18F-DOPA Manufactured by a Modified One Pot Method is of High Enough Specific Activity to Produce Quality Images of the Pancreas when Injected up to 6 Hours Post Manufacture.

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Introduction

PET imaging with 18F-DOPA is the only currently available imaging technique used in patients with congenital hyperinsulinism (CHI). Most centers throughout the world manufacture the 18F-DOPA in close proximity to the imaging center due to its short half -life of 110 minutes. Most use electrophilic method of manufacturing. We report our experience with the neutrophyllic manufacturing process that give us a high specific activity which allows transporting the agent over 200 miles by ground courier and injected between 4-6 hours after end of synthesis (2.25-3.3 half lives).[1-2] The aim of this study is to determine if we could generate adequate images of the pancreas using 18F-DOPA with a higher specific activity that is manufactured at a distance of 200 miles away and injected 4-6 hours later.

Methods

We modified a previously reported one pot technique to manufacture 18F-DOPA. Synthesis was automated in a system utilizing four steps: An isotopic exchange reaction for the radio-fluorination of the 19F precursor using heavy water. Baeyer–Villiger oxidation using meta-chloroperbenzoic acid. Deprotection by acidic hydrolysis. The total synthesis time was about 120 minutes, the radiochemical yields of 18F-FDOPA produced were about 10±7%. The radiochemical and enantiomeric purities were about 98±2%

Protocol:

18F-DOPA manufacture started at 0600 hours and was completed typically by 0800. Two doses of 18 F-DOPA designed to be injected 30 minutes apart were shipped by licensed ground courier. Quality control was performed on the remaining sample which took 1 hour and if passed, the doses were released for use. The dose arrived at destination between 1230 and 1300. The patients were sedated and placed in PET CT scan prior to arrival of the dose. The dose of 0.12-0.16 mCi/kg was administered. The patients had a low dose attenuation CT, followed by 10 minute PET scans at 20, 30, 40, and 50 minutes with a contrast CT between the 30 and 40 minute scans. The 18F-DOPA was manufactured and administered under an IND held by the PI, and under an IRB approved protocol.

Results

33 patients underwent the 18F-DOPA PET CT. 4 of the first 6 production runs failed due to technical problems and 4 of 27 (15%) since then. All 33 images were good quality exams.

The mean specific activity at end of synthesis was 259.2 mCi/mg DOPA. The mean specific activity at the time of injection was 41.4 mCi/mg DOPA. The mean injection time from end of synthesis was 292.5 minutes.

Outcomes of the surgeries are as follows:

26 of 33 patients went to surgery. 2 of the 26 patients had biopsies only. Histology revealed focal, diffuse, Localized Islet Nuclear Enlargement (LINE), and atypical focal.

There were 15 focal surgeries, 12 of which were cured with minimal pancreatectomy. One was cured with removal of head and pancreatico-jejunostomy. One had persistent hypoglycemia despite removal of head and pancreatico-jejunostomy. Another patient had portal hypertension and was in-operable. Overall, focal surgery had a 93% cure rate. There were two LINE surgeries performed. Both patients were cured with pancreatectomy of 30-50%.

Six patients had diffuse surgery with hypoglycemia post 98% pancreatectomy. There were 3 patients with atypical focal surgeries who also had hypoglycemia post-op with 50-98% pancreatectomy.

Conclusions

This modified novel production method of 18F-DOPA results in a product with higher specific activity which allows it to be transported by ground up to 200 miles and injected up to 6 hours after end of synthesis.

References

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