



AUTOMATION OF THE PRODUCTION OF RADIOPHARMACEUTICAL WITH THE AIM TO REDUCE THE OPERATOR'S RADIATION DOSE

Aleksandar VUKADINOVIĆ¹, Miroslav RAVLIĆ², Milovan MATOVIĆ³, Drina JANKOVIĆ¹, Marija MIRKOVIĆ¹,
Magdalena RADOVIĆ¹, Zorana MILANOVIĆ¹, Marko PERIĆ¹, Dragana STANKOVIĆ¹, Milutin JEVREMOVIĆ¹,
Sanja VRANJEŠ-ĐURIĆ¹

- 1) *"Vinča" Institute of Nuclear Sciences, University of Belgrade, Laboratory for radioisotopes, Mike Petrovića Alasa
12-14, Belgrade, Serbia*
- 2) *PRIZMA d.o.o., Dr Zorana Đinđića 13, Kragujevac, Serbia*
- 3) *Faculty of Medical Sciences, University of Kragujevac, Svetozara Markovica 69, Kragujevac, Serbia*



Speaker name: Aleksandar Vukadinović

XXXII Simpozijum DZZSCG
Budva, 04-06.10.2023.

Founded in 1948 **Vinča Institute of Nuclear Sciences** is the most prominent multidisciplinary research institute in the Republic of Serbia.



Speaker name: Aleksandar Vukadinović

XXXII Simpozijum DZZSCG
Budva, 04-06.10.2023.



Vinča Institute of
Nuclear Sciences
Laboratory for
Radioisotopes

$^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ Generator

- Dry column technology
- Exceptional eluate quality
- Proven reliability



Radiopharmaceutical kits

for preparation of $^{99\text{m}}\text{Tc}$ radiopharmaceuticals:

- $^{99\text{m}}\text{Tc}$ -DPD
- $^{99\text{m}}\text{Tc}$ -MIBI (sestamibi)
- $^{99\text{m}}\text{Tc(III)}$ -DMSA (succimer)
- $^{99\text{m}}\text{Tc(V)}$ -DMSA
- $^{99\text{m}}\text{Tc}$ -DTPA (pentetate)
- $^{99\text{m}}\text{Tc}$ -MAA (albumin aggregated)
- $^{99\text{m}}\text{Tc}$ -Sn-colloid (tin colloid)
- $^{99\text{m}}\text{Tc}$ -antimony sulphide colloid
- $^{99\text{m}}\text{Tc}$ -PYP (pyrophosphate)
- $^{99\text{m}}\text{Tc}$ -EHIDA
- $^{99\text{m}}\text{Tc}$ -ciprofloxacin



Speaker name: Aleksandar Vukadinović

XXXII Simpozijum DZZSCG
Budva, 04-06.10.2023.



Vinča Institute of
Nuclear Sciences
Laboratory for
Radioisotopes

Iodine-131 radiopharmaceuticals

- Sodium Iodide (Na^{131}I) capsules for therapy
- Sodium Iodide (Na^{131}I) capsules for diagnostics
- Iodine-131-meta-iodobenzylguanidine (^{131}I -MIBG)
- Iodine-131-ortho-iodo-hippuric acid (^{131}I -Hippuran)

