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Experimental implementation and proof of principle for a radionuclidic purity test solely based on half-life measurement

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HIGHLIGHTS

- Practical use of a new method for testing radionuclidic purity.
- We have investigated limitations and possible impacts of the test.
- We have tested the method on both experimental and simulated data.
- We have developed a GUI in MATLAB for an easy usage.
- The test complies with the requirements in Eur. Ph.

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ABSTRACT

In this paper we present the results of an experimental implementation of the method (Jørgensen et al., 2012) for testing the radionuclidic purity (RNP) of F-18 compounds.

The overall limitations of the experimental methods and their possible impacts on RNP detectability have been identified. We have developed an GUI application for use as an easy and automated test tool in the production procedure.

The test results show that this method fully complies with the requirements in the European Pharmacopoeia (Eur. Ph.) for RNP of FDG and F-18 Sodium Fluoride.

1. Introduction

The widespread use of short lived radiopharmaceuticals for PET have demonstrated the complexity of establishing radionuclidic purity (RNP) spanning a product shelf life of several half-lives. A very important example is F-18 compounds with half-life about 2 h. Here a shelf life of 10 h with a RNP specification >99.9% (as current European Pharmacopoeia requires) necessitates the detection of a long lived impurity containing 1/32,000 of the activity at the time of release.

We have in a previous paper (Jørgensen et al., 2012) examined the mathematical background for using pure half-life determinations to establish such purity levels.

Now we have tested several practical implementations of the half-life method. In this paper we describe the overall limitations of the experimental methods and their possible impact on RNP detectability. The important factors of detector dynamic response and linearity range, signal-to-background, dead time and timing accuracy have been identified in the experimental implementation and their impacts on method sensitivity found.

2. Theory

The RNP test is based on a two component decay model of F-18 and one other contaminating isotope with a half-life of βT_R, where T_R is the half-life of F-18. The level of contamination at the time $t=0$ is α, where α is defined as the fraction between the count rates of the contaminating isotope and F-18, $\alpha = \frac{A_{other}}{A_{F-18}}$.

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The number of counts $N(t)$ is described over time by the equation:

$$N(t) = \frac{N_0}{1+\alpha}\left(\left(\frac{1}{2}\right)^{t/T_R} + \alpha\left(\frac{1}{2}\right)^{t/(\beta T_R)}\right) \quad (1)$$

where N_0 is the initial number of counts.

The RNP is defined as:

$$RNP = \frac{1}{1+\alpha} \quad (2)$$

2.1. Determination of N_0 and the associated uncertainty

The RNP test is based on a comparison of theoretical and measured data for a decay and therefore the initial number of counts N_0 in the exponential decay is of great importance. Thus we have to determine this as accurate as possible from the measured data to establish the theoretical basis for comparison. The limits for RNP, β and time of measurement have to be corrected in order to adapt the associated uncertainty of N_0.

In (Jørgensen et al., 2012) we proposed that N_0 is found as an average of the first 10 data points (normalized), but this gives rise to a systematic error, since a data set with an impurity will cause a value of N_0 that deviates from the "true" value, and this will affect the test result.

For impurities with $\beta < 1$ the estimated value of N_0 will be smaller than the true value and vice versa. Instead we determine N_0 from an exponential fit of the data points within $t \ll t_c$, t_c being the time (in minutes) where the impurity starts to dominate, given by:

$$t_c = \frac{\ln(1/\alpha)}{\ln(2)}\frac{\beta}{\beta-1}T_R \quad (3)$$

Fig. 1 shows a graph of t_c (in minutes) as a function of α and β and it is seen that we safely can make a fit of the data points within the first hour or two for all relevant isotopes and degrees of impurities.

