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We would like to thank Chu and colleagues for their positive and encouraging comments regarding our recent study on the clinical outcomes of multiparametric magnetic resonance imaging (mpMRI)-based active surveillance (AS) for prostate cancer. We certainly agree with the concerns raised regarding variability in mpMRI performance. Establishing a high-quality mpMRI pipeline is certainly the first step before establishing any imaging-based AS programme and, as we state in our article, we do not advocate the latter without first ensuring the former. There are excellent efforts under way to remedy these issues.[1]

We also agree that low positive predictive value (PPV) is a challenge that needs to be addressed, as the premise of detecting oncological progression on imaging relies heavily on the assumption that such progression underpins radiological change.[2] Although visible disease has been reliably associated with aggressive features, exploiting this association for imaging-based surveillance is not trivial: as the authors point out, apart from the designation of a lesion as suspicious being influenced by radiologist experience, efficient lesion sampling is pivotal.

We would like to add that, although concerns regarding PPV are legitimate, an mpMRI lesion can always be re-imaged and/or re-sampled if there is any unresolved clinicopathological suspicion, and such re-evaluation is not in itself problematic if the window of opportunity for treatment is not missed. In contrast, confidently excluding the emergence of significant disease whilst on AS is as important (if not more), because negative or stable imaging findings lead to AS relaxation that could lead to unacceptable treatment delay in cases of missed progression. The negative predictive value (NPV) for significant disease is perhaps high enough in the diagnostic and/or AS candidate selection stage (where upper estimates can reach 96%), but during AS the NPV for disease progression drops [3,4].

Increasing this figure is where established clinical metrics (e.g. prostate specific antigen -PSA- density) and serially collected tissue or blood biomarkers could be of particular value. However, we should mention that, apart from simple metrics such as PSA density, the clinical application of sophisticated biomarker tests is subject to

similar limitations: the optimal timing, testing methods and interpretation of various tests varies considerably, and further studies on their association with long-term clinical outcomes are needed [5]. In addition, these technologies are often more costly or demand special infrastructure that is quite different than that required by mpMRI, which is already available in many healthcare centres. As such, although integrating biomarkers in the imaging AS pathway remains an exciting prospect, their exact clinical translation will need further clarification in coming years. What is more certain is that, in order to achieve personalization of AS schedules, sophisticated methodologies that can successfully integrate all prospectively collected information (clinical data, imaging features, biomarkers) and use them collectively to predict risk dynamically over time. Developing such methods will require a multidisciplinary approach and an expert consensus on exactly how imaging-based AS cohorts should be set up, followed up, analysed and reported, which is somewhat lacking in the existing literature.

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