



Article

Production of Diagnostic and Therapeutic Radionuclides with Uranium and Thorium Molten Salt Fuel Cycles

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Abstract

Targeted radionuclide therapy (TRT) is an innovative and flexible approach for treating various forms of cancer, enabling selective delivery of cytotoxic radiation to cancerous cells while minimizing damage to healthy tissue. Although TRT has proven to be highly promising for treating even advanced-stage cancers, ensuring a stable supply of the radionuclides essential for its use remains a significant challenge today. This is also true for radionuclides utilized in nuclear imaging procedures, such as Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT). Liquid-fueled molten salt reactors (MSRs) are promising for producing large quantities of highly desirable radionuclides for imaging and therapy, offering the ability to recover these radionuclides online without the need for interruptions to power production. In this study, the production of numerous beta- and alpha-emitting radionuclides for use in TRT and diagnostic procedures was studied in two small, geometrically identical, thermal spectrum MSR models—one operating with LEU fuel, and the other with a mixture of HALEU and thorium—using a novel MSR refueling and waste management concept. For therapeutic alpha emitters such as ²²⁵Ac and ²¹³Bi, the impact of thorium utilization on production yields was significant, facilitating greatly increased production.

Keywords: molten salt reactor; SCALE; thorium; targeted radionuclide therapy; isotope production; actinium-225

1. Introduction

1.1. Targeted Radionuclide Therapy as a New Paradigm in Nuclear Medicine

Cancer remains the second leading cause of death in the United States, and is reported as the leading cause of death for individuals under the age of 85 years [1]. The American Cancer Society (ACS) predicts that, in the year 2025, 2,041,910 new cancer cases will arise in the United States, leading to 618,120 deaths [1]. Although a number of anticancer agents and cytotoxic technologies are currently available to patients and are clinically utilized, many of these are inherently limited by their lack of specificity [2]. Most conventional treatment approaches, such as chemotherapy and traditional external beam radiotherapy, focus on causing death in populations of cells which exhibit uncontrolled growth [2]. As a result, rapidly dividing healthy cells, such as those within the gut, may be destroyed alongside malignant cells [2,3]. This poses significant challenges in treating human cancers, often requiring the dosages of traditional anticancer drugs to be limited and resulting in impaired



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quality of life in treated patients [4]. As explained by Chen et al. (2007), for chemotherapeutic agents, oxidative stress, either directly or indirectly caused within noncancerous cells by these agents, is a primary underlying mechanism responsible for the toxicity of anticancer drugs in healthy tissues, including the heart and brain [4]. This collateral damage to healthy, noncancerous tissue by conventional anticancer agents is associated with severe negative side-effects in treated patients, both short- and long-term, with the latter being encountered later on during a patient's lifetime following the completion of their treatment [4,5]. Accelerated aging is one example of a significant, long-term adverse effect which may be caused by traditional anti-cancer drugs, most notably chemotherapeutic agents, and is especially concerning for pediatric cancer patients treated with these methods [5–8]. These complications caused by treatment nonspecificity make managing late-stage, metastatic cancers with traditional anti-cancer agents particularly challenging, thus warranting increased research and development into alternative treatment approaches which can effectively destroy cancerous cells while minimizing damage to healthy tissues.

An alternative class of cancer therapies, known as “targeted therapies,” seek to cause damage to cancerous cells only while minimizing damage to healthy ones [2]. Targeted radionuclide therapy (TRT) is an example of one such treatment approach which has been studied extensively in recent years, showing great promise in treating a variety of cancers, including those which are resistant to other forms of treatment [9]. In TRT, a radionuclide with favorable nuclear decay properties for therapy (e.g., alpha, beta, or Auger electron emitters) is attached to a cancer cell-specific molecule which naturally seeks out and binds to antigens expressed on the surface of tumor cells [10,11]. The same principle approach may be used for nuclear diagnostic procedures like Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT), where a radionuclide suitable for imaging (a positron or gamma emitter, respectively) is attached to a targeting agent, enabling it to be sent to sites where cancerous cells are present and allowing them to be imaged. Suitable targeting agents come in a variety of forms, and can include monoclonal antibodies [12–15], peptides and proteins [16–19], small molecules [20], and nanoparticles [21–24].

While organic radionuclides, such as the nuclear imaging isotopes ^{11}C and ^{15}O , are typically conjugated to a targeting agent through a covalent bond, metallic radionuclides like ^{225}Ac and ^{213}Bi are conjugated via the use of a chelator, which binds to the metal ion and allows it to be attached to the targeting agent [25]. The use of targeting agents which selectively bind to antigens present on cancerous cells facilitates the targeting of these cells directly rather than rapidly dividing cells in general. In the case of TRT, this allows for the delivery of cytotoxic radiation directly to tumor sites while largely sparing noncancerous cells from damage, thus minimizing the adverse effects caused by collateral damage to healthy tissue.

