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AUTOMATED RADIOCHEMISTRY REVIEW FOR NUCLEAR APPLICATIONS

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Automated Radiochemistry Review for Nuclear Applications

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ABSTRACT

Chemical separation of target radionuclides from interferences is a key part of radioanalytical procedures to ensure accurate measurement. Over the last 30 years, automation of radiochemical separation has been pursued because of potential advantages over manual separation, including reduced worker exposure to radioactivity, improved reliability and safety, shorter analysis times, higher throughput, and improved reproducibility. Automation is still a relatively new approach for radiochemical separations, with limited literature reporting on its use compared to more common bench separations.

NPL have recently acquired automated radiochemical separation, and as part of this have undertaken a review of the literature, from the first published work in 1994 to the present day to identify patterns in automated separation with regards to the radionuclides of interest and application area (e.g. nuclear medicine, decommissioning, forensics).

Of the application areas, environmental radioactivity remained a consistent area of interest, with nuclear safeguards, radioecology, and tracer studies having fewer publications. Since the latest review of automated radiochemistry published in 2020, there has been an increase in the number of applications for medical radionuclides, with ^{68}Ga and ^{89}Zr frequently studied. In the areas of emergency preparedness and nuclear waste management, ^{90}Sr is the most frequently studied radionuclide.

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INTRODUCTION

Chemical separation of radionuclides from interferences prior to measurement are a critical part of radioanalytical procedures. There are a number of techniques that have been applied to this, including precipitation, solvent extraction and chromatography. Over the last 30 years, extraction chromatography has become the gold standard for radiochemical separations to deliver high yield, high purity radionuclides in a range of applications.

Extraction chromatography is a technique developed in the early 1990's that combines the selectivity of liquid-liquid extraction with the straightforward operation of volume chromatography. Extraction chromatography has increasingly grown in popularity for radiochemical separations due to its radionuclide-specific separation capability and the diversity of resins available for different applications [1-2]. Separations were initially carried out using gravity, with flow rates of <1 mL min^{-1}. This was improved to several mL min^{-1} using vacuum boxes however, depending on the application, this work can require separation times of several hours or more, with the operator having to perform manual changeover of reagents and collection of separation fractions.

Development of automated radiochemistry focuses on reducing operator time through automatic changeover of reagents during the separation and collection of all separation fractions. This technique also aims to improve the reproducibility of flow rates through the extraction chromatography column. This development was initially seen through the development of flow injection analysis (FIA) and sequential injection analysis (SIA) systems. A review by O'Hara *et al.* explained FIA and SIA instrumentation and their applications for different radionuclide separations, including ^{90}Sr and ^{99}Tc, primarily for environmental monitoring and nuclear decommissioning applications [3].

Automated radiochemistry has also led to the development of commercial instruments such as the Automated System for Radionuclide Separation (ASRS) and the Hidex Q-ARE 50 (Hidex, Finland) [4-5]. Briefly, these instruments consist of a series of tubing connections, valves and pumps that automatically condition the column, load the sample, and deliver the load and elution fractions. Each fraction is automatically collected, with the pumps enabling careful control of the flow rate at each stage. A range of column sizes can be accommodated depending on the application and it is also possible to do tandem (multiple) column separations. An example of the layout of the HIDEX Q-ARE 50 is shown in Figure 1.