Quality control of radiopharmaceuticals

Sealed sources

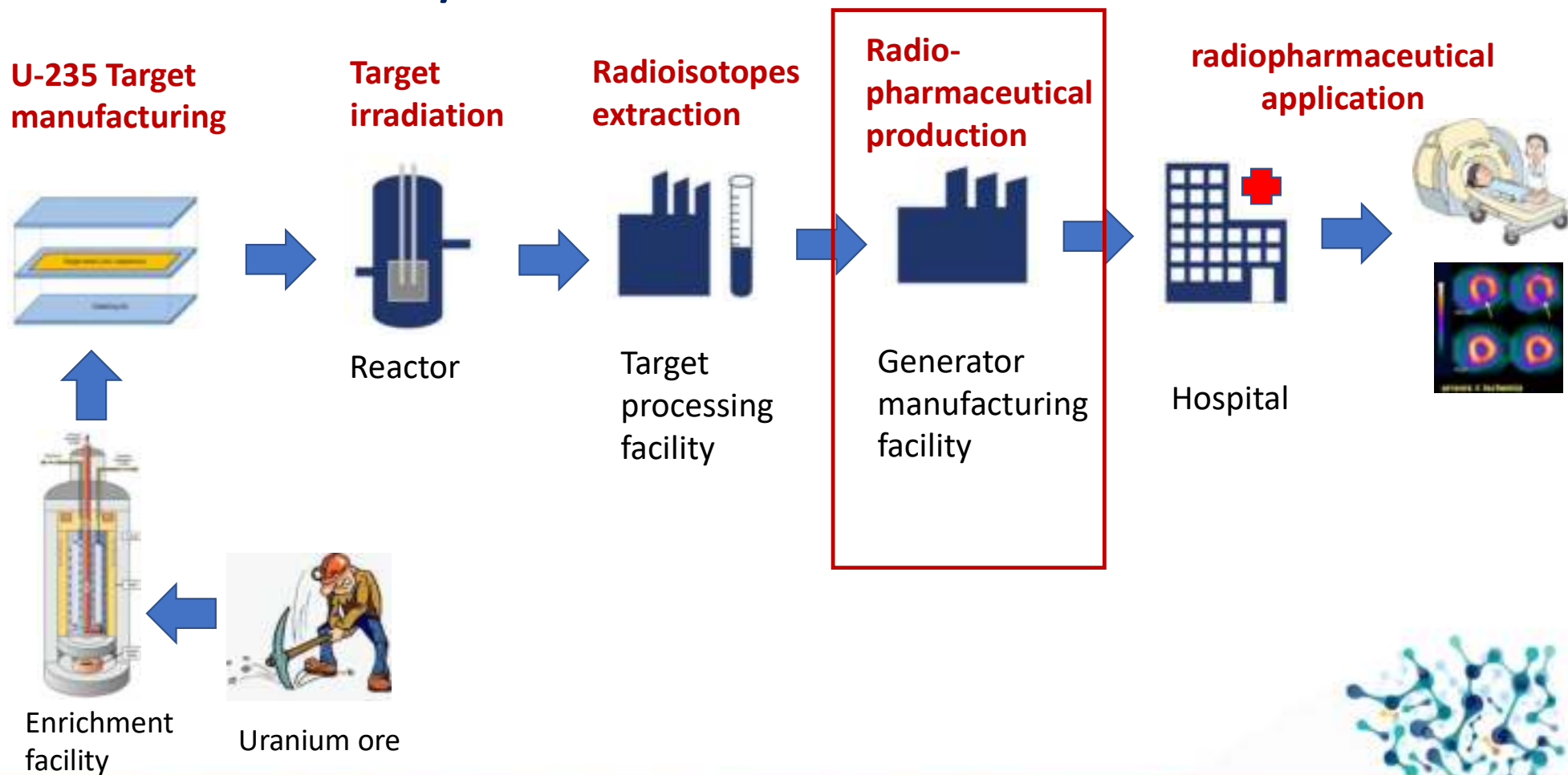
- Sources for industrial processes: measuring densities, thicknesses, levels and concentrations (^{60}Co , ^{137}Cs , ^{241}Am , ^{90}Sr , ^{85}Kr etc.)
- Sources for industrial radiography (^{192}Ir , ^{75}Se)
- Sealed sources for medical uses



Speaker name: Aleksandar Vukadinović

XXXII Simpozijum DZZSCG
Budva, 04-06.10.2023.

OVERVIEW OF Mo-99/Tc-99m SUPPLY CHAIN

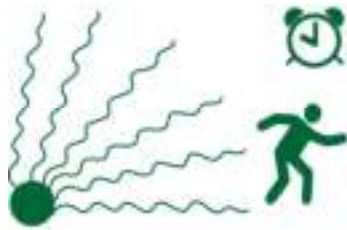


Speaker name: Aleksandar Vukadinović

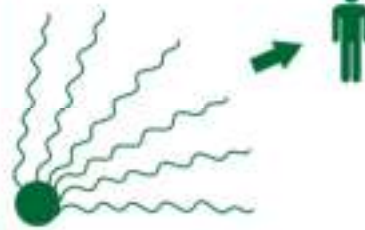
XXXII Simpozijum DZZSCG
Budva, 04-06.10.2023.

