

The impact of generator ingrowth time on bone scan quality

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Abstract

This investigation evaluated the impact of the increased presence of technetium-99 in molybdenum-99/technetium-99m generator elute following a long generator ingrowth time on bone scan image quality.

Methods: The study was a prospective analysis of consecutive bone scans performed on either Monday (72 hour ingrowth) or Tuesday (24 hour ingrowth) of a standard working week in a single nuclear medicine department. Regions of interest (ROI) were drawn to obtain a bone to soft tissue ratio of radiopharmaceutical accumulation in 92 patients. Age, gender, injection to scan time, and bone to soft tissue ratio of the two study groups were compared.

Results: All three variables, age ($P = 0.634$), gender ($P = 0.827$), injection to scan time ($P = 0.386$) demonstrated no statistically significant difference between the Monday and Tuesday cohorts. While the mean bone to soft tissue ratio for the Monday group was lower (2.15) than the Tuesday group (2.30), no statistically significant difference was noted ($P = 0.213$).

Conclusion: No statistical significance between the bone to soft tissue ratios between 24 and 72 hours generator ingrowth time was shown despite evidence of an improvement on Tuesday. Further investigation using a larger, multi-centre trial is recommended.

INTRODUCTION

The concept of image quality is a generic one that applies to all types of images but remains subjective (1). In Nuclear Medicine, image quality may translate, either directly or indirectly, to diagnostic integrity. The quality of bone scintigraphy has been shown to have many variables, including the radiopharmaceutical (2,3), patient age (4), patient gender (5), the interval between injection and scan time (5), and radiopharmaceutical incubation period (6). Radiochemical purity, or the percentage of successfully, is another important factor in bone scan quality (7,8).

Radiochemical impurities are detrimental to image quality as the impurity has different biodistribution in the body from that of normal labelled radiopharmaceutical; contributing to a poorer target to background ratio (7,8).

Both Technetium-99m (^{99m}Tc) and Technetium-99 (^{99}Tc) are daughter products of the parent molybdenum-99 (^{99}Mo), however, ^{99}Tc is also the daughter of ^{99m}Tc (7,9). ^{99}Tc , with a very long half-life of 2.1×10^5 years, decays to stable ruthenium-99 with the emission of a beta particle (7,9).

Chemically, ^{99m}Tc and ^{99}Tc are identical and are the same isotope by definition; although different nuclides (7). During radiopharmaceutical reconstitution, they both compete for the same binding sites (7). In sufficient numbers, ^{99}Tc atoms could result in some of the ^{99m}Tc atoms remaining unbound after bone radiopharmaceutical reconstitution, producing free ^{99m}Tc pertechnetate (7). Bone imaging agents accumulate in bone regardless of whether it is bound to ^{99m}Tc or ^{99}Tc , however, ^{99}Tc will remain undetected during bone scintigraphy.

Given the short half life of ^{99m}Tc (6.02 hours), the very long half life of ^{99}Tc and the decay of both ^{99}Mo and ^{99m}Tc to ^{99}Tc , the proportion of ^{99}Tc on the radionuclide generator column will increase over time (7,9). At 3 hours post elution, ^{99m}Tc represents 72.7% of the total technetium atoms on the column. This decreases to 27.7% by 24 hours post elution (typical elution period) and just 7.7% at 72 hours (typical Monday ingrowth in the absence of out of hours work) (7).

RESEARCH QUESTION

Anecdotally, a number of unusual bone radiopharmaceutical biodistributions have been noted following long weekends. In these cases, the generator ingrowth time was a minimum of 96 hours and possibly as much as 144 hours. The fraction of 99Tc atoms in the eluate would be well in excess of that of 99mTc (less than 5% 99mTc). It was hypothesised that the extended generator ingrowth provided sufficiently high concentrations of 99Tc in the competitive pool to displace 99mTc from binding sites and degrade bone scan quality. The aim of this study was to determine what impact a long generator ingrowth time has on image quality.

METHODOLOGY

The investigation was a prospective analysis of consecutive patients presenting for routine bone imaging to a single Nuclear Medicine department on Mondays and Tuesdays over a period of six weeks. The patients were scanned as per department protocol and referral. Patients were randomly allocated to scan day, injection time and scan time. 99mTc labelled MDP (Radpharm Scientific, Canberra) was employed for all patients. The 99mTc MDP was prepared according to manufacturer specifications using 99mTc eluate of a 99Mo/99mTc 80 GBq Gentech generator (ARI, Sydney).

