AN EMBEDDED SYSTEM BASED COMPUTER CONTROLLED PROCESS AUTOMATION FOR RECOVERY AND PURIFICATION OF ^{99m}Tc FROM (n,γ)^{99}Mo

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Abstract

^{99}Mo produced ^{99m}Tc ($t_{1/2}$=6hr, 140keV γ-ray) is the most useful radioisotope for nuclear diagnostics. High specific activity ^{99}Mo is supplied globally mainly by five old reactors whose routine or unscheduled maintenance shutdown causes supply irregularities that adversely affects patient management in nuclear medicine centres. ^{99m}Tc may also be produced via ^{98}Mo(n,γ) in a natural MoO_3 target in reactor or by ^{100}Mo(n,2n)^{99}Mo or ^{100}Mo(p,2n)^{99m}Tc reaction in cyclotron. To meet the crisis proposals are there to produce ^{99}Mo by ^{100}Mo(n,2n)^{99}Mo or ^{99m}Tc directly by ^{100}Mo(p,2n)^{99m}Tc in a cyclotron. Of the several separation methods of ^{99m}Tc from molybdenum, the most common are adsorption column chromatography, sublimation and liquid-liquid solvent extraction. The conventional methods besides being cumbersome are often hazardous, polluting, require skilled manpower and facilities like fume hood and so are not always practically feasible for hospitals. To address these, VECC and BRIT, Kolkata have collaborated to develop an embedded system based automated ^{99}Mo/^{99m}Tc generator from low specific activity ^{99}Mo using solvent extraction technique, supervised by a PC based GUI.

INTRODUCTION

Technetium-99m ($t_{1/2}$= 6.02h; 140.51 keV (89%), principle γ-emission energy) is known to be the most useful radioisotope in diagnostic nuclear medicine. More than 80% of all diagnostic procedures done worldwide in nuclear medicine centre are performed with ^{99m}Tc. There are several methods [1, 2, 3, 4, 5] for routine separation of ^{99m}Tc from ^{99}Mo, namely, alumina column chromatography technique based on the elution of ^{99m}Tc from high specific activity ^{99}Mo obtained by thermal fission of ^{235}U, the zirconium molybdate gel column chromatography technique based on the elution of ^{99m}Tc from the medium specific activity (n, γ)^{99}Mo and solvent extraction technique based on extraction of ^{99m}Tc with methyl ethyl ketone (MEK) followed by removal of MEK from low-medium specific activity (n, γ) ^{99}Mo. Currently the solvent extraction generators for the separation of ^{99m}Tc from ^{99}Mo produced by neutron activation of ^{98}Mo is achieved by manual solvent extraction with MEK in most of the hospitals in India and other developing countries. Though it is being practiced, but the method is not desirable in hospital set up as the MEK being inflammable solvent, the evaporation of MEK by heating is hazardous and environmentally polluting. Not only is there the requirement of additional facilities such as fume hood and trained and skilled technicians, which may not always be practically feasible for hospitals but the process is cumbersome as well. There is also the possibility of bacterial contamination in the product and radiation exposure to the operating technicians.

To solve the abovementioned problems, an automated closed cyclic module for separation and recovery of various isotopes, radioactive or non-radioactive, using solvent extraction technique, and in particular, for separation and recovery of ^{99m}Tc from low-medium specific activity ^{99}Mo obtained in research reactor has been indigenously developed jointly by VECC and BRIT, Regional Centre, Kolkata. The module may also be used for separation of ^{99m}Tc produced in cyclotron. Its principle of working, scope and advantages are explained in the following sections with a discussion of the process chemistry as well.

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PROCESS CHEMISTRY

The generator system is based on the selective extraction of pertechnetate ($^{99m}TcO_4^-$) in MEK from aqueous alkaline (n,γ)$Na_2^{99}MoO_4$ solution, subsequent purification of the organic phase by passing through an alumina column to remove traces of Mo, alkali etc. and careful evaporation of the organic phase. The residue obtained is reconstituted in physiological saline (10 ml), purified through an on-line 0.22μm membrane filter to obtain pharmaceutical grade ^{99m}Tc and collected in a vacuum vial.

AUTOMATION OVERVIEW

Scope

The process constitutes of sequential mixing, seperation, evaporation and collection of various chemicals and their by-products. The mixing and directing the flow of chemicals to various parts of the system was achieved by a set of solenoid valves and a vacuum pump. By exploiting the difference in density and electrical conductivity of the organic and aqueous constituents, the phase separation was carried out online. The evaporation of the trace organic amount before the product collection was done by temperature controlled heater system set at the boiling point of the organic chemical. A clock system was designed to set the timings of each sequence of operation starting from the initial chemicals to the final product. the integrated design employing a microcontroller based embedded system with a compatible PC based GUI enabling the operator to programme and intervene the process remotely.

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Controller Electronics

A 16-bit microcontroller (Texas Instruments make MSP430FG4619) based control architecture, a customized version of [6], constitutes the heart of the system. On the one hand it communicates with the PC based GUI over the serial link and on the other hand sets in motion the actuator circuitry. From the GUI it receives the configuration words and the process instructions. Based on these it configures a timer and also selects the actuators that are to be operated upon for the corresponding step of the process. Its digital input bank reads the actuator status and sends the update to the front panel LEDs and the GUI. Priorities are programmed in the firmware so as to make the system fail-safe, e.g. command to terminate the process has been given the highest priority that will overrule any operating conditions and will shut down the process, closing all the valves, pump and heater, at any instant the particular command is received. Also on every reset or at the instant the circtuitry is powered, it drives all the actuators to their OFF state.

