

# Evaluation of specific activity and stable impurities in $^{225}\text{Ac}$ derived from ISAC and $^{229}\text{Th}$ decay.

## Introduction

Targeted Alpha Therapy (TAT) is a promising method for the treatment of cancer, due to the high Linear Energy Transfer (LET) of alpha particles resulting in a short range and dense ionization tracks in tissue.  $^{225}\text{Ac}$  (half-life 9.92 d) in particular was identified as one of the most favorable candidates for TAT due to its half-life, multiple alpha decays and favourable chelation chemistry. [1,2] To validate its potential, various studies have demonstrated the effectiveness of  $^{225}\text{Ac}$  treatments of metastatic and late-stage cancers. [1-3] The current supply of  $^{225}\text{Ac}$  for clinical studies has mainly come from  $^{229}\text{Th}$  generators obtained from  $^{233}\text{U}$ . The available supply from these sources, however, is not enough to support large-scale clinical studies, limiting the development of  $^{225}\text{Ac}$ -based radiopharmaceuticals.

## Methods

The Life Sciences group at TRIUMF works in collaboration with Canadian Nuclear Laboratories (CNL) to establish and test various methods of production of  $^{225}\text{Ac}$ . This includes production using the ISAC facility, spallation reaction on thorium, and decay of  $^{229}\text{Th}$  (provided by CNL). A comparison study was performed using ISAC-produced and CNL-produced  $^{225}\text{Ac}$  to compare the specific activity and presence of stable contaminants that may affect radiolabeling with chosen chelators. The aim of this study was to establish the quality and applicability of  $^{229}\text{Th}$ -generated  $^{225}\text{Ra}/^{225}\text{Ac}$  from CNL to enable future use of material in important chelation studies with novel ligands. If high purity and high specific activity  $^{225}\text{Ac}$  can be readily available through the collaboration with CNL, TRIUMF has the opportunity to make significant contributions to the chelation chemistry and in vivo use of  $^{225}\text{Ac}$ .

## Experimental

The comparison study was designed to replicate a concentration dependence experiment, where the radiolabeling of 2-[4,7,10-tris(carboxymethyl)-1,4,7,10-tetrazacyclododec-1-yl]acetic acid (DOTA) and  $N,N'$ -bis[(6-carboxy-2-pyridyl)methyl]-4,13-diaza-18-crown-6 (macropa) with various sources of  $^{225}\text{Ac}$  (ISAC and CNL) were tested. [4] Results of this study lead to changes in the separation procedure of  $^{225}\text{Ra}/^{225}\text{Ac}$  from  $^{229}\text{Th}$  at CNL. The collaboration continues to work to optimize the purification process and work toward using the obtained  $^{225}\text{Ac}$  with higher specific activity for chelation studies that will translate to further in vitro and in vivo testing.

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## References

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## Email Address

mynericj@mcmaster.ca

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**Primary author:** Ms MYNERICH, Jenasee (TRIUMF)

**Co-authors:** Mr ROBERTSON, Andrew (TRIUMF); Dr RAMOGIDA, Caterina (TRIUMF); Mr SAEKHEIE, Meelad (TRIUMF); Dr CAUSEY, Patrick (Canadian Nuclear Laboratories); Dr SCHAFFER, Paul (TRIUMF); Dr PERRON, Randy (Canadian Nuclear Laboratories); Dr RADCHENKO, Valery (TRIUMF); Ms BROWN, Victoria (TRIUMF)

**Presenter:** Ms MYNERICH, Jenasee (TRIUMF)