An accelerator-driven production of Mo-99 at CERN as a long-term solution to the current world crisis in diagnostic medical imaging

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Executive Summary

More than 30 Million medical diagnostic protocols per year in the word are threatened by a global crisis in the production of an essential radionuclide for Nuclear Medicine: Molybdenum-99. In addition to the current crisis, no solution exists to date to provide a global, long-term reliable supply of this fundamental product.

Urgent actions are needed not only to solve a serious problem that is striking most of world countries, but also to protect the development of Nuclear Molecular Imaging which, together with Nuclear Molecular Therapy, are essential tools to provide predictive, preventative and Personalized Medicine that will transform healthcare.

Presently, the worldwide supply chain of Mo-99 is essentially based on the production from 5 nuclear research reactors that serve a market in excess of 300 M€. These reactors are approaching the end of their operational lifetime and the aging of the installations lead to unscheduled shutdown that provokes severe shortage of Mo-99, hitting the nuclear medicine community.

We suggest here to base the Mo-99 production cycle on particle accelerators, which presents many advantages in terms of safety, cost, time to market and environmental and proliferation issues. Only one machine based at the European Organization for Nuclear Research (CERN) and built with a joint international effort could potentially serve the world market and solve a global public health problem.

1 Background

Nuclear Molecular Imaging provides non-invasive, visual and quantitative representations of fundamental biological processes in living subjects, a necessary path for improving patient care. Nanograms of Molecular probes labelled with tracers are sufficient to create metabolic images through PET (Positron Emission Tomography) or SPECT (Single Photon Emission Computed Tomography) scanners, but can also be used for effective treatment of cancer diseases through Molecular Therapy.

Molecular Medicine (Molecular Imaging and Therapy) promises to provide predictive, preventative and Personalized Medicine that will transform healthcare.

One of the most used tracers for Molecular Imaging worldwide is Technetium-99m which labels hundreds of different molecular probes. It is foreseen that the medical protocols using Tc-99m (currently in excess of 30 Millions/year) will be in constant increase for the next years.

Hospitals extract Tc-99m from simple devices called Technetium generators as needed, and instant commercial kits provide pre-packaged chemicals to simplify incorporation of Tc-99m into inorganic molecules. The Tc-99m in a generator is continuosly produced from Molibdenum-99 for a week. The Mo-99 used to manufacture Tc generators is extracted as a fission product by special fuel bars irradiated into research nuclear reactors. Its half-life is 66 hours, the reason why the production cycle of both Mo-99 and Tc-99m generators is one week.

Presently, the worldwide supply chain of Mo-99 is essentially based on the activity of 5 research reactors (NRU Canada, HFR Netherlands, SAFARI-1 South Africa, BR2 Belgium and OSIRIS France) irradiating Highly Enriched Uranium (HEU, containing about 98% of fissile Uranium-235). The greatest part of these reactors is approaching the end of its operational lifetime and the aging of the installations lead to unscheduled shutdown that can last for months. Consequently, a severe shortage of production capacity of Mo-99 is hitting the nuclear medicine community which is seeking alternative solutions to ensure a reliable supply of Tc generators.

Besides the current shortage, no solution exists to date to provide a global, long-term reliable supply of Mo-99. Concerns about such long-term supply have been further exacerbated by the recent decision (May 2008) to discontinue development of the MAPLE reactors in Canada, two new dedicated facilities that were to replace NRU's production of Mo-99 (the NRU and HFR reactors produce together about 90% of world Mo-99 supply).

2 Alternatives for a global, long-term reliable supply of Mo-99

The Association of Imaging Producers & Equipment Suppliers (AIPES) issued a report on the current status of the Mo-99/Tc-99m market in November 2008 [1], highlighting the need to urgently define possible alternatives to the reactor production of Mo-99 such as:

- The partial or total conversion of existing research nuclear reactors into production reactors for radioisotopes for nuclear medicine purposes.
- The reliance of world markets on a network of "smaller" production reactors, with the resolution of associated logistic issues.
- The use of high-current accelerators & hybrid systems for the industrial production of radionuclides, SPECT, PET, therapy and pain palliation nuclides.

It is important to highlight that future production alternatives using Nuclear Reactors are affected by another problem: in the interest of nuclear security and non-proliferation, the U.S. and other countries are increasing the pressure to migrate all non-military applications (such as research reactor fuel and isotope production targets) to use Low-Enriched Uranium (LEU). To understand these issues, one can consult a report issued in 2009 by the US National Research Council [2] with the aim of exploring alternatives to the use of HEU for medical isotopes production. Further technical and economic information about the current status of the Mo-99 production can also be found in this report.

In November 2008 a report was issued by TRIUMF [3], again stressing the need for alternatives to nuclear reactors for ^{99}Mo production, reviewing different alternatives and suggesting a photo-fission method as the most promising one.

