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EDITORIAL

The isotope bone scan: we can do better

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The conventional isotope bone scan using ^{99m}Tc-labelled diphosphonate is perceived as being highly sensitive but non-specific in the detection of skeletal pathology. The poor specificity is a significant clinical issue, as additional investigations are frequently required (X-ray, CT, MRI) to clarify equivocal lesions, such as the presence of degenerative changes, where metastatic involvement is suspected. This inevitably leads to extra cost, heightened concern and frequent delays in management. Where available, specificity (and to a lesser extent sensitivity) has been greatly improved with the use of single photon emission computed tomography (SPECT)/CT [1–3], but can be further significantly improved with the use of ^{18}F-fluoride positron emission tomography (PET)/CT [4–6]. Further, ^{18}F-fluoride can on occasion identify early metastatic lesions at a time when the bone scan is normal [7–10]. Nevertheless, ^{18}F-fluoride is rarely used routinely for bone imaging due to the limited availability of PET, cost and competition for time on the PET scanner.

In addition to the above issues there are significant limitations to the use of the bone scan for its most common application, the detection and assessment of metastatic disease. A frequent request is to monitor the effect of treatment, but it is well recognised that even with successful treatment there will be a significant delay before this becomes apparent on the bone scan due to ongoing altered metabolic activity in bone, and there is the possibility of a flare response if the study is performed too early. In the situation where there is such extensive skeletal involvement that lesions coalesce, effectively superficially 'normalising' appearances (the 'superscan' of malignancy), any change is likely to be difficult to detect and further, it is now apparent there may be significant alterations in the metabolic activity of individual lesions but with no apparent visual difference between studies [11]. In this situation quantitation is required to clarify the issue. Quantitation with a conventional bone scan is problematic and techniques that have been used in the past such as measuring bone to soft tissue or lesion to bone ratios are crude and nowadays rarely, if ever, performed. Quantitation is, however, routine with PET studies, and standardised uptake values (SUVs) are commonly measured using the 'universal' tracer ^{18}F-fluorodeoxyglucose (FDG). As previously stated, ^{18}F-fluoride is not routinely used for bone scanning, although there are research reports demonstrating that SUVs can detect significant metabolic change in individual metastatic lesions even when visual evaluation reveals little if any difference [11].

In oncology there are a large number of new treatments that are either in development or have recently become available, and evaluating skeletal response is critical with regard to the future of a drug's development or to decide upon the optimal management of a patient. SUVs are satisfactory in most routine situations, although one must be aware of their limitations. Care must be taken with regard to quality control, for example if there is significant variation in the time when the scan is performed following injection, as this can impact on SUVs (generally there is increased uptake of tracer in a tumour with time). A more important limitation is that SUVs may not be accurate if skeletal involvement is so extensive that the arterial input function is altered, and in such situations

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true quantitation with tracer kinetic studies to measure skeletal plasma clearance is required [12, 13]. Such studies are, however, complex and labour intensive and are not performed in routine practice. Nevertheless, there is considerable interest in tracer kinetic studies in the metabolic bone field and, in recent years, there have been significant developments that have simplified the methodology to the point where clinical use is becoming more feasible, and accurate measurements of ^{18}F-fluoride plasma clearance can be made at multiple sites throughout the skeleton from a single whole-body scan [14].

The isotope bone scan with ^{99m}Tc-labelled diphosphonate is an old and trusted friend and continues to perform with some distinction. It is apparent, however, that we can do significantly better with ^{18}F-fluoride. In the field of oncology earlier identification of metastatic involvement is possible and, where it is important to assess whether a patient is responding to treatment, quantitation may provide such information [11, 15]. As PET scanners are becoming more widely available there now appears to be a compelling case for the introduction of ^{18}F-fluoride as the 'new' bone scan into routine clinical practice.

The remaining questions are whether bone-specific tracers, such as ^{18}F-fluoride, or tumour-specific tracers, such as ^{18}F-FDG or ^{11}C/^{18}F-choline, are best suited in the different clinical applications of: (1) skeletal staging and (2) response assessment. It is possible that the high sensitivity of ^{18}F-fluoride PET is superior in the former and the high specificity of tumour-specific tracers in the latter [16, 17], although detecting early metastases in the bone marrow before an osteoblastic reaction may only be possible with tumour-specific tracers [16].

Whilst the addition of CT to both PET and SPECT scanners has undoubtedly improved diagnostic specificity in assessing skeletal metastases, the advent of PET/MRI may lead to increased sensitivity by detecting early bone marrow metastases, and may also improve the specificity of the assessment of response to treatment by the use of diffusion-weighted MR imaging [18].

Conflicts of interest None.

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