A number of beta-emitting radionuclides are currently used clinically in human patients for TRT, with a few notable examples including ^{177}Lu , ^{90}Y , and ^{131}I . Two ^{177}Lu -based radiopharmaceuticals, ^{177}Lu -DOTA-TATE (Lutathera[®]) and ^{177}Lu -PSMA-617 (Pluvicto[™]) received approval from the U.S. Food and Drug Administration (FDA) in January 2018 and March 2022, respectively, for use in human cancer patients [26,27]. ^{177}Lu -DOTA-TATE, as a ^{177}Lu -labeled somatostatin analogue, is used worldwide for TRT of somatostatin receptor (SSTR)-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs) in adult human patients [28]. On 23 April 2024, the FDA approved ^{177}Lu -DOTA-TATE (Lutathera[®]) for use in pediatric patients 12 years of age and older presenting with GEP-NETS, further extending the impact of TRT with ^{177}Lu to treating pediatric in addition to adult cancers [27]. ^{177}Lu -PSMA-617, on the other hand, is the first radiopharmaceutical to receive approval from the FDA for treatment of prostate cancer, combining the urea-based small molecule

PSMA-617 with the cytotoxic payload, ^{177}Lu [26]. PSMA-617 exhibits a high affinity for PSMA, which is commonly overexpressed on prostate adenocarcinomas though shows only limited expression in benign tissues, making PSMA an ideal target for TRT of prostate cancer [29]. ^{90}Y -ibritumomab tiuxetan (Zevalin[®]) and ^{131}I -tositumomab (Bexxar[®]) are two additional TRT radiopharmaceuticals which are approved by the FDA for use in human cancer patients, with both being used in the treatment of non-Hodgkin's lymphoma [30,31].

Leveraging upon the success of TRT using beta-emitting radionuclides, recent research has highlighted the significant potential of alpha-emitters in providing safe, efficacious, and minimally invasive treatments for a variety of cancer types. With their high linear energy transfer (LET) and short range in tissue, equivalent to only a few cell diameters [32], alpha particles enable selective tumor targeting, with the cytotoxic effects of radiation being limited to the cancerous cells and the surrounding tumor microenvironment [33]. Damage to healthy tissue is minimized, and fewer particle tracks are needed to cause cell death compared with beta particles due to the significantly higher relative biological effectiveness (RBE) of alpha versus beta radiation [33]. This RBE has been observed to be 2- to 10-fold higher for alpha particle radiation when compared with beta particles [34]. Furthermore, due to its high LET, cell damage by alpha particle radiation exhibits a strongly reduced dependency on oxygenation [34]. This is a significant advantage of TRT with alpha-emitters compared with other forms of radiotherapy, as it allows for treatment of hypoxic tumors, which are challenging to treat with other forms of radiation due to the increased radiation resistance caused by the oxygen-deprived environment [34].

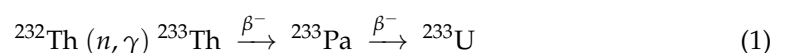
Today, only one alpha-emitting radioisotope, ^{223}Ra , has received approval from the FDA for clinical use in cancer therapy [35]. ^{223}Ra is used in the form of ^{223}Ra dichloride ($^{223}\text{RaCl}_2$) for treatment of metastatic castration-resistant prostate cancer (mCRPC) patients who present with bone metastases, and has been proven to significantly extend the lives of treated patients [36]. Although it offers a safe and effective treatment option, $^{223}\text{RaCl}_2$ is inherently limited to treating only osseous metastatic disease, thus necessitating the exploration of alternative therapeutic radiopharmaceuticals for treatment of other cancer types.

Various alpha-emitting radionuclides are highly promising for use in TRT [37]. Among these, ^{225}Ac , ^{211}At , ^{212}Bi , ^{213}Bi , ^{212}Pb , ^{223}Ra , ^{149}Tb , and ^{227}Th have been identified in the recent literature as the “hopeful eight” due to their favorable nuclear decay properties and the significant body of research available regarding their production and chemistry, positioning them as ideal candidates for continued study [37]. In particular, ^{225}Ac has been at the forefront of many recent studies, both in preclinical animal models and in-human clinical trials, for TAT. Numerous different ^{225}Ac radiopharmaceuticals have been successfully developed and investigated across clinical trials for use in treating prostate cancer, the most notable among these including ^{225}Ac -PSMA-617, ^{225}Ac -PSMA-I&T, and ^{225}Ac -J591 [38]. Highly promising results have also been observed in using ^{225}Ac -based radiopharmaceuticals for treating acute myeloid leukemia (AML) [39,40], breast cancer [41], and ovarian cancer [42]. Although ^{225}Ac has demonstrated significant promise across a number of recent studies, both preclinical and clinical, production of this critical radioisotope remains challenging and presents a significant barrier to the development of TAT [38]. For TAT to be made clinically available to patients in need in the U.S. and worldwide, efficient strategies for producing high-purity samples of ^{225}Ac and other TAT radionuclides must be established. The same is true for ensuring a stable supply of clinically utilized radionuclides for imaging (i.e., PET, SPECT) or therapy, including TRT and palliative therapies.

1.2. Molten Salt Reactors for Clean Power and Radioisotope Production

Although TRT with beta-, alpha-, or Auger electron-emitting radionuclides has been shown to be advantageous for managing advanced and late-stage cancers, ensuring a stable supply of these critical radionuclides for use in TRT, as well as positron- or gamma-emitting radionuclides for imaging procedures like PET and SPECT, remains a challenge [9,38]. Molten salt reactors (MSRs), where the nuclear fuel and coolant are both in the form of liquid molten alkali-halide salts, are advanced nuclear fission reactor designs which are highly promising for use in both clean electricity generation and the production of medical radionuclides [43]. These reactors were studied extensively during the 1960s as part of the Oak Ridge National Laboratory (ORNL) Molten Salt Reactor Program (MSRP) [44], with a landmark achievement of this effort being the development and successful operation of the Molten Salt Reactor Experiment (MSRE) [45]. The MSRE was an 8 MW_{th} demonstration reactor which operated with 33% enriched ²³⁵U dissolved within molten fluoride salts at 1200 °F, which circulated throughout a core of graphite bars [45]. By March 1968, 9000 equivalent full-power hours were achieved with the MSRE using ²³⁵U [45]. Leveraging upon this success, ²³³U was added to the fuel salt to study its performance in an operating MSR, and 2500 equivalent full-power hours were achieved with this fissile fuel [45]. The MSRE was the first reactor in the world to be fueled with ²³³U [45].