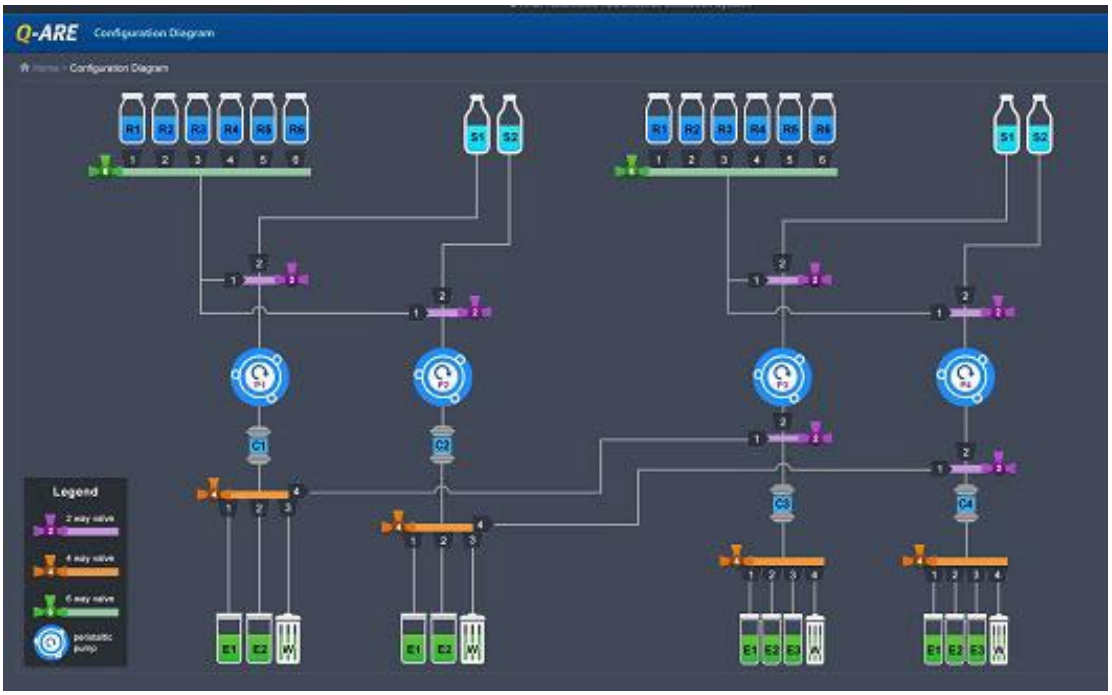

Figure 1: Diagram of Hidex Q-ARE 50 automated separator system including tubing, valve systems, peristatic pumps, and column positions.

Automated radiochemistry allows operators to easily control and test flow rates to optimise the desired separation efficiencies (versus vacuum box method) whilst improving time efficiency of the actual separation. A necessary consideration in automated radiochemistry is to account for the higher dead volume compared to vacuum box methods due to the tubing that the solution needs to pass through. Successfully accounting for these dead volumes and applying to both elutions and line purges should allow for similar performance between automated radiochemistry separators and vacuum boxes.

NPL have invested in automated radiochemistry (a Hidex Q-ARE 50). The main application areas of interest for this instrument are:

- High volume separations to remove the manual addition of high volumes of reagents and collection of fractions from the column:
    - ^{226}Ra separation for measurement in drinking water to comply with drinking water regulations. This builds on work at NPL utilising vacuum box separation and TK100 extraction chromatography resin [6].
    - Uranium/Thorium separation for provision of high yield, high purity ^{232}U as part of a routine Measurement Service [7].
- High precision separations where the behaviour of radionuclides and interferences on the column are very similar, necessitating precise control of reagents and flow rates:
    - Radiolanthanides- the first of multiple applications linked to medical radionuclide production is separation of ^{155}Tb from pseudo-isobaric ^{139}Ce^{16}O. This builds on work utilising a Triskem Ln-resin column and a peristaltic pump with manual changing of reagents and fractions collected [8].

METHODOLOGY

As part of NPLs investment in automated radiochemistry, a literature review was conducted to understand the specific use cases regarding radionuclides and application areas of interest. This was supported by a review of current and prospective users of automated radiochemistry, with an aim of developing a technical working group or similar in the radioanalytical community.

An extensive review of automated radiochemistry was undertaken by J. Qiao in 2020 [9], covering various application areas and radionuclides from 1994 to 2018. The results from this are included in the plots and analysis, alongside a further literature review focused on publications between late 2018 and 2024. The application areas chosen for this review were selected based on the review by J. Qiao, who identified six key areas that use automated radiochemical separations:

- **Environmental radioactivity monitoring-** recording human exposure to radiation by measuring both the general environment and areas surrounding nuclear installations for natural (e.g. ^{210}Po, ^{210}Pb, ^{222}Rn, ^{226,228}Ra, ^{232}Th, ^{236}U) and artificial (e.g. ^{3}H, ^{14}C, ^{89}Sr, ^{90}Sr, ^{99}Tc, ^{237,239}Np, Pu isotopes, ^{241}Am) radionuclides [9].
- **Medical isotopes-** the production of short-lived radioisotopes (e.g. ^{18}F, ^{64}Cu, ^{68}Ga, ^{85}Sr, ^{89}Zr, ^{90}Y, ^{99m,99}Tc, ^{131}I, ^{188}Re, ^{213}Bi) for cancer diagnosis and treatment [10].
- **Nuclear emergency preparedness-** involves measuring radionuclides that would often need to be measured in emergency situations (e.g. ^{89}Sr, ^{90}Sr, ^{99}Tc, ^{137}Cs, ^{237,239}Np, Pu isotopes, ^{241}Am) [10].
- **Nuclear safeguards-** secure reprocessing and recycling of spent nuclear fuel to prevent the illicit development of nuclear weapons (^{236,238}U, ^{237}Np, Pu isotopes) [11].
- **Nuclear waste management-** nuclear decommissioning and operational materials (e.g. concrete, graphite, steel, ion exchange resin, nuclear reactor coolant) for multiple radionuclides (e.g. ^{3}H, ^{14}C, ^{36}Cl, ^{41}Ca, ^{55}Fe, ^{63}Ni, ^{90}Sr, ^{99}Tc, ^{230}Th, ^{233}U, ^{234}Th, Pu isotopes, ^{241}Am, $^{242,243+244}$Cm) [9].
- **Radioecology and tracer studies-** using radionuclides as tracers of environmental processes, including aerosol and transportation of air masses (e.g. ^{7}B, ^{10}Be, ^{22}Na), soil erosion (e.g. ^{239,240}Pu), sedimentation and geochronology (e.g. ^{137}Cs, ^{210}Pb, ^{237}Np), marine ecosystems (e.g. ^{99}Tc, ^{236}U), and climate change [12].

