Are men who are biopsied without a prior prostate MRI getting sub-standard care?

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The article, published in this issue, by a multi-disciplinary group from Dresden who have been offering MRI to their patients since 2012 would suggest so (1).

In their hands, an image-guided biopsy resulted in 29 patients with Gleason score of 7 or 8 being identified who had been overlooked by an optimized 12-core systematic biopsy performed at the same sitting.   Dedicating a minimum of two cores to a 'target' conferred an increase in detection of clinically significant prostate cancer – as defined by Gleason pattern 4 or more – of 43% compared to systematic biopsy alone.

There is reason to think that, if anything, this might be an under estimate of the utility of sampling a target of high propensity for clinically significant prostate cancer versus a strategy that tries to spread the needle around the posterior limits of the gland.   The reason for this is that the operator was aware of the location of the target during the systematic biopsy as these were done after the targeted biopsy. The resulting incorporation bias should not trouble us too much as its effect will be to make systematic biopsy 'better' and therefore diminish any difference between

the two strategies. The fact that the patients had their systematic biopsy under anaesthesia and were in lithotomy (non standard conditions) might add further to both bias and direction.

This study, like many before, incorporates a mixed population that comprises men who were biopsy naïve (around a quarter of the population) and those men who had undergone at least one previous biopsy.   Again, this probably does not matter for our purposes, as the two groups were identical in terms of overall cancer detection (52%) and very similar in terms of the proportion of patients with Gleason pattern 4 or more (80% for biopsy naïve men versus 72% for those who had undergone a previous biopsy). The two groups had a similar number of lesions - around 2 lesions were declared per subject. The two groups did differ in terms of PSA. Men undergoing repeat biopsy had a PSA twice that of men having a biopsy for the first time (12.2 versus 6.1ug/L).

These results appear to be in line with those summarized in a recent systematic review of studies that compared a targeted sampling strategy with another (2). But they do differ substantially to a recent study of over 1000 biopsy naïve men who were randomized to MRI versus a standard systematic TRUS biopsy approach (3).   In this large RCT from Rome the overall detection rate in MRI positive individuals who underwent targeted sampling was 93% (410/440) versus the 52% (137/263) achieved in this study.

Both studies show higher detection rates compared to a standard systematic approach and both show that targeting increases the proportion of men with clinically significant disease. However, exploring the differences between the studies might provide us with insight on how best to refine this new intervention. At present the detection rate of clinically significant cancer (the generally agreed desired outcome of a biopsy when clinically significant disease is indeed present) is contingent on a number of variables (4). They comprise the following: the population sampled; the target condition employed (definition of clinical significance), quality of the imaging; quality of the reporting; the threshold used for declaring a 'lesion' a target; the accuracy of the needle placement; the number of cores deployed to the target; the efficiency of tissue capture. All these differed between the two studies, either explicitly or implicitly.

However, it is likely that the one with the greatest influence on the outcome is the level of certainty attributed to the lesion by the radiologist. There are several scales currently in use and this study used PIRADS – which comprises an ordinal scale ranging from 1 to 5 which are derived from conditions being either met or unmet (5). Ideally, a risk stratification system should influence clinical practice. A PIRADS score of 1-2 should result in avoidance of a biopsy because of the low probability of finding clinically significant disease. A PIRADS score of 4-5 should result in a targeted biopsy because of the high probability of underlying clinically significant disease. A PIRADS 3 should prompt a repeat assessment at a given interval reflecting the indeterminate nature of the prediction.

In the study by Borkowetz *et al.* PIRADS 2 and 3 both were associated with a 10% rate of Gleason pattern 4 or more, suggesting a poor discriminant ability between the two. PIRADS 4 and PIRADS 5, on the other hand, were associated with a 24% and a 60% detection of Gleason pattern 4 or more, respectively. From this we can say that PIRADS 4-5 should be targeted, are positively associated with risk and will confer a high targeting yield. I think we can also say that more work is needed in relation to the inputs that generate PIRADS 2-3. This, fortunately, is in hand as a new version of PIRADS is soon to replace the one used in this article. Hopefully, it will improve the discriminant quality at the lower limits of PIRADS and, as a result, should allow us to avoid incorporating PIRADS 2 into our targeting schedule.

Despite the issues with the finessing of PIRADS and other scoring systems – a task that will never be fully complete - this study adds to the burden of proof. What we can say, quite emphatically (based on this study, the systematic review and other studies published since), is that if patients want to maximize the chances of finding clinically significant prostate cancer if it is indeed present, they should insist on an MRI prior to a biopsy so that targeting can be incorporated into the sampling strategy. To do otherwise would, according to this study, just about halve the chances of detecting clinically significant prostate cancer, if it were present.

Acknowledgements

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