

MRI cognitive fusion biopsy – is near enough good enough?

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Abstract

The evidence supporting the use of MRI-fusion biopsies over blind, systematic methods is mounting quickly and has subsequently led to several institutions embracing this new technique and technology. However, questions still remain whether there is difference between the modes of fusion - cognitive, software-based and in-bore - in terms of cancer detection. While it appears intuitive that software and in-bore approaches would be more accurate than cognitive targeting, many studies have failed to demonstrate a significant difference. This could at least partly be explained by the phenomenon of MRI images underestimating the size of lesions and thus the ultra-precise targeting benefits provided by software and in-bore methods may be superfluous.

The use of multiparametric magnetic resonance imaging (mpMRI) in the diagnostic landscape of prostate cancer (PCa) has grown significantly in recent times. Although the technology itself has existed for some time, developments in T2 weighted imaging, combination with dynamic contrast enhanced and diffusion weighted imaging and higher strength 3-Tesla scanners has increased the sensitivity and specificity of mpMRI for detection of PCa. These superior imaging techniques have been pivotal in progressing the diagnostic field beyond 'blind' transrectal ultrasound guided biopsy, which has been the mainstay for decades. The newfound ability to target suspicious areas of the prostate during biopsy has decreased the likelihood of missing clinically significant disease. This 'fusion' of MRI images to real-time ultrasounds can be performed cognitively by the surgeon or can be digitally overlaid on live ultrasound (US) with the assistance of external platforms. As with all new technologies, its use must be sustainable from a cost-benefit perspective and improve on the outcomes of current

practice. Thus, in a field with finite resources, urologists are left asking the question of whether the use of software to fuse images is essential or an unnecessary luxury?

Despite a number of studies supporting the superior diagnostic capability of fusion technology over 'blind' biopsy techniques, trials comparing cognitive fusion to the use of software are limited. Those that have been reported demonstrate no difference in diagnostic accuracy between the two techniques. In a New York study of 172 consecutive men with suspicious pre-biopsy MRI findings there was no significant difference in cancer detection rates (CDR) between men who underwent MRI-US biopsy using the Artemis system and those who had cognitive fusion(1). However, it should be noted that there was an absolute difference in CDR favouring the platform fusion technique. Importantly, this study included a mixed population – biopsy naïve, previous negative biopsy and those on active surveillance – and demonstrated no significant advantage to either technique. Sampling efficiency measured by cancer core length per positive core and percentage of cancer core length displayed an absolute difference to the visual targeting methods but this did not meet statistical significance. Additionally, Lee and colleagues reported comparable outcomes between the two fusion methods in a large prospective study(2). The absolute detection rate of high-grade cancer was higher in the visual targeting group but this trend reversed when examining CDR for all grades. Neither of these comparisons reached statistical significance in their differences. Furthermore, a recent meta-analysis reported no difference between cognitive and software fusion techniques for overall and clinically significant cancer detection rates(3).

It has been shown that mpMRI underestimates the size of prostate cancer lesions. The suggested fundamental basis leading to this underestimation may lie in the heterogeneous nature of PCa cellularity. Prostate cancer lesions lie on a spectrum and can range in composition from densely packed malignant cells to a mere handful of malignant glands scattered amongst normal prostatic tissue. Regions of tumour with the latter composition, such as those found on the outer edge of prostate cancer lesions, have similar T2 and apparent diffusion coefficient measurements to normal prostatic tissue thus making them almost indistinguishable(4).

Similar to examples from our institution demonstrated in Figure 1, a recent study by Priester and colleagues examined the correlation between tumour dimensions reported by mpMRI images and actual in-vivo pathology. The mpMRI images of 114 men were

used to produce 3-dimensional molds of tumours and were compared to whole mount pathology specimens post radical prostatectomy(5). It was reported that the mean pathological tumour volume was three times greater than the mean region of interest (ROI) volume indicated on MRI($p<0.001$). Specifically, tumour diameter was significantly underestimated by an average of 11mm with the tumour extending beyond the ROI on all anatomical axes. Additionally, it was demonstrated that 50% of lesions extended more than 13.5mm beyond the ROI. This relationship was observed for all Gleason grades. These findings are further supported by Le Nobin and colleagues in an MRI-histology co-registration analysis(6). Histological tumour volumes were on average 1.5 times greater than the ROI in this cohort. Of concern, the discrepancy between MRI and histology was observed to be greater for tumours with an institutional imaging suspicion score (comparable to PIRADS) of 4 or greater on MRI and those with a Gleason score of 7 or more($p<0.001$).

Proprietors of software-based fusion methods have suggested that its use affords unparalleled precision in aiding the localization of mpMRI target lesions. However, with the knowledge that prostate cancer lesions usually extend beyond the reported target zones, the (subjective) superior targeting offered by these platforms may be superfluous. Authors of the above studies have suggested that underestimation of tumour volume may be compensated for during the biopsy process by taking additional cores outside each ROI. Given that no mpMRI labeling of this target penumbra exists, this would be performed in a 'blind' fashion depending on operator cognition. Therefore, these additional 'blind' cores would negate the proposed benefits of efficiency and precision offered by platform fusion software and likely improve CDR by way of increased sampling. The waters are further muddied by the heterogeneity in diagnostic yield between studies in regards to the platform used and the experience of operators.

With ongoing advancements in prostate cancer imaging and fusion-biopsy techniques we are likely to see the development of newer products boasting their superiority in precision of disease localization. The ever-forward march of technology leads us to a decision that must be made as to whether these new tools have evolved ability beyond their utility. In the landscape of the diagnosis of clinically significant prostate cancer, mpMRI software fusion based platforms certainly seem to be nearing this point. Factoring in the discord between mpMRI lesion size and true pathology, another decision must be made; when it comes to biopsy, is near enough good enough?

Niranjan Sathianathan certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (e.g., employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None

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Figure 1. Patient A: Axial T2 3T MRI slice demonstrating index lesion of volume 1.4ml in the right apex (A.i) and corresponding whole mount section demonstrating 2.7cc index tumor highlighted in orange (A.ii). Patient B: Axial T2 3T MRI slice demonstrating index lesion of volume 0.9ml in the posterior apex (B.i) and corresponding whole mount section demonstrating 3.1cc index tumor highlighted in orange (B.ii).

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A.i



A.ii



B.i



B.ii

