Editorial

ProPSMA: a callout to the nuclear medicine community to change practice with prospective, high-quality data

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Conflicts of interest

We performed our first PSMA PET/CT in mid-2014 and it was immediately obvious that this new imaging modality was vastly superior to existing practise of CT and bone scanning, or choline PET/CT. Patient number 1 was scheduled to undergo a prostatectomy with curative intent, but the PSMA PET/CT additionally demonstrated pelvic nodal and distant osseous metastatic disease (Figure 1). His management was changed and he was enrolled in a clinical trial of enzalutamide. When I met this man in his late 70s briefly after a follow-up scan one-year later, he remained symptom free and was very pleased to have forgone the risks of surgery when it had no chance of cure.

The striking images we are now able to produce in nuclear medicine and the precision medicine we practice are not, however, enough to convince governments or insurers to either approve or fund such new technologies. Unbiased comparative effectiveness data comparing PSMA PET/CT to existing technology are a necessary prerequisite. We need to be able to provide precise data on the accuracy, management impact, reproducibility and safety compared to currently used technologies and show health economic benefits.

In late 2015, through The Australasian Radiopharmaceutical Trials network (ARTnet), we put in an expression-of-interest to a grant opportunity from the Prostate Cancer Foundation of Australia (PCFA) funded through Movember. Back then, the world had barely heard of PSMA PET/CT. In close collaboration with our urology, radiation oncology, clinical trials experts and consumer advocates, we put together a successful grant proposal culminating in the proPSMA study(*1*). We established a network of 10-sites around Australia with capability to perform on-site radiopharmaceutical production and PET acquisition according to standardised methods(*2*). The study recruited well and we expanded the study to 300 patients to ensure it was adequately powered. Referrers were engaged and recruitment was complete more than 6-months ahead of schedule. A huge amount of data was collected including an imaging biobank which will form the basis of further research.

The ProPSMA clinical trial results, published in *The Lancet*(3), show that PSMA PET/CT offers greater accuracy than conventional imaging with an accuracy of 92% for detecting pelvic nodal or distant metastases compared to 65% for standard imaging with the combination of CT and bone SPECT/CT (Figure 2). Moreover, PSMA PET/CT led to management change defined by change in treatment modality or change in delivery in 28% of men compared to 15% for conventional imaging. Other outcomes showed fewer equivocal ("uncertain") findings with PSMA PET/CT (23% vs 7%), half the radiation dose with PSMA PET/CT (8.4 mSv vs. 19.2 mSv) and high reporter agreement for PSMA PET/CT. When PSMA PET/CT was performed following conventional imaging as a second-line imaging test, it had a similarly high rate of change in patient management. Conversely, just 5% of patients had their treatment plans modified with second-line CT/bone scans and only 2% had an accurate change in their stage with CT/bone scans.

By now hundreds of thousands of PSMA PET/CT have been performed globally. Doctors with experience adopting this new technology generally have no doubt that it is a high-impact modality and superior to conventional imaging. More than 1500 manuscripts have been

published, mostly retrospective analyses without comparison to a reference standard. By comparison, proPSMA study has imaged a small number of men - only 300 - but this has resulted in a rich dataset which has generated definitive data. This will hopefully provide the necessary data for reimbursement of PSMA PET/CT, enabling widespread availability of PSMA PET/CT for men globally.

Precision medicine has often been at variance with evidence based medicine. In the former, individual results inform patient management whereas in the latter results are informed by randomised controlled trials and meta-analyses. ProPSMA tries to bridge the gap between these two worlds. As nuclear medicine specialists, we need to generate more unbiased, prospective, multi-centre data. Establishing collaborative networks, working together and upskilling the next-generation of specialists in clinical trial methodology is key to achieving this. As new radiotracers emerge, there is a pressing need to develop and enrol patients on well-designed clinical trials.This is our best chance to properly evaluate the impact of our tests and enable widespread access to patients.

