Let's follow the golden mean – using MRI to determine the need for biopsy in men on active surveillance

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Re: Changes in Magnetic Resonance Imaging Using the Prostate Cancer Radiologic Estimation of Change in Sequential Evaluation Criteria to Detect Prostate Cancer Progression for Men on Active Surveillance

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O'Connor and colleagues are to be congratulated on this analysis of their cohort of men on active surveillance (AS), in this month's issue of European Urology Oncology[1]. Magnetic Resonance Imaging (MRI) is used as a tool for re-assessment on surveillance and they report a series of 391 men who have at least one MRI and associated biopsy during surveillance. For progression from Gleason Grade group (GG)1 to GG3, they report a negative predictive value of 94% with stable MRI.

Whilst men with GG2 are permitted in many surveillance programmes, it is universally accepted that the presence of GG3 should prompt active treatment in men who are fit for it. It is therefore welcome that O'Connor and colleagues address this specifically in their cohort, of whom a quarter enter the programme with GG2. Follow up data at 29 years from the SPCG-4 trial [2] suggests that GG2 disease is associated with the same risk of prostate cancer death as GG1 (and less benefit for radical treatment), whilst GG3 confers over a five-fold increase in risk of prostate cancer related death. Work from University College London (UCL) has shown a significant difference when comparing MRI-visible and non-visible GG2 lesions: MRI-visible GG2 seems to behave more aggressively when compared to non-visible disease.[3] There is growing recognition therefore, that imaging findings are a key component of risk stratification in surveillance.

O'Connor and colleagues use the Prostate Cancer Radiologic Estimation of Change in Sequential Evaluation (PRECISE) criteria[4] to assess repeat MRI scans, where progression on MRI is defined as an increase in the size or conspicuity of lesions, or development of a new lesion. During the PRECISE consensus meeting, there was much debate about the use of volume, or one or two diameter measurements to accurately assess change, and it was concluded that data on this element was lacking, and would be addressed in the next iteration.

The MAPPED study[5] looked at variability in tumour volume measurement in T2-weighted imaging in a cohort of 40 men who underwent MRI at baseline, 3 and 6 months, with half of men randomised to an intervention thought to reduce tumour size. In men on placebo, where stability in such a short time period was assumed, there was up to 25% variation in serial measurements over the 6-month period. O'Connor and colleagues further refine the PRECISE definition of radiological progression as 1mm change in tumour size on MRI measurement, which may lie within measurement variation. Using this definition, they classified 268/621 (43%) of MRI intervals with a PRECISE score of 4, denoting progression. This compares with the UCL PRECISE cohort, where 240/553 (43%) of men showed

radiological progression with a median follow-up of the overall population of 76 months (52–100.5 months). [6]. It is likely that in the UCL cohort, 1mm change in lesion size would be denoted as stability. It should be noted that the NIH cohort was calculated on a per scan basis, whilst the UCL cohort is on a per patient basis. An update of PRECISE, taking into account data collected since its publication, will seek to address the issue of size measurement, and measurement repeatability which will be vital to increasing the usefulness of the PRECISE score.

The NIH team have a well-developed MRI programme, and have previously reported their learning curve for MRI-targeted biopsy, noting that, the detection of clinically significant disease rises, and that of indolent disease falls[7]. They rightly acknowledge that ensuring the quality of MRI for each man having one is a high priority worldwide, with the recent publication of PI-QUAL[8], that represents the first step towards the standardisation of a scoring system to assess the quality of prostate MRI prior to reporting. What's more, results such as these can support increased dissemination of MRI in AS, yielding increased experience for radiologists and urologists and further improving the already excellent accuracy of MRI in AS.

There are some men who have significant pathological change on biopsy, in this cohort and others, which was not detected on MRI. It is vital that we offer these men biopsy despite a stable MRI. At our institution we offer biopsy when there is a change in PSA density, and in this analysis, this is shown as a significant predictor for both upgrading to GG2 and GG3.

This cohort does not analyse the predictive value of digital rectal examination (DRE), and it is not clear if this was done. Whilst it has been a key component of previous predictive models, in the era of MRI, it seems likely that this will become outdated. MRI provides greater morphologic information than DRE, and adds information on vascularization (contrast enhancement) and cellularity (diffusion-weighted sequences) which have no correlate with DRE. In a similar fashion, PSA density, and changes in PSA density may overtake the use of PSA.

In an era of reluctance to attend hospital for non-urgent matters, and a desire to reduce the incidence of infection associated with prostate biopsy, the ability to safely reduce the use of routine biopsies in AS is very welcome. Men on surveillance are often at their most anxious, and willing to have additional testing at the start of AS. Data shows that in the later years of surveillance, the adherence to a routine biopsy schedule is in the order of 10%, reflecting

reluctance both on the part of the patient and the physician [9,10]. However, it is likely that their risk of progression increases as they age. In this analysis, the overwhelming majority men can omit a 2-year biopsy if their MRI and PSA density are stable. We look forward to this approach being more widely adopted and incorporated into risk calculators in due course. When Aristotle described the principle known as ‘The Golden Mean’, he meant that virtue lies between the extremes of excess and deficiency. We should then follow the ‘Golden Mean’ during AS, in order to allow men at lowest risk to have the lightest touch surveillance, and those at greater risk to be followed more closely.

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