David Armany[1]

[1]Department of Urology, Blacktown Mount Druitt Hospitals, Mount Druitt, New South Wales, [2]College of Health and Medicine, Australian National University, Canberra, Australian Capital Territory, and [3]Blacktown-Mount Druitt Clinical School, School of Medicine, Western Sydney University, Blacktown, New South Wales, Australia

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[Correction added on 27 January 2024, after first online publication: Anderson et al. 2024 has been added to the References in this version.]

Correspondence: Henry Woo, Department of Urology, Blacktown Mount Druitt Hospitals, Mount Druitt, New South Wales, Australia.

e-mail: hwoo@urologist.net.au

Magnetic resonance imaging-targeted prostate biopsy changed everything (so everything has to change)

I have a favourite cartoon. Entitled 'In the days before television', it shows a family sitting on the couch staring at the wall. What makes the cartoon funny is that we are removing a technology from a situation and assuming nothing else changes. When we run this in reverse, adding in a technology but keeping the rest of the world the same, the results can be tragic, cavalry charges against machine gun nests in World War I being perhaps the most well-known example.

MRI-targeted biopsy is no less a transformative technology in prostate cancer care than television was to home entertainment or machine guns to warfare. It also follows the same inevitable laws of technology such that if one thing changes and others do not, bad things can occur. Unfortunately, this is exactly what has happened with MRI and prostate cancer: we changed how we looked for prostate cancer but did not change how we graded or treated it.

In terms of treatment, the 'Will Rogers' phenomenon is well known [1]. If you transfer the higher-risk patients of those in a low-risk category to a higher-risk category, average risk falls in all groups. When MRI was introduced, some patients who would have had no or Grade Group (GG) 1 cancer on systematic biopsy were reclassified as GG 2, 3 or even 4 on MRI-targeted biopsy. But even though the average risk of patients in GG 2–4 has changed due to the introduction of MRI, our treatment guidelines have not. They are based on studies conducted in the pre-MRI era and are likely now miscalibrated for a situation where many men have MRI-targeted biopsy.

With respect to pathology, a key consideration is how to grade if there are discordant cores. For systematic biopsy, we quite sensibly adopted the rule that the true grade is the highest grade. If, for instance, a patient has one core from the right mid-gland that showed 4 + 3, and a second core from the left base with 3 + 3, the lower-grade cancer elsewhere in the prostate does not affect the risk of the 4 + 3 lesion and the patient would be assigned GG 3. But with MRI, everything changed: the multiple cores no longer come from different areas of the prostate but from the very same lesion. It is trivial to show, using basic anatomy and geometry, that a rule of 'the true grade is the highest grade' for MR-targeted cores will lead to upgrading of tumours [2].

Tragically, previous attempts to make these sorts of obvious and basic points have often been met with tribalism—a 'them and us' attitude dividing the world into MRI advocates against MRI opponents—and accusations of Luddism ('we can't just to go back to blind biopsy'). But the central conclusion of the first major paper to raise concerns about MRI-targeted biopsy was: 'Consideration should be given to changing guidelines on grading of MRI cores and those regarding treatment of

MRI-detected high-grade prostate cancer' [3]. This is not about being 'against MRI', it is about being against changing technology but keeping everything else constant. The problem is not MRI, it is that we changed the diagnostic pathway but have not changed pathology and treatment.

The paper by Jabbour et al. [4] therefore comes as a relief: at last we seem to be taking a serious, evidence-based approach to how we should be moving forward as a field in the light of the transformational effect of MRI on our diagnostic pathways. The authors' central finding is that grading guidelines taking into account the special nature of MRI (International Society of Urological Pathology [ISUP] 2019) are more accurate than grading guidelines that were written before MRI-targeting became a common aspect of clinical practice (ISUP 2014). This finding has immediate and important clinical implications because many centres continue to follow the ISUP 2014 approach and because the most common change if ISUP 2019 is followed instead, downgrading from GG3 to GG2, is associated with important treatment deintensification. This is not an academic debate about definitional niceties, it means that an important proportion of men can be managed conservatively, or if treated with radiotherapy, avoid extended androgen deprivation therapy. We can only hope that other authors follow Jabbour et al. in systematically evaluating how best to interpret pathology specimens from MRI-targeted biopsy so that we can best risk-stratify our prostate cancer patients.

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Disclosure of Interests

Andrew Vickers is a co-inventor of the 4Kscore, a commercial test for predicting prostate biopsy outcome. He receives royalties from sales of the test. He owns stock options in Opko, which offers the test.

Andrew Vickers

Department of Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center, New York, NY, USA

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Candid choices: optimising patient selection in prostate cancer focal therapy

Focal therapy (FT) for prostate cancer (PCa) involves using both advanced imaging and ablative techniques to precisely target and treat specific areas of clinically significant PCa within the prostate. By focusing on the index lesion rather than the entire gland, it aims to reduce side-effects often associated with more aggressive treatments [1]. In contemporary urological practice, FT represents a groundbreaking advance that fundamentally alters the field of localised PCa treatment. This disruptive innovation has created a new market of technological interaction [2]. More importantly, FT implies a process of systematic risk assessment to identify, evaluate, and mitigate potential risks. Risk monitoring and review of variables start at the initial clinic and go through energy selection, treatment, and follow-up (Fig. 1). Precise selection of patients is crucial for accurate results.

We were very pleased with the manuscript from Kaufmann et al. [3], which features a clear example of dedication and effort. This paper presents the outcomes of a 3-year study on focal high-intensity focused ultrasound (HIFU) for treating PCa. The fruit one harvests from the tree in this work is the major importance of selection for the eventual indication of FT. The authors deployed a solid approach of transperineal template saturation biopsies and MRI/TRUS fusion-targeted biopsies with targeted prostate cores taken from any lesion Prostate Imaging-Reporting and Data System (PI-RADS) ≥3. Although this diagnostic approach seems rather aggressive, it provides a solid base to indicate partial gland ablation. A total of 91 patients participated, primarily with Grade Group ≥2 disease and the authors strictly assessed them with follow-up biopsies, showing 44–65% of patients free of clinically significant cancer at 3 years. With Professor Eberli's group, we share a strong belief that at this point of FT development, follow-up biopsies remain essential as eventual detection of cancer recurrence using MRI and PSA might be still limited in