In this interval the deviation between the pure and the impure curve will be very small. The relative deviation can be found as:

$$d(\%) = \frac{N(t)_{impure} - N(t)_{pure}}{N(t)_{pure}}\cdot 100\,\% = \frac{\alpha}{1+\alpha}\left(\left(\frac{1}{2}\right)^{((1-\beta)/\beta T_R)t} - 1\right)\cdot 100\% \quad (4)$$

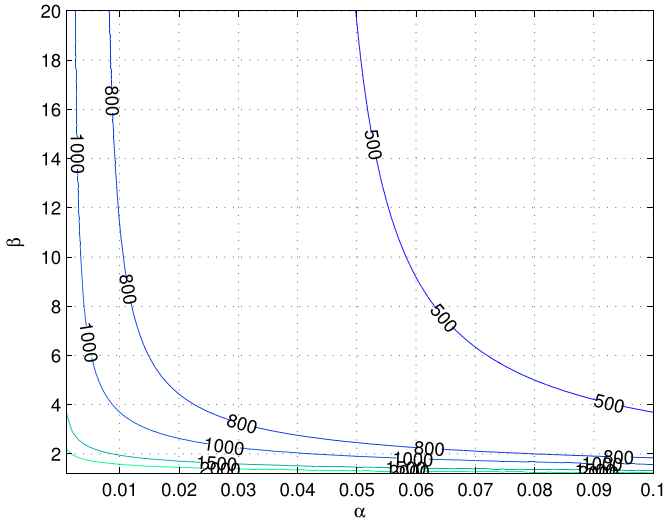

Fig. 1. The figure shows a graph of t_c (in minutes) as a function of α and β.

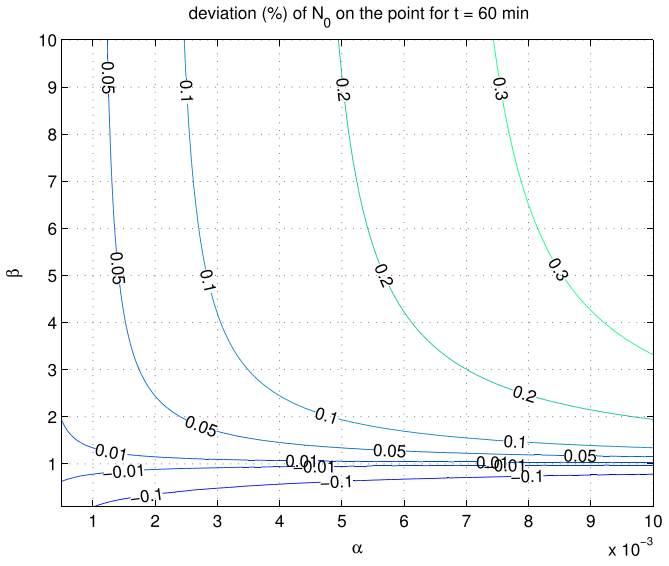

Fig. 2. The graph shows the relative deviation (in %) between the pure and the impure graph after the first hour as a function of α and β.

Fig. 2 shows the relative deviation (in %) between the pure and the impure graph after the first hour, and it is clear that deviations that small will have no significant impact on the determination of N_0.

The uncertainty σ_{N_0} of N_0 is the standard deviation found from the calculation of the exponential fit. In this calculation we have included the poisson statistical uncertainty on the first few measurements contributing to N_0.

2.2. Uncertainty of time

Timing imperfections in the detector chain used increase the uncertainty of each measurement. One example of that could be the uncertainty in time which can be converted to an equivalent uncertainty in the count value by:

$$\sigma_{equiv,time} = \left|\frac{dN(t)}{dt}\right|\cdot\sigma_{time} \quad (5)$$

From this (see Appendix A) it is obvious that the uncertainty in time will have a greater influence on the counts, the higher the count rate is. The question is then, how large the initial counts can be without the equivalent uncertainty gets dominating. We choose $\sigma_{equiv} \le \sigma_{poisson}$:

$$\frac{\log(2)}{T_R}\cdot N_0\cdot\left(\frac{1}{2}\right)^{t/T_R}\cdot\sigma_{time} \le \sqrt{N_0\cdot\left(\frac{1}{2}\right)^{t/T_R}} \quad (6)$$

which gives (for $t=0$):

$$N_0 \le \left(\frac{T_R}{\log(2)\cdot\sigma_{time}}\right)^2 \quad (7)$$

Using the timing error in the counter setup as the uncertainty in time, $\sigma_{time}=1/14$ min (see results section), we get the value of the initial counts, $N_0 \le 5.1\cdot 10^6$. Below this limit the poisson noise forms the greater part of the uncertainty, see Fig. 3.

2.3. Total uncertainty of the data points

The uncertainty of N_0 propagates through the calculations and contributes to the uncertainty of each data point. This is calculated in Appendix B.

Hence, the total uncertainty for each data point in the