REDUCING RADIATION EXPOSURE

To reduce radiation exposure:



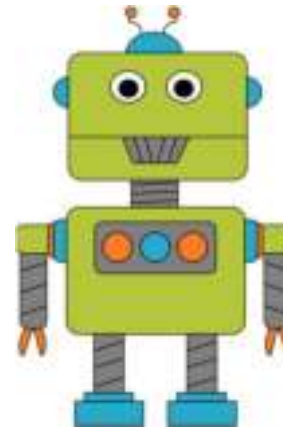
Limit Time



Increase Distance



Use Shielding



AUTOMATION OF PRODUCTION PROCESSES

Types of $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generators



RADIOIODINE CAPSULES



REPUBLIC OF SERBIA
INNOVATION
FUND

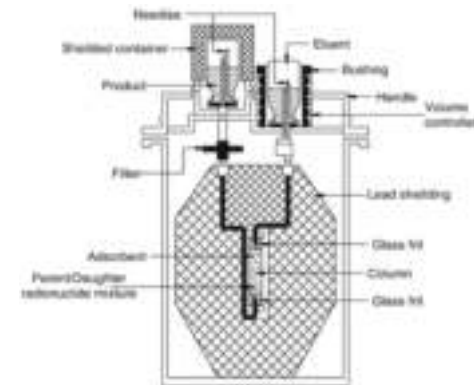


Speaker name: Aleksandar Vukadinović

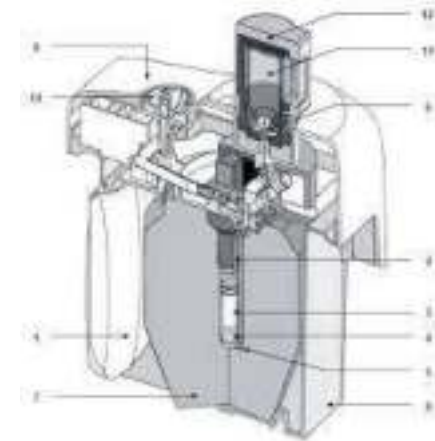
XXXII Simpozijum DZZSCG
Budva, 04-06.10.2023.

Types of $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generators

- DRY COLUMN GENERATORS



- WET COLUMN GENERATORS

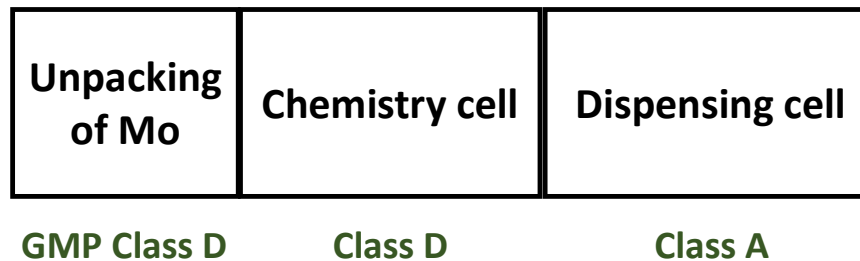


Speaker name: Aleksandar Vukadinović

XXXII Simpozijum DZZSCG
Budva, 04-06.10.2023.