Following the success of the MSRP, research into MSRs continued at ORNL, and commercial interest in these reactor designs has increased in recent years with their selection by the Generation IV International Forum (GIF) as one of the six most promising advanced reactor designs for future development [46]. In addition to the numerous advantages offered by the use of liquid molten salt fuels, including a more highly negative fuel temperature feedback coefficient (FTC) of reactivity, these unique reactor designs also boast the ability to operate with thorium-based fuels, employing the ²³²Th/²³³U fuel cycle. With this fuel cycle, fissile ²³³U fuel is bred from fertile ²³²Th, which is incorporated into the fuel salt alongside a startup fissile material (typically ²³⁵U). Following the capture of a neutron, ²³²Th undergoes beta decay to produce ²³³Pa, which subsequently beta decays to ²³³U. This is represented by Equation (1) below [47]:



In addition to clean power production, MSRs have recently gained research attention regarding their use in the production of desirable radionuclides for use in diagnostic and therapeutic medical procedures. With MSRs, valuable radioisotopes may be extracted online without interruptions to power production, with the liquid nature of the fuel enabling the use of chemical separation procedures such as evaporation/distillation, chemical reduction, electro-deposition, and/or chemical oxidation [43]. Furthermore, the use of thorium-based fuels enables the production of neptunium-chain radionuclides, which see only limited production in a traditional uranium fuel cycle. The production of medically desirable radionuclides in liquid-fueled MSRs has previously been explored with promising results in a number of different studies, particularly with Monte Carlo modeling tools like the SCALE [48] and Serpent-2 [49] codes.

Chen et al. (2021) used SCALE TRITON to study the production of ¹³¹I and ⁹⁰Sr in a modular MSR model, specifically examining equilibrium times, yields, and cooling times for isotopic impurities [50]. This study showed significant production of both radionuclides, with high purity samples being capable of recovery in the MSR for medical use [50]. Using HF-H₂ bubbling for transfer of ¹³¹I from the fuel salt to the off-gas system, it was shown that 3.49E5 TBq of ¹³¹I could be extracted from the salt each year, with 1296 TBq being available for extraction from the off-gas system using the electric field method of

recovery [50]. Zhang et al. (2023) used the Serpent code to model the production of ^{99}Mo in an LEU-fueled MSR design based on the MSRE, with the model being benchmarked against JMCT and historical MSRE data from ORNL design reports [51]. Additional studies modeling ^{99}Mo production in MSRs have been performed with SCALE TRITON [52], with Cornejo et al. (2021) concluding that MSRs can supply ^{99}Mo in quantities which far exceed global demand [53].

With their ability to employ both traditional uranium-based as well as thorium-based fuels, detailed analysis into the impact of fuel cycle choice on radionuclide production is desirable for MSRs which are to be used for this purpose. In this study, the production of both diagnostic and therapeutic radionuclides will be examined in two geometrically identical, small, 400 MW_{th} MSR models: one operating with LEU fuel, and the other with a mixture of HALEU and ^{232}Th . These MSR models both utilize a novel refueling and waste management strategy previously explored by the authors in neutronic studies using uranium and thorium fuel cycles [54–56] and which was first proposed by Wheeler and Chvala (2021) in [57]. Referred to as the “Sourdough” refueling and waste management strategy, this concept has demonstrated promise for use in liquid-fueled MSRs as a way to rapidly grow an MSR fleet and postpone the need to manage high-level waste (HLW). The prior work by the authors included modeling batch and continuous refueling with this novel refueling strategy in these MSR designs to assess its performance over extended operation, with long-term depletion being simulated with SCALE 6.3.1 TRITON. Recently, the production of diagnostic and therapeutic radionuclides was examined in these models in preliminary works by the authors of [58,59]; however, these studies were very limited in their scope, with only a small number of radionuclides being studied. Furthermore, in [58], radionuclide production was only tracked within the active fuel salt, with no consideration being given to the significant quantities of valuable radionuclides which are produced in the offgas system or are routinely removed as noble metal fission products. The present study will build upon the authors’ previous research to perform a detailed analysis of the production of 16 different diagnostic and therapeutic radionuclides using a revised modeling framework to include active tracking of radionuclides removed as gaseous or noble metal fission products. Additionally, this work provides a unique contribution to the overall study of modeling medical radionuclide production in MSRs, with it being the first detailed fuel cycle comparison study of radionuclide production using the novel Sourdough strategy.

2. Materials and Methods

In this study, an MSR model previously developed and studied by the authors in the SCALE 6.3.1 code system, EIRENE, is utilized for modeling radionuclide production during simulated depletion. EIRENE (Example Integral REactor for Nuclear Education) is a small, 400 MW_{th}, graphite moderated, thermal spectrum MSR model fueled by low enriched uranium (LEU). The fissile uranium fuel is incorporated in a FLiBe fuel salt with 63.333% LiF, 31.667% BeF₂, and 5.000% UF₄, with a nominal ^{235}U enrichment level of 2.65% [54]. The fuel salt flows upwards through the fuel channels, with these channels existing in three separate regions: Region I (R-I), Region II (R-II), and Region III (R-III), each region containing fuel channels of a specific radius. Region I contains the smallest fuel channels, each having a radius of 1.1570 cm, whereas Region II fuel channels are slightly larger, with radii of 1.2198 cm [54]. The largest fuel channels are within Region III, each one having a radius of 1.3485 cm [54]. The fuel channel design and overall geometry of EIRENE is adapted from the Integral Molten Salt Reactor (IMSR) model developed by Carter and Borrelli in [60]. EIRENE additionally features six SS316 shutdown rods positioned symmetrically within the core, a Hastelloy-N reflector, core blanket, and vessel, and an upper plenum filled with

pure helium gas. This upper plenum is positioned immediately above the outlet plenum, and exists to accommodate the growth of in-core fuel salt volume from refueling, a feature which was studied previously by the authors [54].

