Research Letter

Magnetic Resonance Imaging and Detection of Metastases in Prostate Cancer: Learning Lessons from History

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In February 2017 the inventor of the magnetic resonance imaging (MRI) scanner, Sir Peter Mansfield, died at the age of 83 [1]. He was awarded the 2003 Nobel Prize for medicine, and MR scanning has since become ubiquitous and indispensable in most fields of cancer, but not quite yet in urological oncology, particularly for advanced and high-risk prostate cancer staging. Why have we been so slow to evaluate its utility properly and to put it to work to best effect in this disease, especially in the critically important area of detection, localisation, and quantitation of metastases?

The review by Woo et al [2] in this issue of European Urology provides an overview and meta-analysis of the literature on the utility of MRI in detecting bone metastases, and compares this in terms of sensitivity and specificity to the existing urological “workhorse” and traditional 40-yr-old cornerstone of metastatic prostate cancer staging, the technetium bone scan [3]. It also highlights the weakness of the uro-oncological literature in this area and draws our attention to the paucity of high-quality clinical science in evaluating and using MRI as a staging tool in the advanced prostate cancer setting.

The relatively low sensitivity (79%) and specificity (82%) of bone scintigraphy is well known. In modern, modern practice dictates that scintigraphy cannot stand alone in the staging process, as supplementary imaging is required to complete the assessment of soft-tissue disease status and to confirm the nature of lesions that are scintigraphically “equivocal”. Is it time to move to MRI as the primary imaging modality? Do the data presented here show or help clinicians to understand how good MRI is as an alternative, and if it is better, what type of MRI scanner or scan protocol should be used?

By definition, the review provides level 2a evidence of accurate MRI-based detection of bone metastases in prostate cancer. It is a meta-analysis of ten predominantly prospective studies and it concludes that overall per-patient MRI sensitivity and specificity is 96% and 98%, respectively. However, while the study methodology is fundamentally sound, the individual studies analysed are generally weak, with significant heterogeneity and inherent bias that limit the overall interpretation. Heterogeneity between studies is recognised by the authors in their submission, and following meta-regression analysis the number of imaging planes was the only significant explanatory factor. When two or more planes were used, the sensitivity and specificity increased to 99%, but data in relation to this were only available in a small number of the studies. The meta-analysis also found no statistically significant difference between diffusion-weighted imaging (DWI) and standard MRI sequencing between studies. This seems surprising at first glance, but the data have limited numbers for comparison and information relating to standardisation or co-alignment of protocols is fundamentally weak or missing. It seems clear that while DWI looks better, it needs further definitive clarification before safe conclusions can be drawn.

The authors acknowledge the methodological limitations in their study, including the per-patient analysis of imaging and the predominant use of a best value comparator (BCV) over histological confirmation as a reference standard. This lack of per-lesion analysis hinders interpretation of the MRI in classifying metastatic burden, but it is only fair to recognise that the BCV used represents current practice for metastatic confirmation owing to the difficulty and clinical impracticality of taking multiple metastatic biopsies. The analytical study factor with the potential to exaggerate the overall statistical result was incorporation of only the highest scan accuracy interpretation when multiple independent readers were used. The final result also fails to incorporate “real world” interobserver scan report variability, which may expose less reliable MRI capabilities. Another major drawback in all the studies is that in the absence of a truly definitive reference standard, there has been no reported long-term follow-up of lesion regression or progression, which might

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have bolstered the reader’s confidence in the absolute veracity of the results.

Is help for the confused clinician at hand to help in deciding which imaging modality to use? The relative comparison and replacement of scintigraphy with MRI has been characterized by a slow and patchy evolution, but uro-radiologists and uro-oncologists now seem to be rising to the challenge of modernisation by recognising that the traditional imaging modalities are probably unfit for purpose in the modern era. Expert groups have now been established to develop a rational and usable collaborative framework for MRI use and reporting [4]. This is a significant step forward that will help in establishing the advantages and disadvantages of switching techniques. However, this alone is not sufficient. It is also incumbent on clinicians and cancer trial designers to incorporate tightly drawn imaging protocols within clinical trials and collaborative registration studies so that robust evidence can be gathered for the future. As a community we have been slow to develop this unified approach to imaging, but it is hoped that lost ground can be recovered and perhaps, with the help of highlight reviews such as this, we can avoid making the same mistake with positron emission tomography scanning, for which a headlong rush to publish multiple articles—often of low quality, frequently uninformative, and sometimes misleading—based on case series of ever larger volume is evident [5]. Would it not be good to know in a short number of years that we are imaging usefully and cost-effectively and that decisions to switch modalities are based on a solid foundation of evidence? Perhaps, in our future decision-making and data-gathering, we should learn the lesson of history to avoid repeating the mistakes of the past.

Conflicts of interest: The authors have nothing to disclose.

References


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