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Active surveillance for prostate cancer – will MRI help us address the current controversies in traditional surveillance approaches?

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Corresponding Author:	Caroline M Moore, MD FRCS(Urol) UCL: University College London UNITED KINGDOM
First Author:	Caroline M Moore, MD FRCS(Urol)
Order of Authors:	Caroline M Moore, MD FRCS(Urol)
	John Withington

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Active surveillance for prostate cancer – will MRI help us address the current controversies in traditional surveillance approaches?

John Withington[1,2], Caroline M Moore[1,2,]

[1] Division of Surgical and Interventional Science, University College London [2] Department of Urology, University College London Hospitals Trust

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UCL Urology
Division of Surgical and Interventional Science 3rd Floor Charles Bell House
43-45 Foley Street
London
W1W 7TY

caroline.moore@ucl.ac.uk

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We congratulate Willemse and colleagues on their paper on active surveillance for localised prostate cancer, in this month's issue of European Urology (1). They should be commended for their precise focus on some of the most controversial questions in contemporary AS practice, which did not achieve consensus in the recent European Detective study (2). These were: inclusion of patients with intermediate-risk disease; optimal thresholds regarding biopsy characteristics and how they should influence inclusion, exclusion and reclassification; and the nature and frequency of repeat biopsy during active surveillance. Conclusions on these aspects from previous systematic reviews have been mixed (3). This partly reflects contemporary literature on AS comprising many single centre, non-comparative cohort studies.

To what extent do Willemse and colleagues resolve the points of controversy identified in the DETECTIVE study? Based on their systematic review, they recommend that selected patients with Gleason 3+4 disease, or other single-feature intermediate risk characteristics, can be offered AS, provided strict monitoring protocols are followed. Furthermore, they recommend that men with higher volume Gleason 3 + 3, (based on systematic biopsies, with > three cores positive or maximum core involvement >50%) should have initial reclassification biopsies, and be monitored closely, whilst these volume thresholds in Gleason 3+4 disease, should exclude men from AS. They also recommend that confirmatory biopsies should be performed within two years of commencing AS and repeat surveillance biopsies performed at least every three years for the first decade of AS.

Of course, as the authors acknowledge, a more fundamental question remains: are routine, scheduled repeat biopsies needed at all? It is notable that their conclusions refer only to men on an active surveillance programme 'where the use of MRI is not mandatory, or absent'. We believe that MRI should be a mandatory part of active surveillance, both at inclusion and for subsequent monitoring.

A patient who had been on AS for over a decade described to us his relief when he stopped having regular, protocol based biopsies: "I had felt like a pin cushion!" Perhaps even more concerning, is the proportion of patients who simply drop out of AS programs, and undergo unnecessary radical treatment, because they find AS intolerable. Estimates of the proportion of patients who undergo active intervention for reasons other than disease progression, based on systematic reviews of qualitative studies investigating the experience of men on AS, range from 20-40% (4). The reasons for this are multifaceted and individual, but there is clearly something about AS that some men find intolerable over time. Meanwhile, in our own centre's 5-year follow-up AS cohort of 672 patients, only one man discontinued due to anxiety without objective change on MRI or biopsy (5).

What is different about AS in our institution? We would suggest that a hugely important factor in optimising the tolerability of AS for our patients is a shift away from routine biopsy, in favour of MRI-led AS. Men have a confirmatory MRI at one year, followed by a risk adapted approach using baseline risk and changes in PSA density to determine the frequency of MRI. MRI-visible disease, and Gleason 3+4 disease at diagnosis were associated with increased likelihoods of moving to active treatment, with

around 1 in 3 men with MRI-visible Gleason 3 + 4, having treatment at 5 years. Men at lowest risk had non-visible Gleason 3 + 3 disease.

The question of whether MRI can effectively lead decisions to biopsy in AS is considered in this review. They conclude that evidence to date remains insufficient to recommend that MRI can safely replace repeat biopsy. However, among the 333 cohorts they reviewed, only a minority included MRI within their protocols at diagnosis (n=17), during surveillance (n=47), or at the point of reclassification (n=26) (1). This reflects the reality of international AS practice to date. Multiparametric prostate MRI, while available widely in the UK setting and other European countries, is available less reliably in other contexts, notably the US (6).

The challenges in introducing MRI into active surveillance include ensuring sufficiently high quality MRI to allow protocol based biopsy to be omitted. There is now a formal framework for assessing MRI quality which is useful in this context (7). The second is of determining what to do with the MRI findings. In surveillance using standard biopsies, huge efforts have been made to define appropriate triggers for active treatment in terms of change in tumour burden, based on both grade, and estimates of tumour volume, as well as in PSA or digital rectal examination. We would challenge the traditional metric of percentage core involvement as a threshold, and advocate for maximum cancer core length to better reflect tumour volume. For example, 66% of a 3mm core is still only 2mm, but could trigger action based on the short core rather than tumour volume. A metric of > 3 positive cores is only relevant when those cores are done according to a standard protocol, and should not be applied to a targeted biopsy strategy. MRI allows us to accurately measure tumour volume, and thresholds for biopsy and treatment based on MRI tumour volume should be explored.

In addition, it is recognised that MRI-targeted biopsies show ‘grade inflation’ compared to standard biopsies (8), and this should be factored in when assessing risk.

The first step to developing MRI based thresholds for recommendations is standardised reporting of MRI in active surveillance, according to the PRECISE framework (9). The second step is incorporating these data, along with other variables, into a dynamic risk prediction model, which balances change in biological risk, with patient co-morbidities and preferences.

We look forward to the PCASTt/SPCG17 randomised trial of MRI-led AS, comparing standardised with MRI-led surveillance (10). Ensuring that high-quality multiparametric MRI is available to patients with prostate cancer, whoever they are and wherever they live is a necessary precondition to unlocking the full potential of AS. Until that time, the systematic review by Willemse and colleagues, and the DETECTIVE program which prompted the review, are a valuable contribution to understanding contemporary international practice in AS.

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Disclosure

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[1] Division of Surgical and Interventional Science, University College London [2] Department of Urology, University College London Hospitals Trust

Conflict of interest statement

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