Acknowledgements

References

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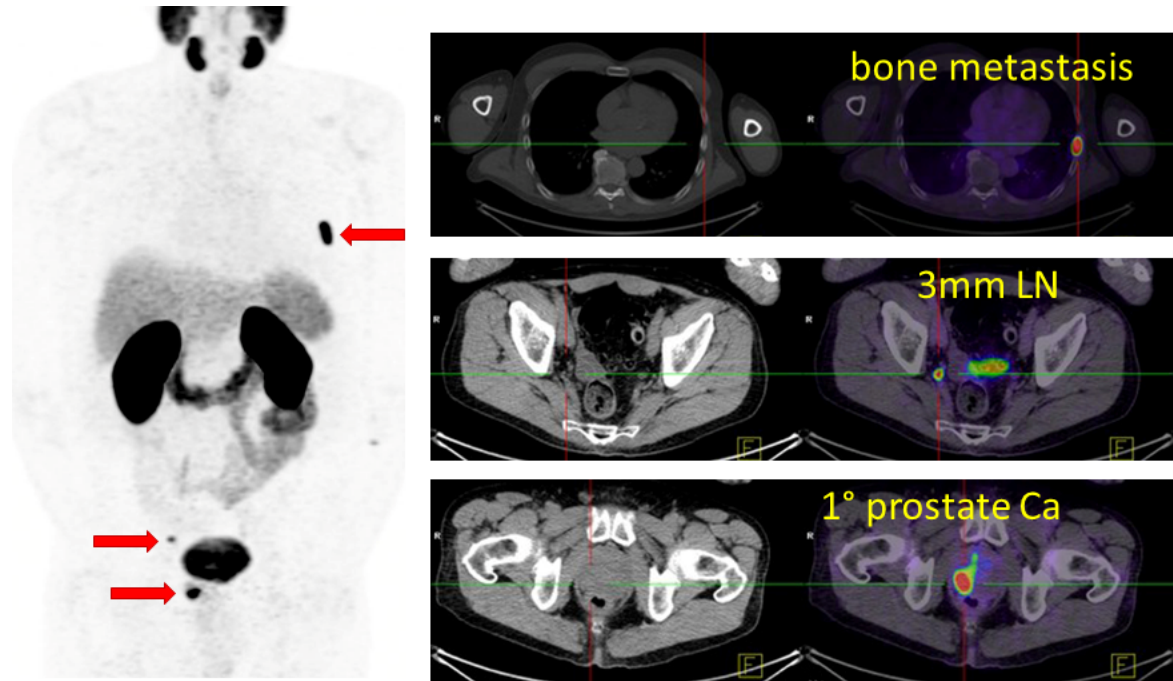
Figure 1: Man with newly diagnosed Gleason grade group 4 prostate cancer, with no evidence of metastatic disease on CT, bone scan or MRI of the pelvis. PSMA PET/CT demonstrated a <5mm pelvic nodal metastases and a bone metastasis. The patient's management was directed away from a curative-intent prostatectomy.
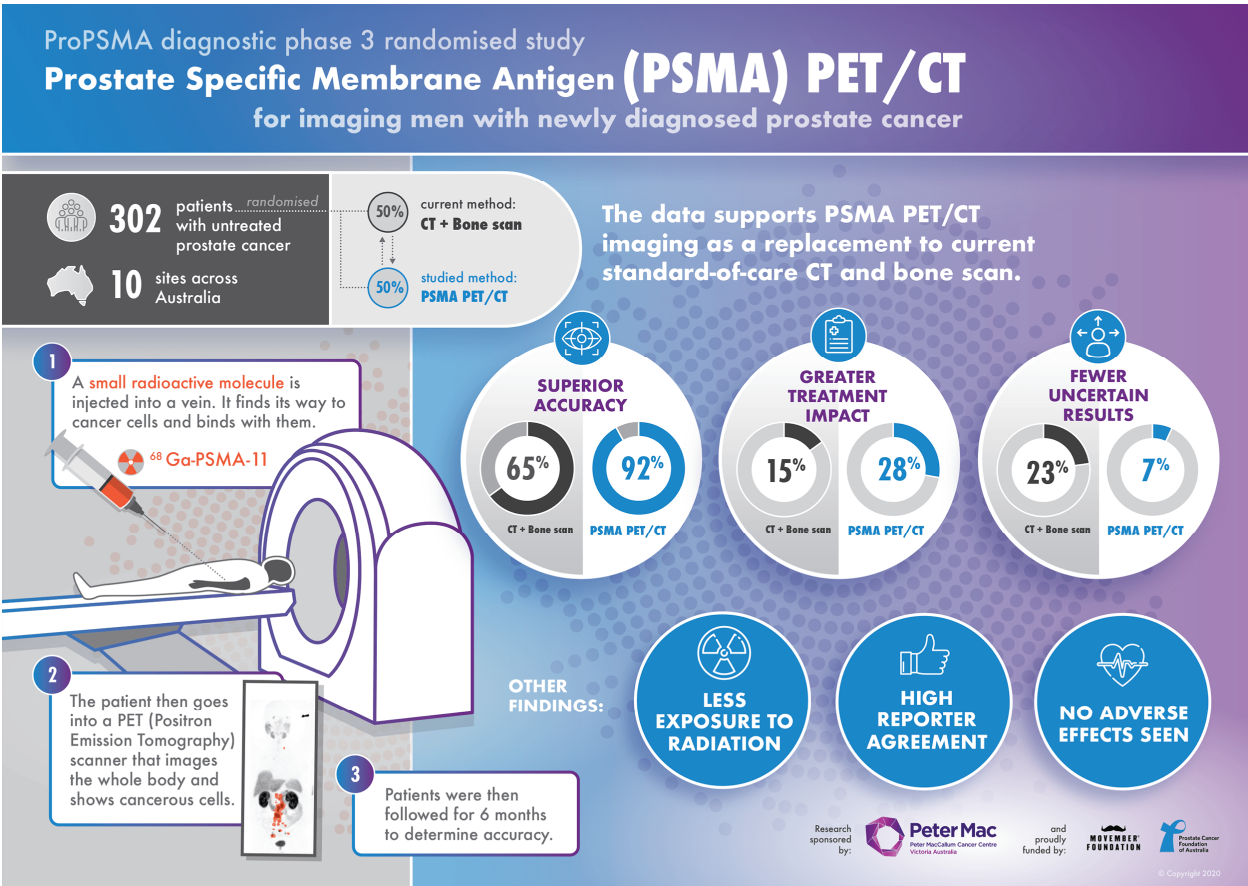
Figure 2: Infographic summarising the proPSMA clinical trial results