MRI Pathways

By Kalli Spencer

Pre-prostate biopsy MRI can yield a 27–49% reduction of patients undergoing transrectal ultrasound (TRUS)-guided biopsy. A meta-analysis of seven clinical trials with 2582 patients found that MRI with or without a targeted biopsy offered a 57% increase in clinically significant prostate cancer (csPCa) detection, a 33% decrease in the total number of biopsies, and a 77% reduction in cores per biopsy procedure[1]. The PRECISION trial further reported 13% fewer insignificant cancers in an MRI-targeted biopsy group compared with a systematic TRUS-biopsy group[2]. High level evidence shows that a diagnostic pathway is able to identify clinically significant disease and detect fewer insignificant cancers. From July 2018, patients in Australia meeting the Medicare Benefits Schedule (MBS) criteria were able to undergo multiparametric MRI (mpMRI) with no out-of-pocket expenses[3]. This addition of mpMRI to the diagnostic pathway has led to a reduction in biopsies in younger men.

Once the decision to biopsy is made, the biopsy route then needs to be selected and the international literature has varied recommendations. The transperineal (TP) route has significant advantages in terms of minimal post-operative infection and access to the anterior gland when compared to transrectal (TR) biopsies. The current standard in Australia is the TP approach. General anaesthetic TP biopsies (TPB) take longer to schedule compared to TR biopsy, impacting diagnostic target time. There has been a recent trend towards a local anaesthetic approach for TP biopsy with fewer cores to limit scheduling delays. Several biopsy techniques have been proposed, currently a systematic biopsy (SB) is recommended in the setting of a negative MRI and in the work-up of focal therapy, SB with a targeted biopsy (TB) is considered as the standard in patients with a MRI target. TB alone might be considered in the active surveillance setting, and saturation TB approaches have recently been proposed as a means of reducing the number of cores and biopsy related complications, with high detection rates reported especially in those with low PSA levels and small prostate volumes.

In a study led by Professor Manish Patel at the University of Sydney the team found that adding SB to TB increases the detection of csPC[4] by 16% and diagnosis of a higher Gleason Grade Group by 19% at the expense of slightly increased cost of an insignificant cancer diagnosis (5%). Furthermore, increasing PIRADS score is associated with higher rates of csPC on SB; thus, the authors recommend a combination of both techniques for diagnostic accuracy especially those with higher PIRADS scores.

A retrospective study was conducted at the Royal Brisbane hospital examining the experience of a mpMRI-based triage system at a tertiary referral, public teaching hospital[5]. They looked at progression to a TPB, with (target or systematic +target) or without (TPB only) cognitive fusion, for cancer detection. This referral pathway resulted in a reduced number of men proceeding to prostate biopsies with a cost benefit while also achieving a high diagnostic accuracy. They found that significant cancer was identified in 60.5% of all biopsied men and 78.6% of men with a MRI classification PIRADS score ≥ 3 who underwent biopsy. These numbers are higher than those reported in the PRECISION (38%) and PROMIS (50%) trials. The distribution of PIRADS scores was different in their series in comparison to the other studies. In their cohort, 56% of men were assigned a PIRADS 2 and 8.8% (58/653) of men a PIRADS 3 on mpMRI. This contrasts to lower numbers of PIRADS 1–2 mpMRI being reported

in the PRECISION (28%) and PROMIS (27%) trials. They deduced that the subspecialty interest and experience of radiologists in collaboration with urologists at their hospital allowed for a smaller number of indeterminate reports. A selective approach to biopsy in patients with PIRADS 2 or 3, which included age, clinical factors, PSA kinetics and density has allowed them to achieve greater yield of patients with csPCa. Patients who had a biopsy were significantly younger for both PIRADS 2 and 3 cohorts, while those in the PIRADS 2 cohort had significantly higher PSA density. If considering the entire PIRADS 2 and 3 cohort, irrespective of men proceeding to biopsy, the overall detection of prostate cancer was 6.5% and 21%, respectively. However, this approach resulted in 70% and 50% less biopsies for patients in PIRADS 2 and 3 cohorts. For men who then had a prostate biopsy, the diagnostic yield was higher than other studies, specifically 22% for PIRADS 2 (a threefold improvement) and 43% for PIRADS 3 (a twofold improvement) cohorts.
Even though 30% of patients with PIRADS 2 mpMRI were biopsied in their cohort, the proportion of overall patients who avoided a biopsy (47.3%) was higher than in PRECISION (28%) and higher than what would have been achieved in PROMIS (27%) if only patients with PIRADS ≥ 3 proceeded to biopsy. This was possible mainly because of the high proportion of PIRADS 2 scans and to a lesser degree due to the discretionary approach employed for PIRADS 3 scans. Reducing the number of patients subjected to biopsy has clear benefits in minimising complications and cost.

The team postulates that PSA density may further risk stratify patients with equivocal MRI results. It has been previously reported that in patients with PIRADS 1–2, a PSA density of less than 0.15 increases the negative predictive value (the ratio of patients truly diagnosed as negative to all those who had negative test results) from 79 to 89%. In their study, when employing a PSA density cutoff of 0.15 to patients with PIRADS 2 who underwent biopsy, a statistically significant difference in detection of significant cancer was apparent (37% vs 16%).

The biopsy detection rates were maintained across the study period, suggesting that the clinicians were beyond the learning curve. Cognitive fusion is a widely used, inexpensive and reproducible. The biopsies were performed by training registrars with consultant supervision, showing that a cognitive fusion biopsy technique is a skill readily acquired by training registrars and clinicians. Their results correlate with previous studies suggesting no difference in cancer detection of targeted lesions between experienced physicians and residents.

In this study, only 7.8% of patients underwent targeted-only biopsy, but in these, the detection rate of csPCA was 96.3%, suggesting that extra cores were appropriately avoided. In those who had separate systematic and targeted cores (stTPB), systematic cores detected cancer with a higher Gleason grade than targeted biopsies in 3.2% and 5% of men with PIRADS 4 and 5 MRI lesions, respectively. While the additional yield is small (3.2–5%), systematic biopsies may alter treatment decisions by detection of higher-grade cancer even in the presence of a high-risk lesion seen on mpMRI, likely due to inaccuracies in characterisation of multifocal disease and tumour volume by mpMRI and limitations in identifying microscopic foci with current imaging modalities.

The MRI pathway has evolved alongside the development of several biopsy methods and techniques. The currently available array of alternatives enables centres to offer biopsy procedures tailored to individual patient-specific risk, comorbidity, and preference. Combining

imaging, TP biopsy and a more widespread use of local anaesthetic in an outpatient setting seems a reasonable solution to balance costs and benefits. Local choices, however, are likely to depend on the expertise and experience of clinicians and on the technology available.

References

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