Results are shown for application area and radionuclides of interest. A full set of plots summarising the outcomes of the literature review are given in Appendices A, B, and C.

RESULTS

APPLICATION AREAS

Figure 2 summarises the application areas where automated radiochemistry has been used.

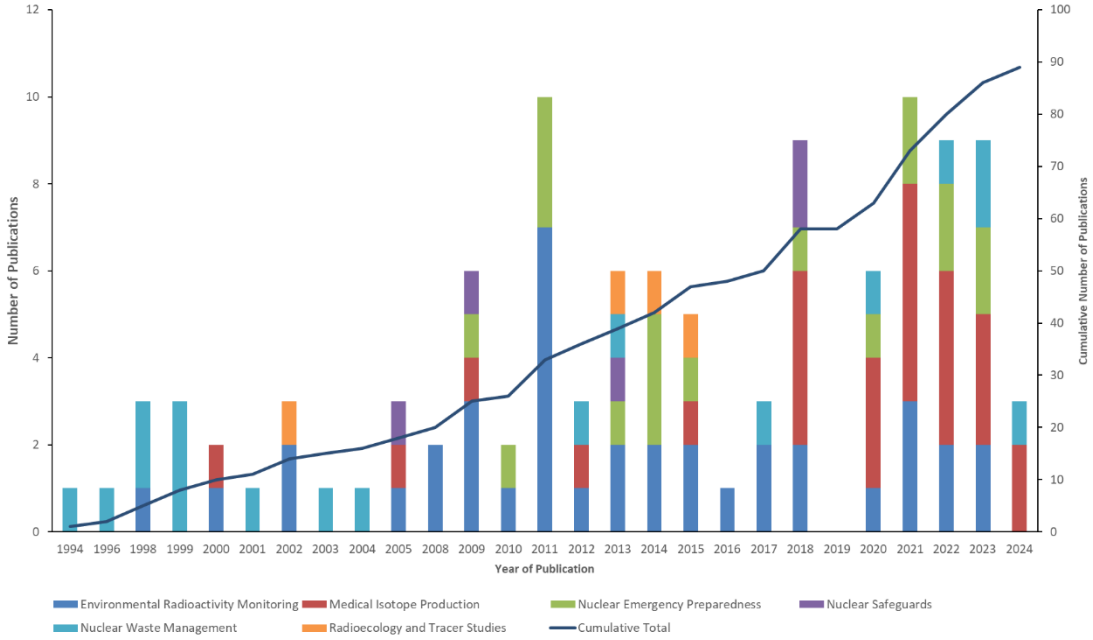

Figure 2: Relationship between application area and the number of publications per year between 1994 and 2024.

- **Environmental radioactivity monitoring** is continually reported on between 1994 and 2024, with no significant change in the number of publications since the 2020 review paper [9, 12-21].
- **Medical isotope production** publications have increased significantly (2018-2024) since the last review on automated separation, averaging three publications a year [9, 22-41].
- **Nuclear emergency preparedness** has been a continual area of interest since 2009, averaging one publication a year since the last review paper on automated separation (2018-2024) [9, 18-20, 42-46].
- **Nuclear safeguards** remain an application area of minimal interest, with only five total publications between 1994 and 2024, with no significant change since the 2020 review on automated separation [9, 21, 47].
- **Nuclear waste management** was highly reported on between 1994 and 2004, averaging one publication a year. After a period of no reporting on this application area, the number of publications per year has increased back to one per year (2020-2024) [9, 19-20, 48-49].
- **Radioecology and tracer studies** remain an application area of minimal interest, with only four total publications between 1994 and 2024, with no significant change since the last review on automated separation [9].
- **The cumulative total** has significantly increased since the 2020 review on automated separation from 51 to 89 publications, with a change in the average increase in the number of publications from 2.4 to 5.9 [9, 12-49].

RADIONUCLIDES OF INTEREST

Figures 3 and 4 show the link between the number of publications for each radionuclide.

