Accepted for oral presentation in the SNM 59th Annual Meeting 2012 Miami, Florida/US

Optimization of [^{18}F]-FDG production with terminal sterilization by autoclave.

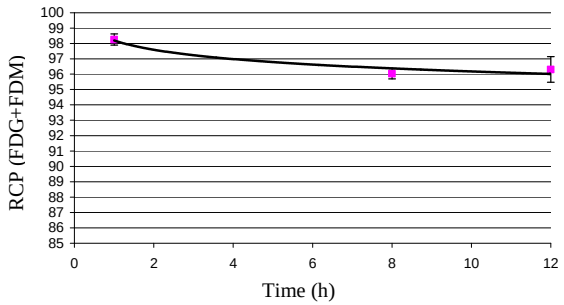
A.J. Abrunhosa[1], F. Alves[1,2], I. Oxley[3], R. Boumon[3] and C. Gameiro[3]
[1]ICNAS Institute for Nuclear Sciences Applied to Health, University of Coimbra, Portugal; [2]ESTeS-C College of Health Technology, Polytechnic Institute of Coimbra, Portugal; [3]Ion Beam Application (IBA), Louvain la Neuve, Belgium

Objectives: Due to the short half-life of [^{18}F]-based radiopharmaceuticals some of the mandatory pharmacopeia tests are only completed after the product is released for use. This is the case, in Europe, for the sterility and pyrogen tests. In these cases, the Ph. Eur. allows a so called "parametric release" in which a comprehensive set of in-process tests and controls are used as an alternative to routine testing of the finished products. For this purpose, a fully validated and highly reproducible manufacturing process, ideally including heat sterilization in the final container, is required. In this work, we will report a [^{18}F]-FDG formulation able to withstand terminal sterilization using a fully automated process with commercially available equipment in a validated EU GMP lab.

Methods: Syntheses were performed on an IBA Synthera automated synthesis module linked with a Comecer Theodorico W dispensing system with robotic arm and equipped with an autoclave.

Results: Synthesis time was 26 minutes with non-decay corrected radiochemical yields always above 60%. After correction for pH/isotonicity, final FDG solution was dispensed and autoclaved for 3 minutes at 135ºC in the final container. The entire process is automated allowing very low doses to the operators. Batches of up to 222 GBq were produced with a radioactivity concentration of 185 MBq/ml at 8h calibration point and tested according to Phar. Eur. for up to 12 hours in normal (room temperature) and accelerated conditions (AC, 40ºC). All results were within specification at all time points for all validation batches (n=5).

The figure below shows radiochemical purity ([^{18}F]-FDG+[^{18}F]-FDM) over time for up to 12h.



Conclusions: Results obtained were used to submit a Marketing Authorization in an EU member State that was successfully granted in December 2011. Besides the advantages regarding Quality Assurance, laboratory requirements are also less stringent when terminal sterilization by autoclaving is used reducing the time to establish a new facility, training of personnel as well as the setup and operating costs.

References:

Karwath, P et al. Appl Radiat Isot. 2005. 62(4):577-86
Varelis P et al. Appl Radiat Isot. 1996. 47(8) : 731-733