The EIRENE model was initially developed for the purpose of demonstrating a novel refueling and waste management concept, the “Sourdough” fuel cycle, in which fissile fuel salt is allowed to grow within the reactor core from routine refueling rather than maintaining a constant fuel salt volume. Chemically identical or compatible “refuel” salt is added to the core either continuously at a defined rate, or in batches at set time intervals [54,57]. While drainage of fuel salt from the core would typically be simulated alongside refuel additions in a typical MSR fuel cycle modeling approach, with the Sourdough fuel cycle, no drainage is implemented, with the total in-core fuel salt volume growing with each refuel salt addition [54,57]. After enough time, the total fuel salt volume will double with respect to its starting quantity, with the time at which this occurs being referred to as the “doubling time” [54,57]. With this refueling approach, the entire fuel salt volume maintains criticality throughout depletion, meaning that when doubling of the volume occurs, half of it may be removed and transferred to another reactor of identical design for use as startup fuel [54,57]. In this way, critical fuel salt is “grown” from an initial fuel “starter,” facilitating the rapid growth of an operating MSR fleet in addition to postponing the need to manage high-level waste (HLW) streams due to fuel salt simply being transferred from one reactor to another [54,57]. Further details on this fuel cycle and its applications, in addition to its implementation within EIRENE, may be found in a previous work by the authors, which examined the neutronic performance of the Sourdough fuel cycle with SCALE 6.3.1 TRITON [54]. The batch refueling procedure outlined in [54] is utilized in this present study with SCALE 6.3.1 TRITON; however, rather than simulating different refuel salt enrichment levels, only one enrichment level, 19.75%, is defined and used for refueling in this study. This enrichment level was chosen to allow for direct comparison between EIRENE and its thorium-fueled counterpart, Th-EIRENE.

Th-EIRENE is a structurally and geometrically identical model to EIRENE, with the only difference being its fuel salt. Fertile ^{232}Th is incorporated into the FLiBe fuel salt of Th-EIRENE in the form of ThF_4 , with a salt molar composition of 61.333% LiF, 30.667% BeF_2 , 1.420% UF_4 , and 6.580% ThF_4 . A nominal ^{235}U enrichment level of 19.75% is utilized for Th-EIRENE, which is significantly higher than the 2.65% defined for EIRENE to allow sufficient reactivity for breeding ^{233}U from ^{232}Th . Figure 1 includes a radial and axial side profile view of the EIRENE and Th-EIRENE models in SCALE 6.3.1, whereas Table 1 provides relevant design parameters for both models. All scripts used in developing these two models are made openly available in a public GitHub repository (Link to repository: <https://github.com/cerikam/IMSR>, accessed on 19 December 2025).

In the batch refueling simulations performed in this study, refuel salt with a ^{235}U enrichment level of 19.75% is utilized for both EIRENE and Th-EIRENE. Using the same procedure presented in [54], fresh refuel salt is added to the core every 7 days, with a new SCALE 6.3.1 TRITON model file being created after each refuel salt addition to account for growth of the total fuel salt volume. As an update to the previously utilized Python framework in [54], an executable ORIGEN script is generated for each depletion step and used to mix the burned salt with the fresh refuel salt. Execution of this script results in the generation of three isotope composition .f71 data files: one for the active fuel salt, another for the off-gas system, and one for noble metal fission products removed from the fuel salt during simulated operation. This allows for tracking of the compositions of desirable radionuclides in not only the active fuel salt, but also those which are routinely removed online.

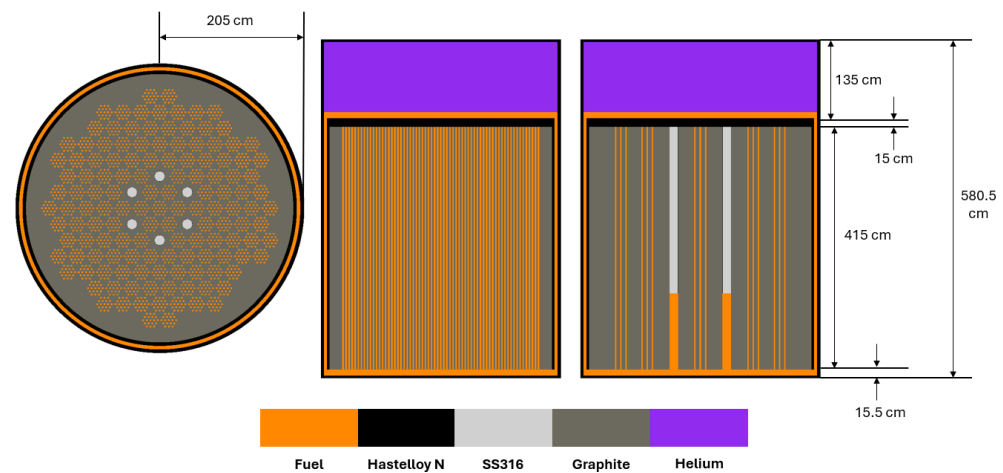


Figure 1. Radial (left), axial side (middle), and axial front (right) views of the EIRENE model in SCALE 6.3.1.