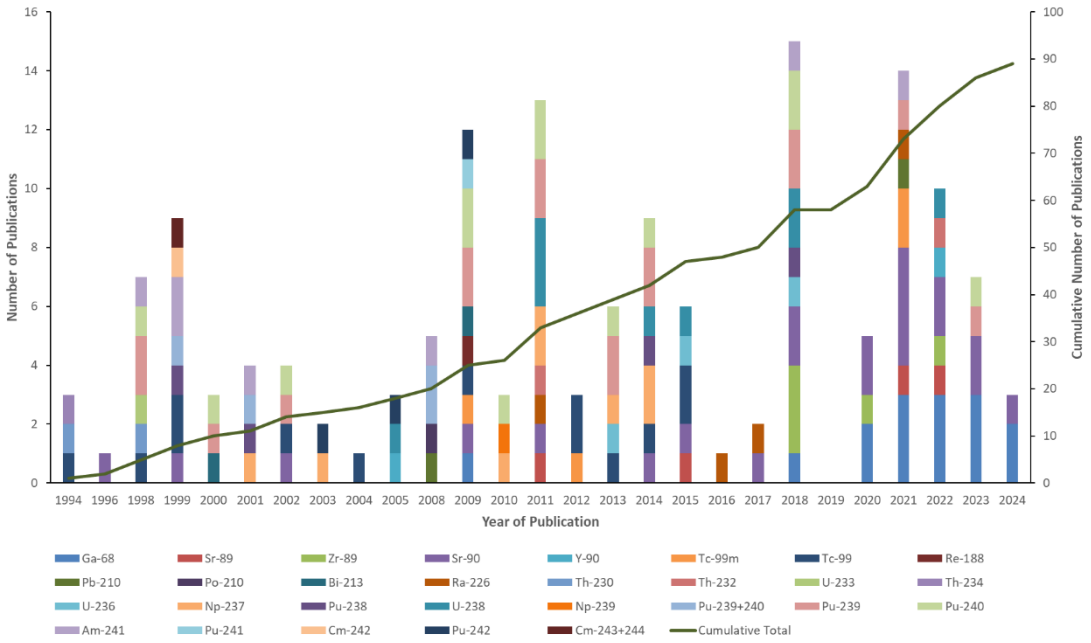

Figure 3: Graph showing the radionuclide and the number of publications per year between 1994 and 2024.

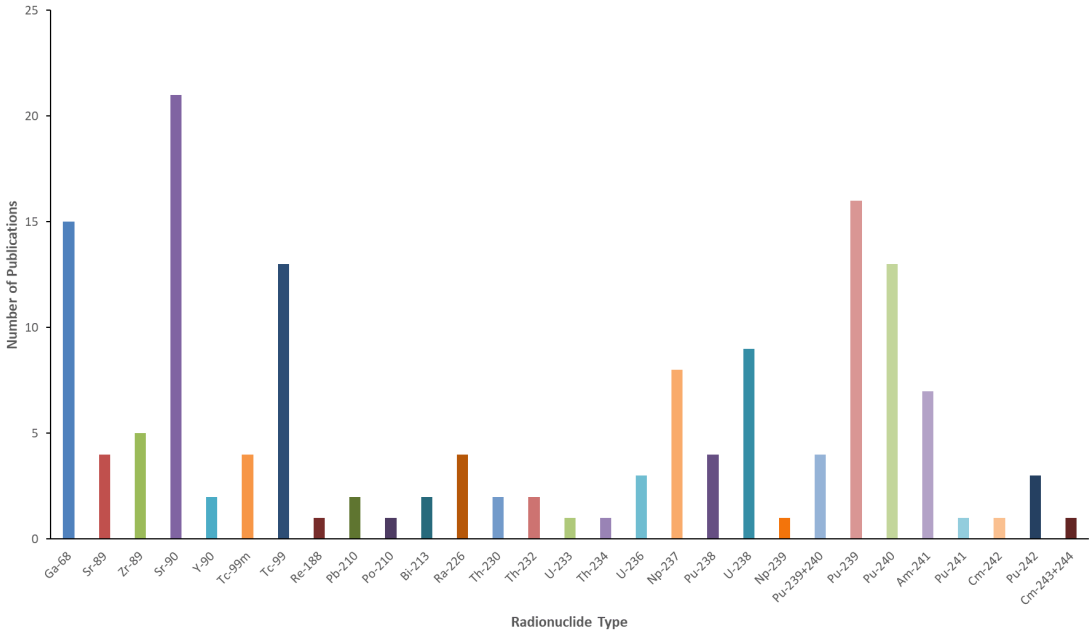

Figure 4: Graph showing the radionuclide and total number of publications between 1994 and 2024.

- **^{68}Ga** is a radionuclide of increasing interest, going from one publication in the most recent automated separation review to two publications per year, on average, between 2018 and 2024 [9, 22, 25-26, 28-30, 31-33, 37-41].
- **^{89}Zr** is a radionuclide of increasing interest, going from one publication in the most recent automated separation review to five publications between 2018 and 2024 [9, 23-24, 27, 36].

- **^{90}Sr** is a radionuclide of increasing interest, going from eight publications in the most recent automated separation review to two publications per year, on average, between 2018 and 2024 [9, 12-14, 18-20, 42-46, 48-49].
- **^{89}Sr, ^{90}Y, ^{99m}Tc, ^{210}Pb, and ^{232}Th** are reported on an equal amount before and after the most recent review on automated separation [9, 13, 16, 31-33, 45].
- **^{226}Ra, ^{236}U, ^{238,239,240}Pu, ^{238}U, and ^{241}Am** are reported on less since the most recent review on automated separation [9, 14-17, 21, 42, 47].
- **^{99}Tc, ^{188}Re, ^{210}Po, ^{213}Bi, ^{230,234}Th, ^{233}U, ^{237,239}Np, $^{239+240,241,242}$Pu, and $^{242,243+244}$Cm** have not been reported on since the most recent review on automated separation [9].