$^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generators production process

- COLD** → 1. Sterilization of the column system with needles
- COLD** → 2. Assembly of the generator components
- HOT** → 3. Preparation of the Mo-99 loading solution
- HOT** → 4. Dispensing of the loading Mo-99 solution into the generators under the aseptic conditions



Hot cell system for the post-loading process



$^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generators production process

Development of the system for production $^{99\text{m}}\text{Tc}$ generators

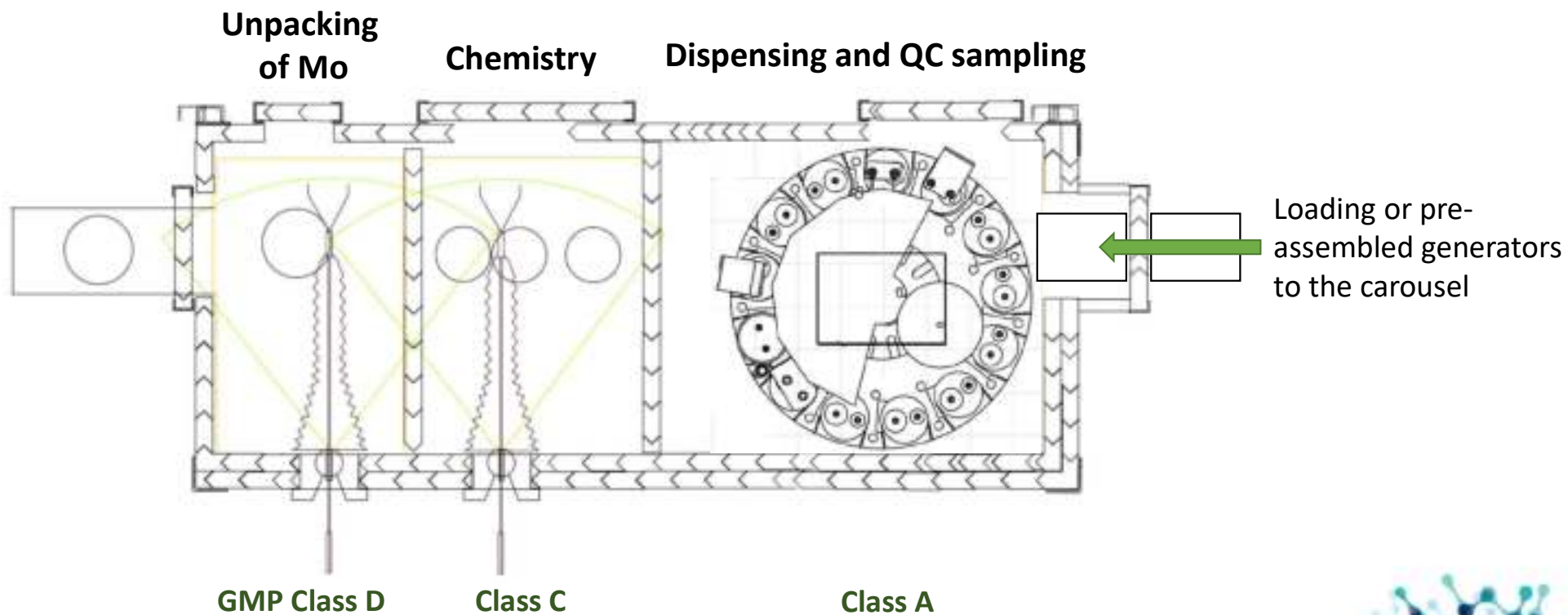
Goals:

- Suitable for production of small batches (under 30 generators per batch)
- Automation of all HOT production steps
- To be affordable
- To meet the GMP requirements



$^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generators production process