Patient age, gender, and time between injection and scanning were recorded. Bone scan images were then examined subjectively for evidence of thyroid accumulation (free pertechnetate) or any other unusual biodistribution. Two simple ROIs with total count rates determination were used to calculate bone to soft tissue ratios. The ROIs were of the same size and ROIs excluded any areas of pathology. Where possible, a femur to thigh ratio was performed, however, spine to adjacent non-renal soft tissue, humerus to arm, or tibia to calf ratios were calculated in some patients.

This research approved by the Ethics in Human Research Committee of the School of Biomedical Sciences, Charles Sturt University, Wagga Wagga, Australia.

RESULTS

The study population included 92 patients. One patient was excluded on the basis of widespread metastatic disease, two patients were excluded due to poor skeletal uptake and four patients were excluded due to out of hours generator elution. All remaining 85 patients had either a normal bone scan or findings that did not interfere with the evaluation of images. Seventy three patients had femur/thigh ratios calculated, six

patients had humerus/arm ratios calculated, five had tibia/calf ratios calculated, and one had a spine/adjacent non-renal soft tissue ratio calculated. No statistically significant difference was noted between the Monday and Tuesday cohorts for age (P = 0.634), gender (P = 0.827) or injection to scan time (P = 0.386) (table 1).

Figure 1

Table 1: Distribution of patients in the two groups according to age and gender, and the average injection to scan time.

SCAN DAY	AVERAGE AGE (YEARS)	GENDER DISTRIBUTION (%)		AVERAGE INJECTION TO SCAN TIME
		Female	Male	
MONDAY	54.7	48.6	51.4	3 hrs 2 mins
TUESDAY	57.1	52.0	48.0	2 hrs 59 mins

The mean target to background ratio of the Monday group was 2.28 (95% CI = 2.10 to 2.47). The mean target to background ratio of the Tuesday group was 2.39 (95% CI = 2.24 to 2.54). The overlap of the 95% CI supports the students t-test in suggesting no statistically significant difference between the two groups (P = 0.390).

In an effort to better control variables known to influence bone scan quality, patients were excluded if they were younger than 20 years, if a femur : thigh ratio was not calculated, if the injection to scan time was outside the 2.5 hours to 3.5 hours window. No statistically significant difference was noted between the Monday and Tuesday cohorts for age (P = 0.898), gender (P = 0.916) or injection to scan time (P = 0.667) (table 2). The mean target to background ratio of the Monday group was 2.15 (95% CI = 1.98 to 2.33). The mean target to background ratio of the Tuesday group was 2.30 (95% CI = 2.15 to 2.44). The overlap of the 95% CI supports the students t-test in suggesting there was still no statistically significant difference between the two groups (P = 0.213).

Figure 2

Table 2: Distribution of patients in the two groups according to age and gender, and the average injection to scan time.

SCAN DAY	AVERAGE AGE (YEARS)	GENDER DISTRIBUTION (%)		AVERAGE INJECTION TO SCAN TIME
		Female	Male	
MONDAY	60.6	50.0	50.0	3 hrs
TUESDAY	61.2	48.7	51.3	2 hrs 59 mins

DISCUSSION/CONCLUSION

While the difference in the bone to soft tissue ratios at 24 and 72 hours post previous elution was not deemed to be statistically significant, the results show that the Tuesday patient group had a higher bone to soft tissue ratio. This raises the possibility that generator ingrowth time may affect

bone scan image quality. Many clinical centres do not routinely elute their generators over standard weekends, resulting in a generator ingrowth time of 72 hours if the generator is eluted on a Friday and then Monday.

Generator ingrowth times greater than 72 hours may result in statistically significant differences being observed, and a more obvious degradation in bone scan image quality. This is especially important over a long weekend, particularly the four day Easter weekend. A limitation of this study was that any extravasation of the radiopharmaceutical at the injection site was not ascertained. Obviously a large extravasation could impact on bone to soft tissue ratio. This study was limited in the size of the patient population; a larger study population would provide a more definitive indication of whether generator ingrowth time effects bone scan image quality. Thus, further investigation is warranted to include a larger, multi-centre investigation that captures the Easter long weekend and which incorporates chromatography quality control of reconstituted radiopharmaceuticals.

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