TRENDS

Figure 5 shows the application area, radionuclide of interest and total number of studies.

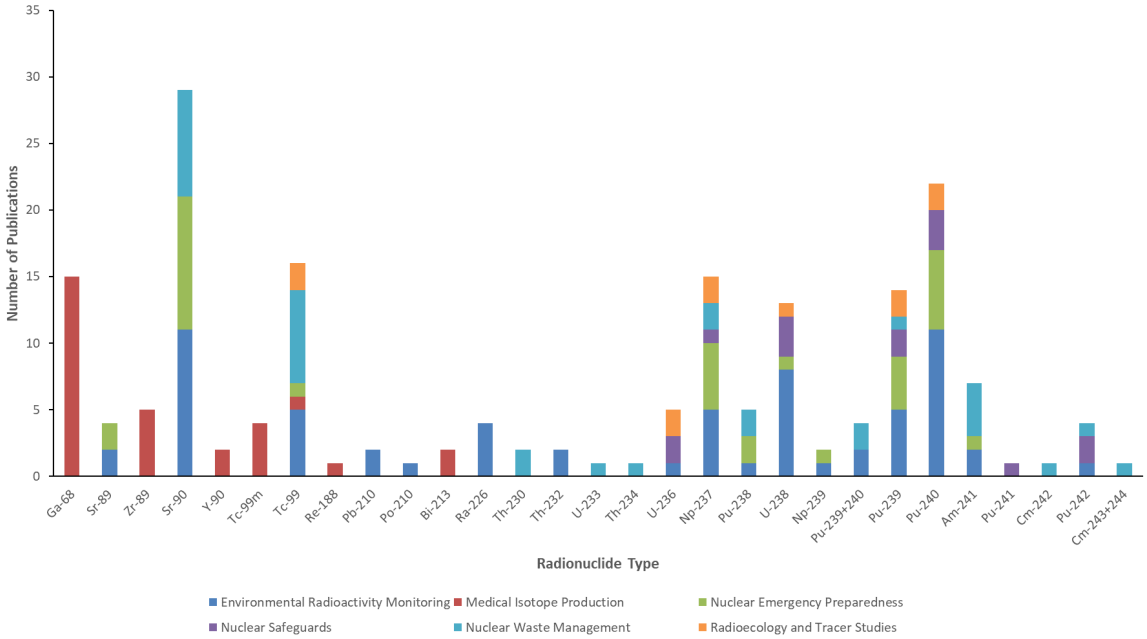

Figure 5: Graph showing the relationship between radionuclide type and the number of publications in each application area per year between 1994 and 2024.

- **There is a significant increase in interest for medical isotope production** since the most recent review on automated separation. This is reflected in the increase in the number of publications for **^{68}Ga and ^{89}Zr**, as well as the continual coverage of **^{90}Y and ^{99m}Tc** in literature [9, 14-21].
- **There is a large increase in interest for nuclear emergency preparedness** since the most recent review on automated separation. This is reflected in the increase in the number of publications for **^{90}Sr**, as well as the continual coverage of **^{89}Sr** in literature [9, 22-41].
- **There is some increasing interest for nuclear waste management** since the most recent review on automated separation. This is reflected in the increase in the number of publications for **^{90}Sr** [9, 18-20, 42-46].
- **There is persistent interest in environmental radioactivity monitoring** both before and after the most recent review on automated separation. This is reflected in the continual coverage of **^{89}Sr, ^{90}Sr, ^{210}Pb, and ^{232}Th** in literature [9, 21, 47].

- **There is minimal interest in nuclear safeguards** both before and after the most recent review on automated separation. This is reflected in the decrease in the number of publications for **^{236}U, ^{237}Np, ^{238}U, and ^{239,240,241,242}Pu** [9, 19-20, 48-50].
- **There is minimal interest in radioecology and tracer studies** both before and after the most recent review on automated separation. This is reflected in the decrease in the number of publications for **^{99}Tc, $^{236.238}$U, ^{237}Np, and ^{239,240}Pu** [9].

CONCLUSIONS AND FUTURE WORK

Automated radiochemistry continues to be considered as a technique of interest for multiple radionuclides and application areas. This review shows that improved separation efficiency of medical radionuclides is an area of growing interest, in line with the drive to produce the next generation of medical radionuclides for improved cancer treatment. Several papers outside of this review focused on automated radiolabelling of medical radionuclides post-separation, including ^{225}Ac, ^{161}Tb and ^{177}Lu [43-46]. Terbium isotopes of interest to cancer diagnosis and treatment (^{149}Tb, ^{152}Tb, ^{155}Tb and ^{161}Tb) are a priority for automated separation at NPL.

Following contact with the Hidex manufacturer, several other labs using the Q-ARE system for automated radiochemical separation have been identified. NPL will aim to set up a technical working group to discuss progress and any issues, working closely with the manufacturer and presenting these at relevant working groups and conferences.

