Does the grade hotspot match the volume hotspot? A 3-D model reconstructed using Template Prostate Mapping Biopsies from the MRC PROMIS trial
Ahmed El-Shater Bosaily1, Massimo Valerio1, Yipeng Hu2, Alex Freeman3, Charles Jameson1, Louise Brown1, Richard Kaplan4, Mark Emberton1, Chris Parker5, Richard Hindley6, and Hashim Ahmed1

1Division of Surgery and interventional science, University College London, London, United Kingdom, 2Centre for Medical Image Computing, University college London, London, United Kingdom, 3Pathology, University College London Hospitals NHS Foundation Trust, London, United Kingdom, 4Clinical Trials Unit, Medical Research Council, London, United Kingdom, 5oncology, Royal Marsden Hospital/Institute of Cancer Research., London, United Kingdom, 6Urology, Hampshire Hospitals NHS Foundation Trust, Hampshire, United Kingdom

Introduction
Prostate cancer shows grade heterogeneity not only per patient, but also per lesion. Currently, MRI guidance and planning is part of a rapidly growing trend of targeted prostate biopsies. Despite the assumption that the maximum cancer grade (grade hotspot) lies within the maximum dimension of the lesion (volume hotspot), some argue that it might not always be true and that areas of higher cancer grade may show different signal characteristics and may be identifiable on MRI hence, the use of biopsies targeted to the maximum diameter of a lesion on MRI might misclassify some lesions if the hotspots were not concordant. The aim of this study is to assess the concordance between the grade hotspot and the volume hotspot in biopsy-naïve patients with elevated PSA who underwent 5mm Template Prostate Mapping (TPM) biopsies as part of the MRC PROMIS trial.

Methods
A 3-D histopathological model was reconstructed using the outputs of TPM biopsies from the pilot phase of the multicenter MRC PROMIS study, which is a paired validating cohort study investigating the diagnostic performance of multi-parametric MRI against standard TRUS biopsy using TPM biopsies as reference test. For the purpose of the study, the prostate is fully sampled with 5mm intervals; each core is separately labelled, analysed, inked and orientated in space to determine the location of cancer lesions 3-dimensionally. After identifying the heterogeneous lesions with respect to grade the concordance between the volume hotspot and grade hotspot was calculated.

Results
133 lesions were identified in 66 patients with mean age 63 years (SD±6) and median PSA 6.9ng/ml (range 0.89-14.5). With a median of 2 cores (1-47) constituting one individual lesion, the median derived volume was 0.31cc (SD±0.7) per lesion. 60% lesions (80/133) were homogeneous, so grade and volume hotspots were always concordant. In the remaining heterogeneous lesions (40%; 53/133), calculated median maximum cancer core length was 6mm (1-24); maximum Gleason score was always 7 with primary and secondary Gleason pattern 4 in 10 and 43 lesions, respectively. In 49% (26/53), there was concordance between the volume and the grade hotspot, whereas in 51% (27/53) the hotspots were in different positions separated by a mean of 8.2mm (SD±2.4). 

Figure1: 3D reconstruction models.

Conclusions
Our study demonstrates that guiding one biopsy needle to the maximum cancer diameter, would lead to correct grade attribution in 80% of all lesions (80/133) and 49% of heterogeneous ones if a true hit was obtained. Further correlation of these histological lesions, their MRI appearance and the detectability of these hotspots on MRI will be undertaken once more PROMIS results are released. In order to correctly risk stratify most lesions and overcome errors of needle placement a number of deployments, yet to be defined, would be required to fully risk stratify individual cancer lesions.