capsule, tumour and BPH nodules respectively. *AMACR* (marker for PCa) expression inversely correlated with T2 MRI intensity-based radiomic features ($r = -0.763$), consistent with the tumour being hypointense. Differential gene expression analysis between hyperintense peri-tumoural and hypointense tumour regions revealed enrichment for genes involved in mucosal immune response.

Conclusion

In this study, we report preliminary experience of mapping MRI with ST using machine learning to identify genotypic changes based on radiomics. With further validation, this

“Radio- Spatial Genomics” model may allow the detection of aggressive PCa genotypic features from diagnostic mpMRI imaging.