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APPENDICES

APPENDIX A: APPLICATION AREAS

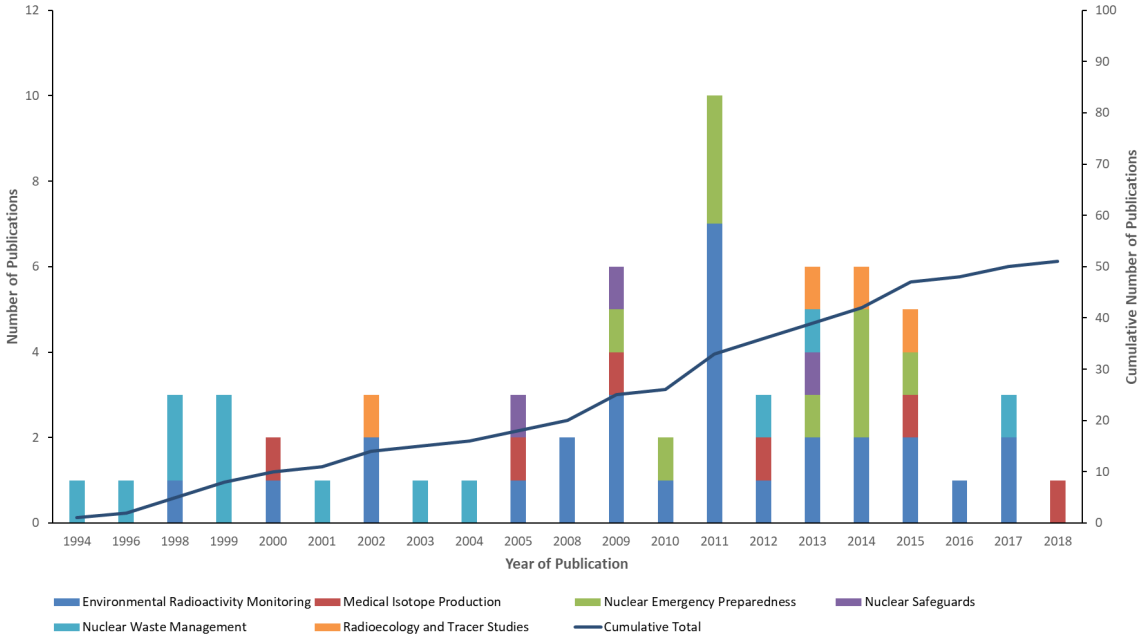

Figure A1: Graph showing the relationship between application area and the number of publications that year between 1994 and 2018.

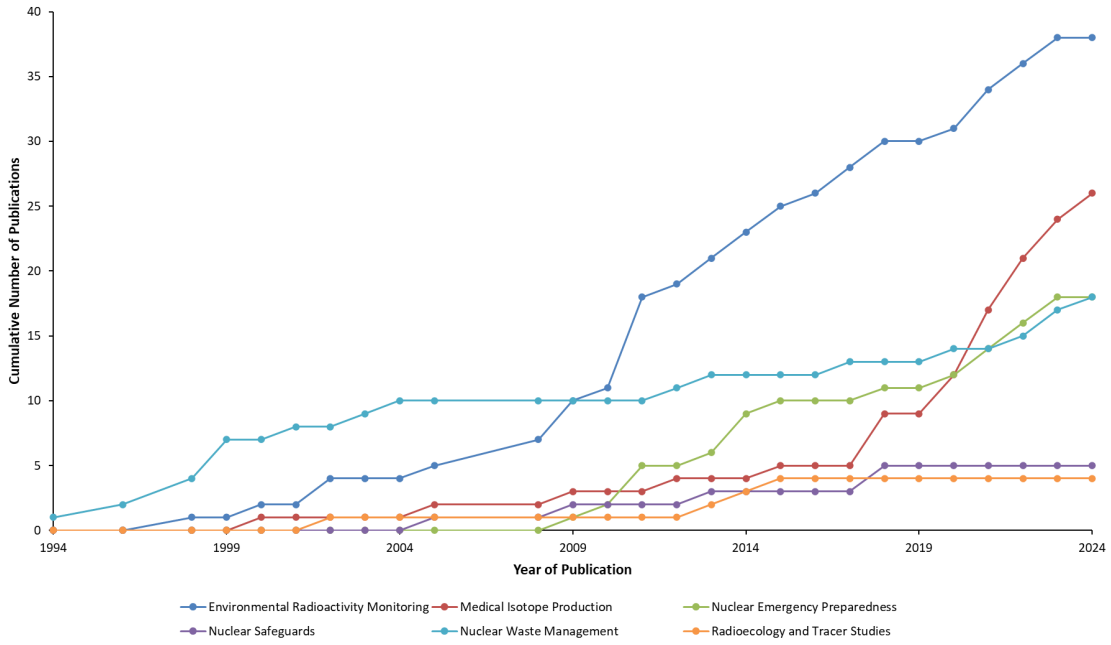

Figure A2: Graph showing the relationship between application area and the cumulative number of publications between 1994 and 2024.