Sensors and Actuator Hardware

A relay based driver circuitry is designed for actuation of the solenoid valves and the pump. This section is driven by the controller whose first stage selects the actuator channel that is being operated upon and also isolates the digital circuitry from the analog one. A driver circuitry, of the corresponding channel, then triggers the associated relay that serves the dual purpose of activating/deactivating the particular actuator and offers yet another level of isolation between the driver power and the electrical power. An isolated feedback path is designed to read the status of the actuating relays and sends the data, over a single channel, to the microcontroller via a digital multiplexing arrangement.

The conductivity detector system is set at the threshold standardized by the process chemistry. It senses the electrical conductivity of the process chemicals and sends the status to the controller via a comparator block that finally dictates the operation of the valves associated with that section of the process.

A temperature controlled heater system is designed to warm up a water bath at a temperature set by the DAC of the controller. AD590 based instrumentation senses the temperature and is utilized as feedback to regulate the temperature of the heater system. The kanthal wire based 180W heater coil was developed for the purpose and is powered by a 30V DC supply. The water bath sets the upper limit of the heater temperature, which is normally operated at temperature higher thatn the boiling point of MEK. The temperature setting is done by DAC, set by the controller and amplified according to the electronics requirement and the readout is buffered from the AD590 feedback signal and conditioned before feeding to the ADC.

GUI

A Visual Basic based GUI was designed (Figure 1) on defined RS-232 based serial communication protocol between the embedded controller and the PC. It gives the user access to change the timings of the sequence of the process and start, halt/resume or terminate it as well. The process is also supervised via animated objects that informs the conductivity status of the process chemical as read by the detector, the status of the actuators and the temperature of the water bath. Manual checks and unavoidable operator interventions during the process are reminded by the GUI in the form of flashing comments as and when required. After each cycle completes, the GUI enforces the operator to refresh the heater setting and the process timings.

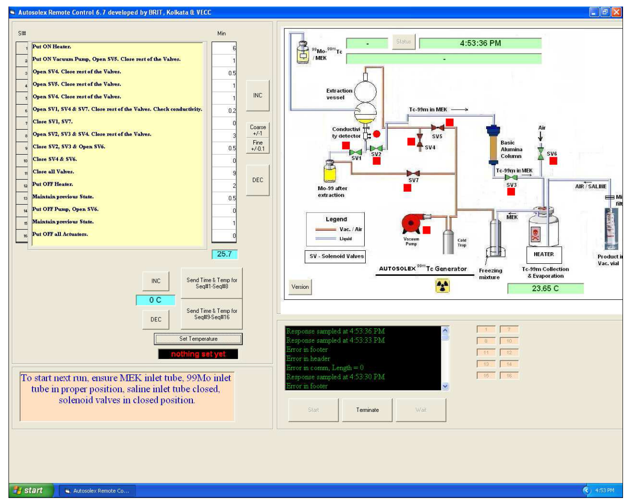

Figure 1: Operator Interface of the PC based GUI.

The important benefits that the system offers are

- As the greater part of the process involves computer control, there is no or little chance of exposing the operator to radiation dose.
- The overall assembly including the solenoid valves can be conveniently used in hospital radiopharmacy.
- The used MEK after extraction may be reused for next extraction, excluding the disposal problem.
- As the organic and aqueous phase separation is controlled by a conductivity detector there is no or very less chance of MEK remaining in the aqueous layer.
- As the aqueous layer containing ^{99}Mo after ^{99m}Tc extraction is unloaded from the solvent extractor a fresh loading of ^{99}Mo/^{99m}Tc may be done for another extraction and purification of ^{99m}Tc at the same day. The absence of volume restriction improves the versatility of the system.
- The process of air bubbling through the product at elevated temperature to remove traces of MEK from the final ^{99m}Tc product proved to be more effective than the conventional way of air flow at room temperature.
- The controller has been configured to include 16 actuators but the design modularity allows a scope for extension without any major hardware modifications.
- The software provides online display of communication status and a time-stamped background log of the actuator information that helps in easier maintenance.

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Figure 2: Hardware assembly consisting of (clockwise from top left) Process Assembly in fumoid, Solenoid Valve Assembly, Electronics Assembly inside the 19” Controller rack, Front panel of Controller Unit.

BENEFITS, FUTURE SCOPE AND CONCLUSION

In summary the system greatly simplifies the operation by minimizing manual intervertion while enforcing strict adherence to embedded protocol, eliminating chance of wrong procedure. This, supplemented with a fail safe approach at several levels of its design and the system economics, advocates high potentiality for its application in nuclear medicine centre.The new generator system, developed primarilyfor separation of ^{99m}Tc from reactor produced low-medium specific activity ^{99}Mo, can also be used for separation of ^{99m}Tc directly produced from ^{100}Mo by (p, 2n) reaction in a cyclotron. The automated radiochemistry used is a remarkable development and it can be adapted in any radiochemical separation in general and production of new PET pharmaceuticals in particular. Thus this will be extremely useful in routine production of new radiopharmaceuticals in the upcoming medical cyclotron project in Kolkata.

It has been succesfully tested and demonstrated at RPL, BRIT, VECC, Kolkata and BRIT, Mumbai and is currently being evaluated at RMC, BARC, Mumbai.

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