Table 1. Key parameters for the EIRENE and Th-EIRENE SCALE 6.3.1 models, BOC fuel [61].

Parameter Name	EIRENE	Th-EIRENE	Units
Fuel salt density	2.5492	2.8405	g/cm ³
Graphite density	1.8400	1.8400	g/cm ³
Control rod density	2.700	2.700	g/cm ³
Hastelloy N density	8.8900	8.8900	g/cm ³
Helium gas density	0.00017850	0.00017850	g/cm ³
UF ₄ in fuel salt	5.0	1.420	mol%
ThF ₄ in fuel salt	0.0	6.580	mol%
Operating temperature	923.15	923.15	K
R-I fuel channel radius	1.1570	1.1570	cm
R-II fuel channel radius	1.2198	1.2198	cm
R-III fuel channel radius	1.3485	1.3485	cm
Inner core radius	190.00	190.00	cm
Height of reactor vessel	580.50	580.50	cm
²³⁵ U enrichment level	2.65	19.75	%

An overview of the Python-based simulation framework utilized in this work is provided in Figure 2. This flowchart is adapted from the one previously presented in [54], though it has been revised to include implementation of ORIGEN for salt mixing and nuclide inventory tracking. For modeling batch refueling in both EIRENE and Th-EIRENE, the simulation begins with initialization of the BOC model. TRITON is then executed for the defined depletion step length of 7 days, and the burned fuel salt vector is obtained from the active fuel salt .f71 data file. Python is then used to write fresh refuel salt vectors for various refuel salt volumes (5 in the current implementation) ranging from low to high to be mixed with the burned salt. A new KENO-VI input file is written and executed for each of these refuel salt amounts, and the resulting reactivity data are fitted with a linear regression model to determine the critical refuel volume which yields $\rho = 0$. This critical volume is then added to the core, and the new total fuel salt volume is compared with the BOC volume to determine whether or not volume doubling has occurred. In the instance that it has, half of the total fuel salt volume is removed, and a new TRITON input is created which reflects the new fuel salt volume. If doubling has not yet been attained, a new TRITON input is written which simply uses the current volume. The new TRITON file will then be executed, progressing to the next depletion step, the process repeating until the total simulation time defined by the user has been reached.

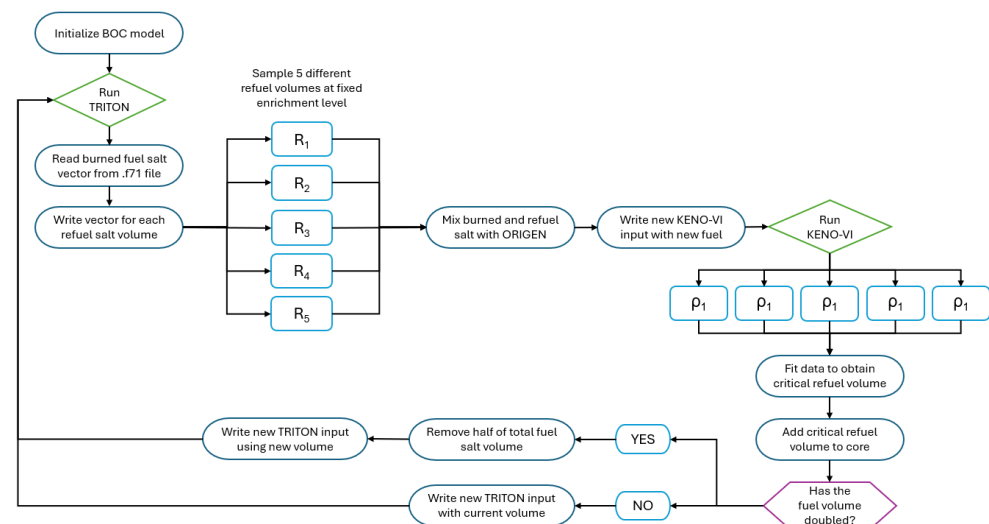


Figure 2. Flowchart illustrating the developed framework for simulating batch refueling with the Sourdough concept in SCALE 6.3.1.

As was implemented previously in the EIRENE model in [54], gaseous and noble metal fission products are continuously removed at fixed rates during each depletion simulation. In the present work, noble metals are defined to include isotopes of Zn, Nb, Rh, In, Ga, Mo, Pd, Sn, Ge, Tc, Ag, Sb, As, Ru, and Cd, with each of these having a fractional removal rate of $1.15741 \times 10^{-4} \text{ s}^{-1}$ as specified in SCALE 6.3.1. Gaseous fission products, which are defined as including isotopes of xenon and krypton, are each removed at a fixed rate of $2.00 \times 10^{-2} \text{ s}^{-1}$. These removal rates are based on the Molten Salt Breeder Reactor (MSBR) SCALE model developed by Hartanto et al. (2024) in [62].