APPENDIX B: RADIONUCLIDE TYPE

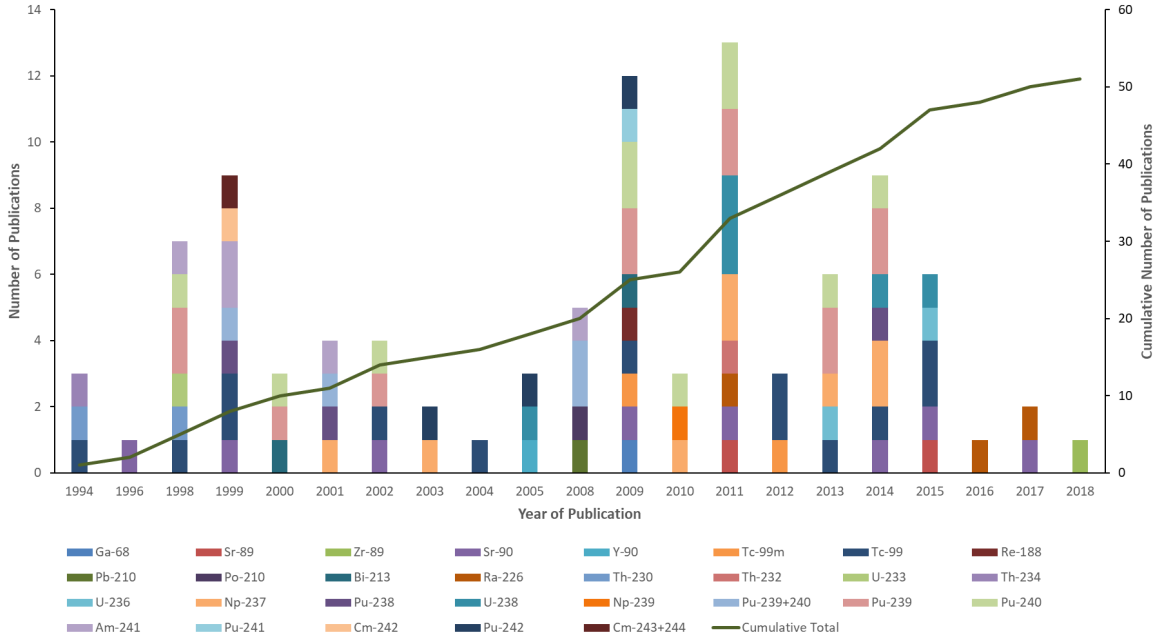

Figure B1: Graph showing the relationship between radionuclide type and the number of publications that year between 1994 and 2018.

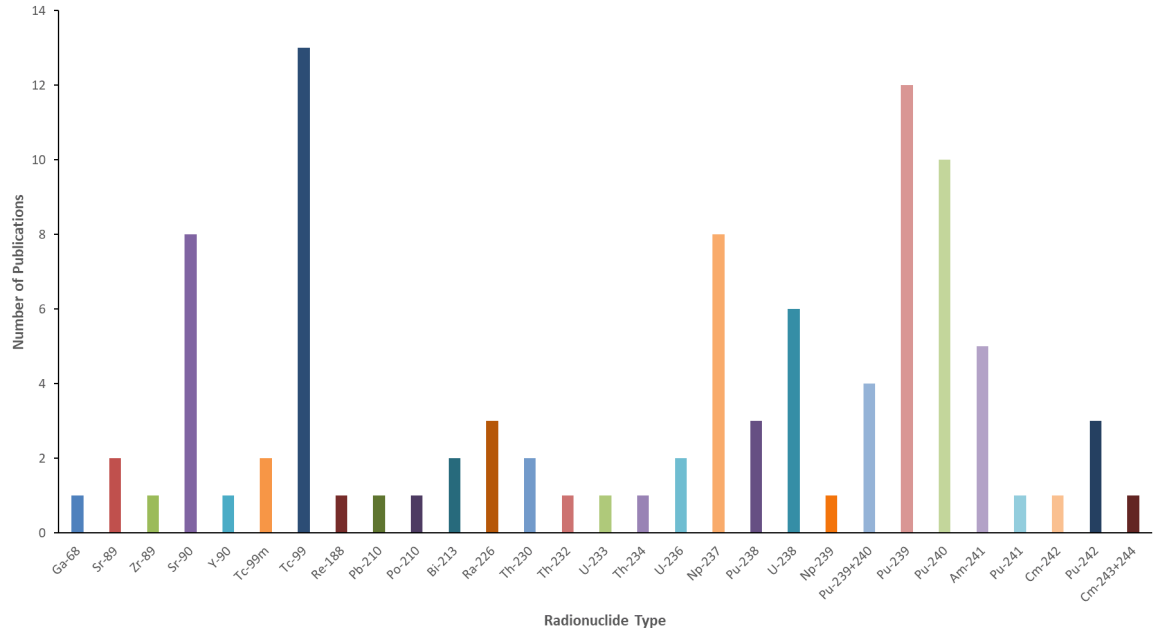

Figure B2: Graph showing the relationship between radionuclide type and the total number of publications between 1994 and 2018.

