Imaging in active surveillance for prostate cancer: where should we focus our research?

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We would like to thank Professor Loch and Dr Fulgham for their editorial comments on our article[1, 2]. Before replying to specific points, we should like to emphasise that our study was initiated 11 years ago as an exploratory study rather than to definitively "prove" the utility of the apparent diffusion coefficient (ADC) in active surveillance. The authors identify limitations to our study with regard to selection, follow-up, and treatment which we shall discuss below.

Although our selection criteria may not now be considered optimal, the majority of our patients were D'Amico low risk (84%), with a median PSA of 6.7 ng/ml, in keeping with published studies. Furthermore, there remains no internationally agreed standard for patient selection or initiation of radical treatment in active surveillance[3]. With regard to biopsy correlation with index lesions, this was done by ensuring a positive trans-rectal ultrasound (TRUS) biopsy core from the relevant octant. As 94 % of patients had peripheral zone lesions, this was possible in nearly every patient. While template biopsy would have been the optimal approach, this was not in routine use at the time of study setup.

As evidence regarding the usefulness of MRI in active surveillance emerged during the latter part of this study, some patients had additional MRIs for monitoring which we acknowledge as a potential source of bias. However, it is important to reiterate that only 35 % of patients in the study had repeat MRI, and this did not occur until a median of 2.8 years (IRQ: 2.3-3.6) after enrolment. We note the authors interest in TRUS for monitoring during active surveillance, and their claim, based on limited evidence, that this is at least as good as MRI in predicting outcome[4]. This may be the

case, but the weight of evidence for multi-parametric MRI is significantly greater, and it has the advantage of being less invasive[5-7].

Finally, the authors state: "It is debatable whether radiation therapy should be considered radical treatment for prostate cancer". However, radiotherapy is accepted and recommended as a curative treatment option by both the National Comprehensive Cancer Network (NCCN) and European Association of Urology (EAU) guidelines. Furthermore, although non-randomised, the comparative evidence suggests that radiation compares favourably with surgery in terms of biochemical outcome[8]. Recently published studies using modern radiotherapy techniques, including the CHHiP trial randomising over 3000 patients, report a PSA relapse-free survival of 85-90 % at 5 years[9, 10].

In summary, we agree that there is a need for robust clinical trials of imaging in active surveillance, particularly to reduce the invasive nature of biopsy follow-up. We feel that multi-parametric MRI is the correct focus for these studies, and that our current study has identified a potential fruitful area for further investigation.

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