Whereas some gaseous fission products such as ^{135}Xe act as neutron poisons and negatively impact neutronic performance, noble metals exist as insoluble species within the fuel salt and may deposit onto surfaces within the reactor primary loop [63]. Accumulated deposition of these noble metals can lead to significant adverse effects, including fouling of the heat exchanger or the creation of decay heat hot spots within primary circuit components [63,64]. Removal of noble metals can prevent this, and can be performed online without the need for interruptions to power production. Furthermore, a number of noble metal fission products are highly desirable for use in nuclear medicine, including (but not limited to) ^{99}Mo . As these nuclides are being continuously extracted from the active fuel salt during reactor operation, their harvest may be simplified, making them more readily available for recovery. With this, the modeling of gaseous and noble metal fission products, in addition to active fuel salt nuclides, comprises a significant component of this study. A specific strategy for noble metal removal (e.g., helium bubbling) is not modeled in the current versions of EIRENE and Th-EIRENE, with this being beyond the scope of this study and left for future work.

Using the developed batch refueling methodology, the atom densities and masses for key nuclides of interest are recorded at each depletion step and actively tracked in both the EIRENE and Th-EIRENE depletion simulations. Table 2 contains the isotopes which were studied in this work, including relevant nuclear data and notable example radiopharmaceuticals for each. Production of these radionuclides within the active fuel salt of EIRENE and Th-EIRENE will be compared between both models, including the produced masses and maximum activity available for harvest, to reveal any potential advantages of traditional uranium- or thorium-based fuel cycles on the yields of these radionuclides. Radionuclides for which significant quantities are removed from the active fuel salt as gaseous or noble metal fission products, and/or exist as decay products of those

which are, will also be studied, with the concentrations and masses of these being recorded using the ORIGEN off-gas and noble metal tracking framework. Radionuclides studied herein include a number of alpha- and beta-emitters which are highly desirable for use in TRT and/or nuclear imaging procedures, in addition to radionuclides such as ^{90}Sr and ^{99}Mo which are used as generators for key medical radionuclides.

Table 2. Radionuclides whose production and recovery is studied in the EIRENE and Th-EIRENE models using 19.75% enriched refuel salt.

Isotope	Decay Mode	Half-Life	Primary Use	Example Radiopharmaceuticals
^{225}Ac	α , 100.0%	9.919 d	Targeted alpha therapy	^{225}Ac -PSMA-617 [65–67] ^{225}Ac -PSMA-I&T [68–70] ^{225}Ac -J591 [71] ^{225}Ac -hu11B6 [72] ^{225}Ac -YS5 [73] ^{225}Ac -SibuDAB [74] ^{225}Ac -RPS-074 [75] ^{225}Ac -PSMA-DA1 [76]
^{212}Bi	β^- , 64.06% α , 35.94%	60.551 min	Targeted alpha therapy	^{212}Bi -anti-Tac [77–79]
^{213}Bi	β^- , 97.872% α , 2.128%	45.607 min	Targeted alpha therapy	^{213}Bi -J591 [80,81]
^{223}Ra	α , 100%	11.44 d	Targeted alpha therapy	^{223}Ra -Cl ₂ [82–84]
^{224}Ra	α , 100%	3.63 d	Targeted alpha therapy; ^{212}Pb generator	^{224}Ra -CaCO ₃ [85]
^{227}Th	α , 100%	18.69 d	Targeted alpha therapy	^{227}Th -trastuzumab [86]
^{230}U	α , 100%	20.23 d	Targeted alpha therapy; ^{226}Th generator	N/A
^{131}I	β^- , 100%	8.0252 d	Diagnostic imaging; targeted beta therapy	^{131}I -tositumomab [87–89] ^{131}I -MIP-1095 [90]
^{103}Ru	β^- , 100%	39.247 d	Diagnostic imaging; targeted beta therapy	^{103}Ru Cl ₃ [91] ^{103}Ru -BOLD-100 [92]
^{106}Ru	β^- , 100%	371.8 d	Occular brachytherapy	N/A
^{89}Sr	β^- , 100%	50.56 d	Palliative therapy	^{89}Sr -Cl ₂ [93]
^{90}Sr	β^- , 100%	28.91 y	^{90}Y generator	N/A (generator)
^{143}Pr	β^- , 100%	13.57 d	Targeted beta therapy	Pr ₂ O ₃ [94]
^{99}Mo	β^- , 100%	65.936 h	$^{99\text{m}}\text{Tc}$ generator	N/A (generator)
^{133}Xe	β^- , 100%	5.25 d	Diagnostic imaging	N/A
^{111}Ag	β^- , 100%	7.421 d	Diagnostic imaging; targeted beta therapy	^{111}Ag -hydroxyapatite [95]

3. Results

Depletion was simulated in SCALE 6.3.1 TRITON for approximately 2400 effective full power days (EFPD) at a reactor power level of 400 MW_{th} in both the EIRENE and Th-EIRENE models, with 19.75% enriched refuel salt being added every 7 days. Mass quantities in grams for each of the radionuclides listed in Table 2 were tracked throughout each simulation, with these data being plotted for both EIRENE and Th-EIRENE with respect to EFPD to compare the production yields between the two models. Data for

all radionuclides (including those which are removed as gaseous or noble metal fission products) were recorded within the active fuel salt, whereas the production yields of the radionuclides ^{103}Ru , ^{106}Ru , ^{99}Mo , and ^{111}Ag were additionally studied as removed noble metals outside of the active fuel salt. ^{133}Xe , as a gaseous fission product, is tracked in the off-gas system, along with ^{89}Sr and ^{90}Sr , which are produced as decay products of ^{89}Kr and ^{90}Kr , respectively. Figure 3 shows the simulated activity data in Curies (Ci) plotted for the alpha-emitting radionuclides ^{225}Ac (a), ^{212}Bi (b), ^{224}Ra (c), and ^{230}U (d), whereas Figure 4 presents activity data for the beta-emitting radionuclides ^{131}I (a), ^{143}Pr (b), ^{89}Sr (c), and ^{90}Sr (d).

