68Ga MAA – Investigations into a potential PET Lung Perfusion Agent

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Introduction

The labelling of MAA with 68Ga for lung perfusion imaging has been previously proposed. Over the last 25 years several groups have reported findings with Ga68 MAA to take advantage of the image resolution improvements afforded by PET over conventional Technetium-99m-MAA imaging[1-3]. However, whilst labelling was feasible, the methods described were mostly impractical for clinical use due to complexity involved in the preparation of 68Ga for labelling. In 2008, a study performed by Mathias and Green utilising the current generation of generators demonstrated a quick and reliable of labelling 68Ga to MAA[4]. This study aimed to modify and extend the method of Mathias and Green in order to identify methods that would further reduce the time and complexity in labelling

Method

Pre-labelling preparation involved "washing" the contents of a commercial MAA kit(s) (an expired preparation by Radpharm) with Milli-Q deionised water to remove contaminants. 68Ga was eluted from the generator with 1mL 0.5M HCl and adjusted to a pH of 5-6 using sodium acetate buffer pH 6-7. This was followed by two methods of labelling:

- Passive Label: 68Ga solution was added to the washed MAA and left to incubate for 35 minutes, inverting slowly every 5 minutes
- Short Label: 68Ga solution was added to the washed MAA and immediately placed into a 200mL 70^{o}C water bath for exactly one minute, after which the solution was removed and inverted slowly for 5 minutes

Labelling efficiency and stability tests were performed post-labelling by centrifuging the 68-MAA solution and measuring both the sediment and the supernatant. Microscopic analysis was also performed both before and after labelling to determine any changes to particle size.

Results

Success in labelling is determined by the percentage of activity present in the sediment compared to the total activity of the sediment and the supernatant combined, corrected for decay. Results from the passive label demonstrated labelling efficiency of between 82% - 90%. Similarly, labelling efficiency of the short label ranged from 80%-95%. Stability of the label was found to be no less than 95% after one hour. Microscopic observation before and after labelling showed no significant change of particle size.

Discussion

The stability of >95% at one hour after labelling, indicated that irrespective of the initial labelling efficiency, after centrifuging and resuspending, at least 80% of the initial activity (decay corrected) will remain with a binding rate of 95% thereafter (important in reducing the amount of free 68Ga within the body). The labelling method was also validated by a member of the MRRG, achieving a labelling efficiency or 90% on their first attempt compounding the simplicity of the labelling method as described. Finally, the study also found that heating the MAA for the one minute does not affect the particle size of the MAA.

References

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Relevance Statement

This study aimed to develop an alternative lung perfusion agent (to Technetium-99m labelled microaggregated albumin) using the generator-produced PET isotope Gallium-68. A Ga 68 lung perfusion has the potential to (A) provide the superior imaging characteristics offered by PET over conventional nuclear medicine and (B) provide a convenient method of obtaining 68Ga as a PET lung perfusion agent. From the research, MAA was successfully labelled to 68Ga with high efficiency and stability as well as suitable particle size. This product is potentially ready for clinical trial and use.