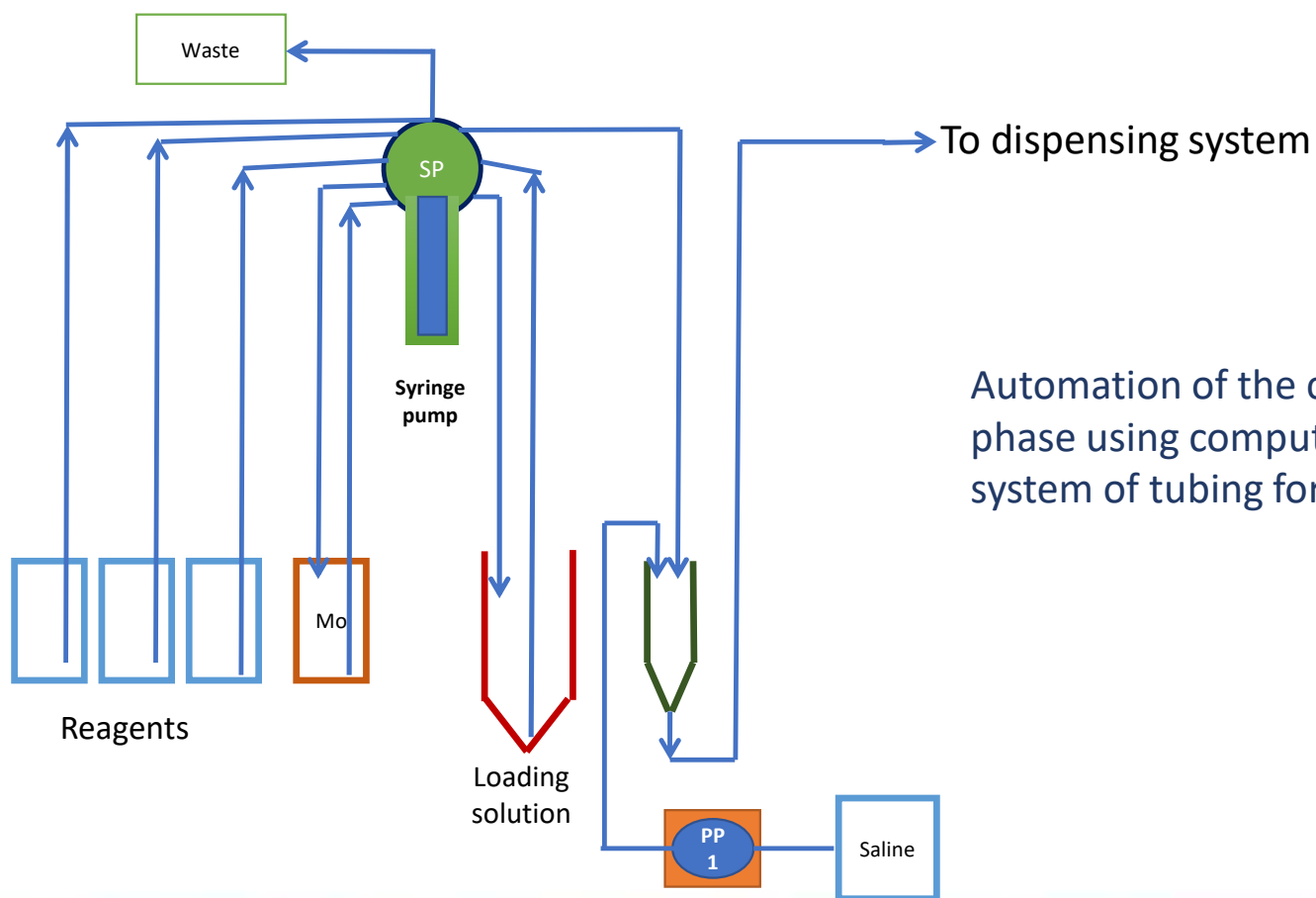
POST-ASSEMBLY LOADING PROCEDURE



Speaker name: Aleksandar Vukadinović

XXXII Simpozijum DZZSCG
Budva, 04-06.10.2023.

$^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generators production system