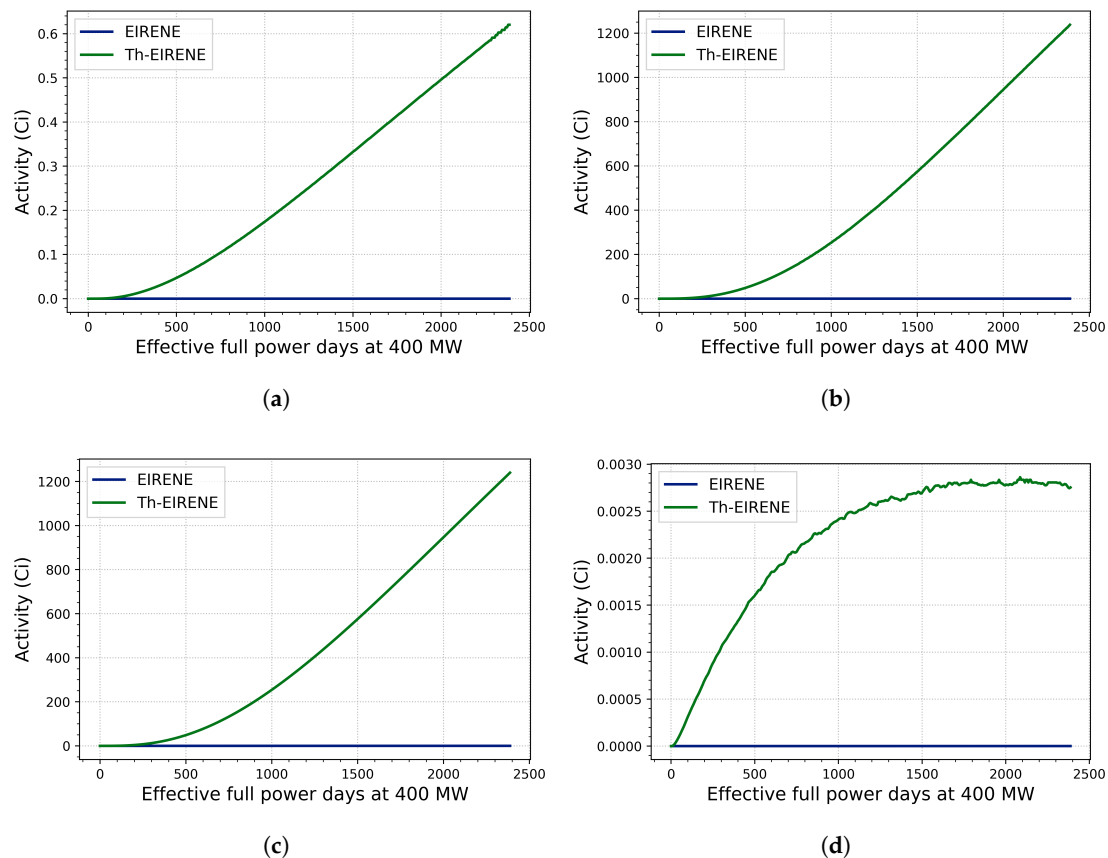


Figure 3. Plotted activity data in Ci for (a) ^{225}Ac . (b) ^{212}Bi . (c) ^{224}Ra . (d) ^{230}U .

From examining the activity data for the alpha-emitting radionuclides in Figure 3, it can be seen that production of these radionuclides is significantly greater in the Th-EIRENE model when compared with EIRENE, highlighting the beneficial impact of ^{232}Th inclusion within the fuel salt. For the beta-emitter ^{131}I , similar activity values are observed between both EIRENE and Th-EIRENE, with slightly greater quantities being recorded early on in the depletion simulation for EIRENE before being exceeded by Th-EIRENE later on, as shown in Figure 4. For the beta-emitters ^{89}Sr , ^{90}Sr , and ^{143}Pr , significantly greater production is seen in the Th-EIRENE model when compared with EIRENE, though large quantities of these radionuclides are available for harvest in both models.

Activity data for the removed noble metal fission products ^{103}Ru , ^{106}Ru , ^{99}Mo , and ^{111}Ag were additionally recorded and plotted with respect to EFPD for both the EIRENE and Th-EIRENE models. These data are presented in Figure 5 for EIRENE (a) and Th-EIRENE (b), with activity values being plotted in kilocuries (kCi). From these data, large production yields are observed for ^{99}Mo , ^{103}Ru , and ^{106}Ru for both reactor models, though overall yields are higher in EIRENE than in Th-EIRENE for these nuclides.

^{111}Ag is produced in significant quantities in both models, though visibly much less when compared with ^{99}Mo , ^{103}Ru , and ^{106}Ru when plotted on a kCi scale.