3 An accelerator-driven production of Mo-99 at CERN

In 1999, at the European Organization for Nuclear Research (CERN), Nobel Laureate Carlo Rubbiainvented a method to efficiently produce Mo-99 from a high power accelerator using Adiabatic Resonance Crossing (ARC) [4]. The ARC method was further developed by a CERN spin-off, Advanced Accelerator Applications (AAA), for the production of innovative products for brachytherapy [5].

We contemplate using a high power accelerator (1 mA of protons at 1 GeV, giving 1 MW beam power) which would be capable of providing a flux of neutrons equivalent to a research reactor but with the "quality" suited to enhance the ARC effect and therefore the production of Mo-99 from Natural Enriched Mo-98.

As a result of preliminary calculations based on experimental data [6], the ARC method, used jointly with only one accelerator of this size, could cover 100% of the current world demand of Mo-99 using a more acceptable production cycle based on Natural Mo-98 and not on fissile, proliferative HEU.

As a unique and totally acceptable commercial drawback of using this method, the specific activity of the Mo-99 produced with an accelerator using the ARC method would be equivalent to the one using LEU fuel with Nuclear Reactors [6]. LEU is already routinely used for commercial purposes at the Ezeiza Atomic Centre in Argentina since 2002 [7].

A MW accelerator is a reality. The Paul Sherrer Institute (PSI) has successfully operated such a machine for years, using also a liquid metal target [8], a technology that could be extremely useful for the implementation of the ARC method.

We believe that the best place to build such machine could be CERN for many reasons:

- CERN has naturally all the competences to build an accelerator. With the end of the construction of the LHC (the Large Hadron Collider), there are potentially resources and competencies available.
- With the necessary resources and investments it is feasible to build a production facility in 5 years, while a new reactor may require up to 10 years.
- CERN has already an interest in building high power linear proton machines for different research purposes. A few designs already exist for such machines.
- Many cost savings could be realised at CERN. For example there is the possibility of using CERN existing tunnels to limit investments in infrastructures or to use

components (accelerating sections) dismounted from the former CERN accelerator (LEP) and left unused.

- CERN could contribute to solve a serious Public Health problem, showing that many years of public investments in fundamental physics research from its member states, can, one day, give also important contributions to everyday's life.
- The potential revenues from a Mo-99 worldwide market in excess of 300 M€ can significantly contribute to future CERN budgets and programs.
- The industry cannot invest in such a facility alone but needs public support, as it has always been the case until now with the use of research reactors. A country has difficulties in making the effort alone to give such support (Canada has given up). CERN is an International Organization and can solve an "international" problem using "international" funds from their member states, which are all suffering the world supply crisis and are being asked by the medical community to contribute to solve the problem.

4 Accelerator vs. Reactor production

Accelerator production of Mo-99 presents numerous advantages:

- The production cycle is based on machines whose safety and public acceptance is not an issue.
- The production capacity is potentially higher: only one accelerator could cover more than the world demand of Mo-99. This is not currently possible with reactors.
- The time needed to build a new accelerator can reasonably be 5 years, which is unrealistic for a nuclear reactor. Most of current reactor Mo-99 productions could be dismissed in 5 years from now due to the aging of the installations.
- The cost of an accelerator would be lower than the one of a dedicated reactor. The decommissioning of a particle accelerator is also extremely less expensive than the one of a nuclear reactor.
- The process starting from Natural Enriched Mo-98 is economic, non proliferative, safe and clean: only Mo-99 is produced from an accelerator, while in a reactor Mo-99 represents only 6% of all the Fission Fragments created, which have to be reprocessed in dedicated nuclear facilities. Also the spent core of a nuclear reactor needs expensive reprocessing.
- Operating cost of an accelerator should also be lower, as much less staff and safety-related issues are involved.

5 Conclusions and next steps

Particle accelerators for the production of Molibdenum-99 present many advantages in terms of safety, cost, time to market and environmental and proliferation issues. Only one machine based at CERN and built with a joint international effort could potentially serve the world market and solve a public health problem at global level.

A dedicated team including CERN and AAA staff could prepare a project to assess the cost and timetable to build such a machine. The project's business model could be built on the following driving ideas:

- CERN would invest in the machine and operate it with its staff. The machine would include an ARC target with irradiating channels.
- Based on a call for tender, a consortium of industries could provide the targets to be irradiated in the facility, build and operate a reprocessing unit in CERN to produce purified Mo-99 for all companies producing Tc Generators. The purified Mo-99 would be sold to companies belonging or not to the consortium. The consortium would take care of transport and commercialisation.
- CERN would be paid by the consortium with a fraction of total sales proportional to the respective investments and running costs.
- All companies producing Tc Generators could buy Mo-99 from the consortium, with priority to companies from CERN member states or from other countries that could financially support the project.

While preparing the project, the medical community and AIPES should alert CERN member states governments and other stakeholders of the importance of such a project.

On the basis of the final project, CERN council members should ask their governments a special budget to allocate to this project. Other countries could join the effort to ensure priority in the supply.

6 References

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