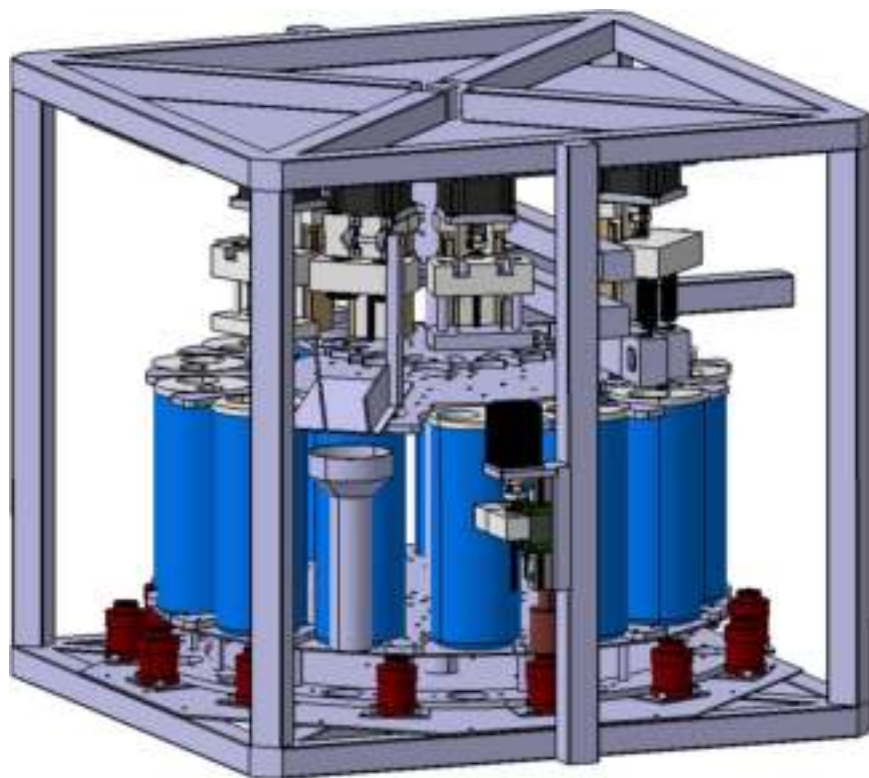
Automation of the chemistry production phase using computer-controlled pumps and system of tubing for liquid handling.



$^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generators production system