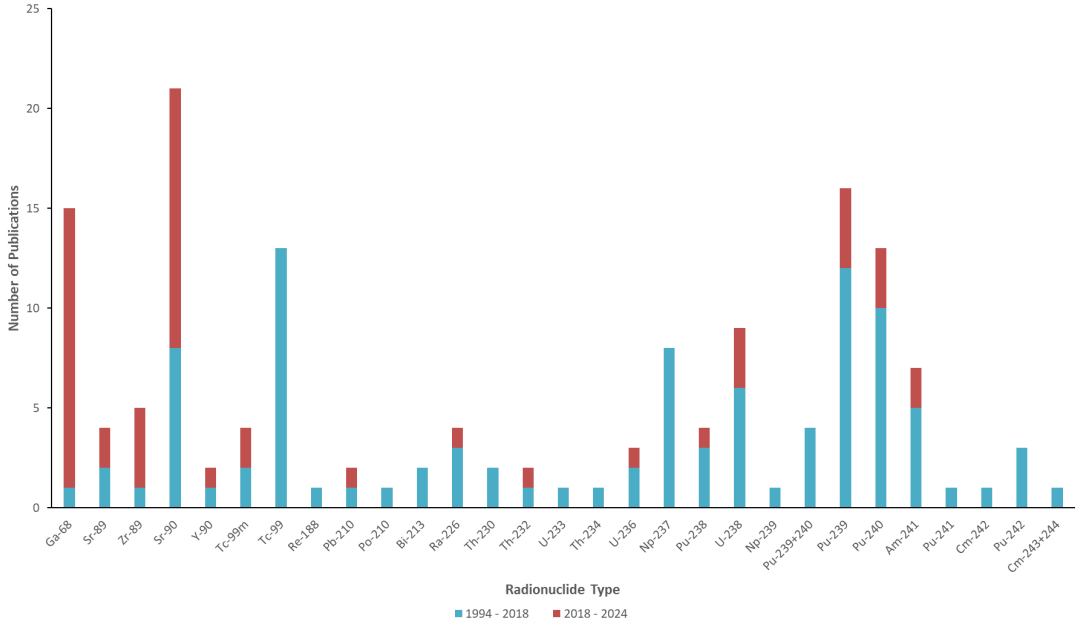

Figure B3: Graph comparing the number of publications for each radionuclide in the periods 1994-2018 (blue) and 2018-2024 (red).

APPENDIX C: TRENDS

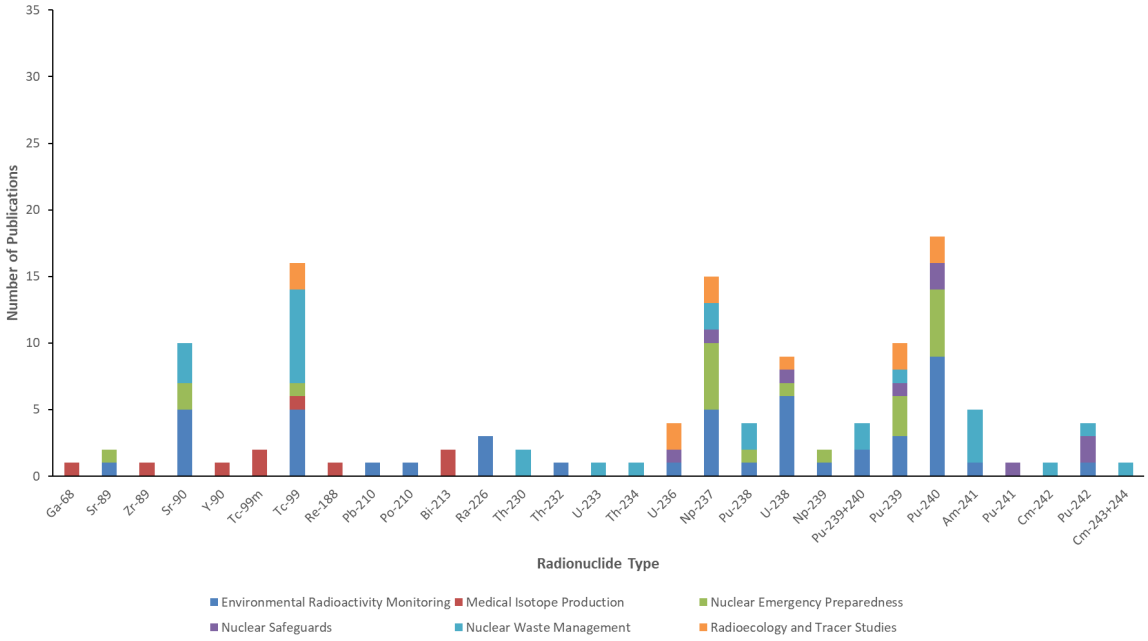

Figure C1: Graph showing the relationship between radionuclide type and the number of publications in each application area per year between 1994 and 2018.