Automation of the dispensing phase and QC sampling

Machine frame

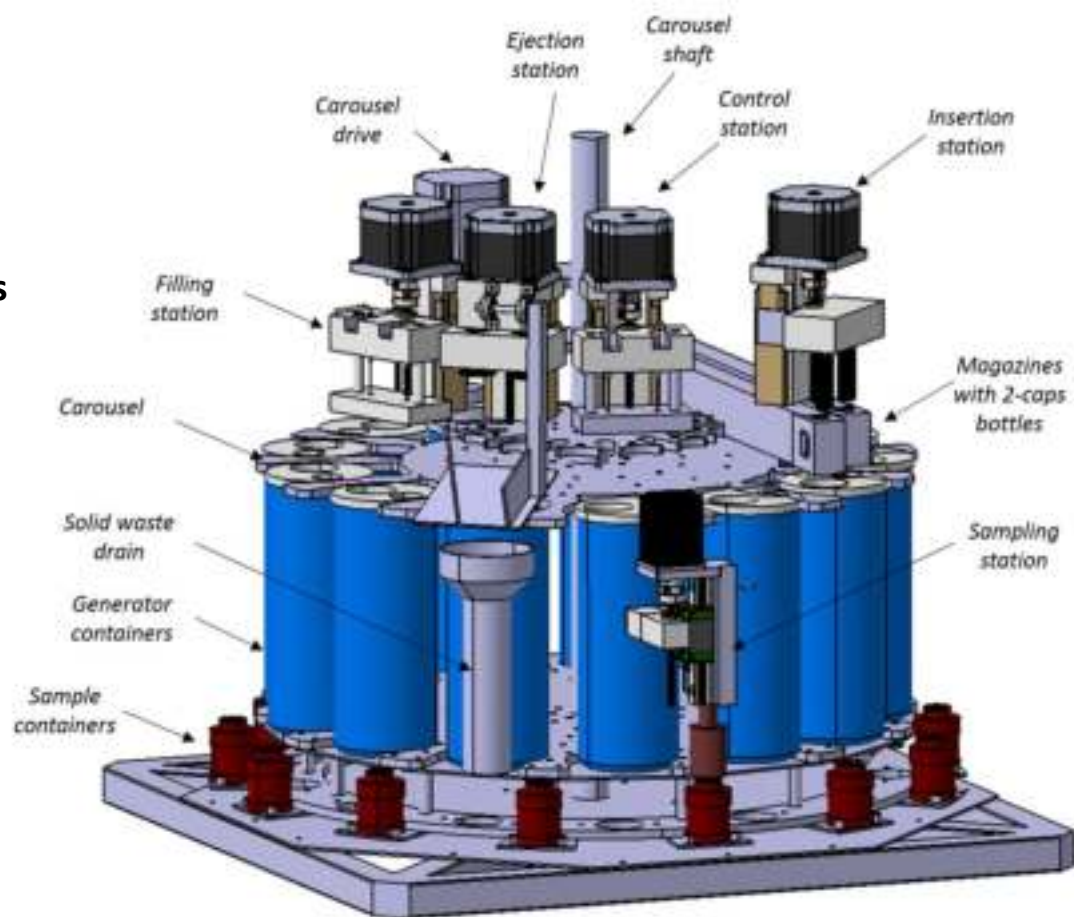


Speaker name: Aleksandar Vukadinović

XXXII Simpozijum DZZSCG
Budva, 04-06.10.2023.

$^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generators production system

Functional parts



Speaker name: Aleksandar Vukadinović

XXXII Simpozijum DZZSCG
Budva, 04-06.10.2023.

RADIOIODINE CAPSULES



OPERATION STEPS:

1. The first step in the whole process is the filling of the known volume of ^{131}I solution into the syringe.
2. The next step is filling-out needed volume (i.e. activity) in the capsule and closing it with the appropriate cap.
3. The third step includes measurement of ^{131}I activity in the capsule (dose calibrator) and printing its value on the self-adhesive label.
4. The final step is transport of the capsule to a lead container.



Radioiodine Capsules

Affordable system

Easy to use

Computer controlled

Every capsule can be different as ordered
by a physician

Dispenses volumes from 0.2 μl – 250 μl

Suitable for small batches of custom
ordered capsules



Speaker name: Aleksandar Vukadinović

XXXII Simpozijum DZZSCG
Budva, 04-06.10.2023.

Automatic production systems

DOES IT MEET GMP REQUIREMENTS? **YES**

- If Hot Cell and equipment is qualified (URS, DQ, IQ, OQ, PQ)
- If cleaning and sanitization process is validated
- If production process is validated
- If environmental monitoring is conducted
(microbiological monitoring, air particulate monitoring)
- If personnel is trained
- If the documentation is in order



Automatic production systems

RESULTS:

- All HOT production steps are automated
- Exposure of the operators to the ionizing radiation is ALARA
- Systems are suitable for production of small batches
- Are affordable
- Meet the GMP requirements



What is next...



Speaker name: Aleksandar Vukadinović

XXXII Simpozijum DZZSCG
Budva, 04-06.10.2023.

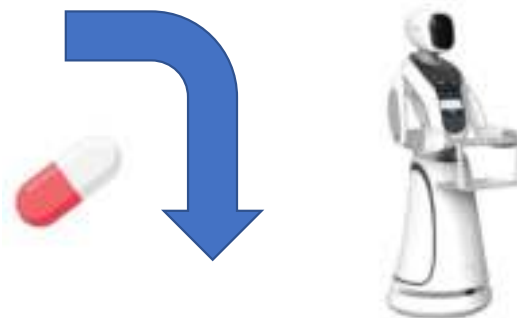
What is next...

ORDER



MANUFACTURE

DELIVERY



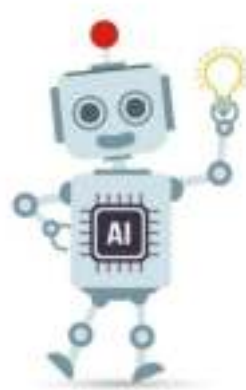
IMAGING/TREATMENT



THE 4th INDUSTRIAL REVOLUTION



Automation



Speaker name: Aleksandar Vukadinović

XXXII Simpozijum DZZSCG
Budva, 04-06.10.2023.



Thank you for your attention

vukadinovic@vinca.rs

Visit us:

www.vinca.rs/en/

www.radioizotopi.rs



Speaker name: Aleksandar Vukadinović

XXXII Simpozijum DZZSCG
Budva, 04-06.10.2023.