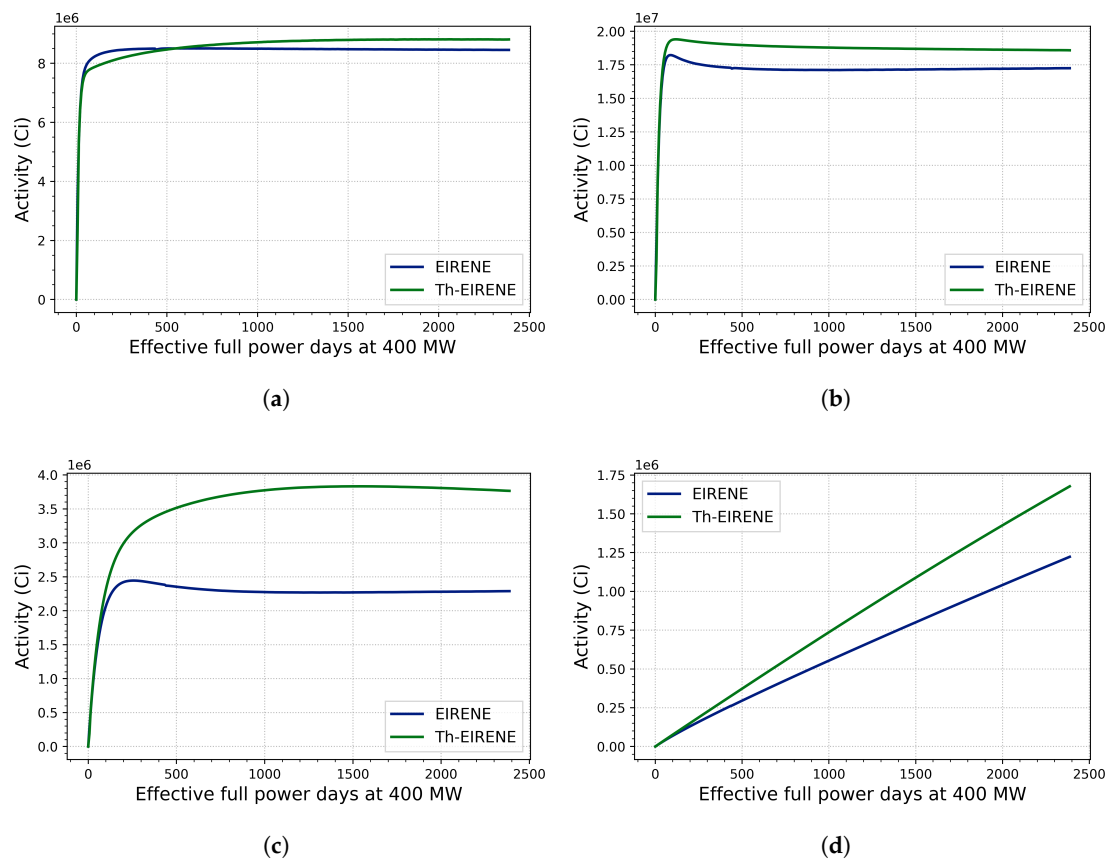


Figure 4. Plotted activity data in Ci for (a) ^{131}I . (b) ^{143}Pr . (c) ^{89}Sr . (d) ^{90}Sr .

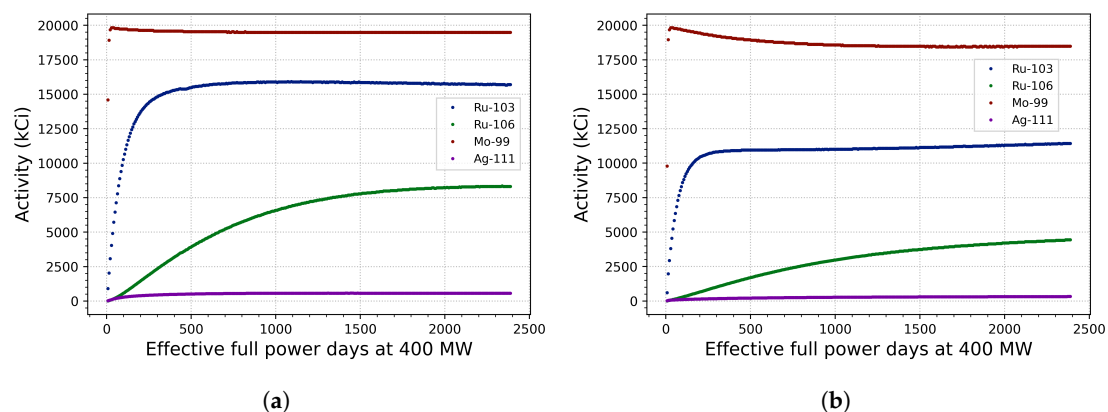


Figure 5. Simulated activity data in kCi for the removed noble metal fission products ^{103}Ru , ^{106}Ru , ^{99}Mo , and ^{111}Ag in (a) EIRENE; and (b) Th-EIRENE.

For ^{99}Mo , due to activity data being sampled every 7 days in the current methodology and assuming no ^{99}Mo is being extracted, decay of ^{99}Mo is prevalent in the data. Maximum activity values for ^{99}Mo reach a maximum value early on in the depletion simulations before gradually starting to decrease with respect to burnup in EFPD. However, even in later periods of the depletion simulation when the ^{99}Mo activity has decreased with respect to its maximum value, ^{99}Mo quantities available for harvest are still significant in both EIRENE and Th-EIRENE. The Organisation for Economic Co-operation and Development (OECD) estimated in 2012 that global ^{99}Mo demand fell between 9500 and 10,000 6-day Ci

per week, with a 6-day Ci representing the simulated ^{99}Mo activity 6 days following its departure from the processing facility [96]. With ^{99}Mo activities recorded in EIRENE and Th-EIRENE reaching nearly 20,000 kCi (20,000,000 Ci), with this representing only a single operating reactor and not considering any additional reactors which have been “grown” from the initial “starter” using the Sourdough refueling strategy, production of ^{99}Mo with both uranium- and thorium-based fuels is shown to be highly promising with this fuel cycle concept.

From the recorded mass data, activities in Curies (Ci) for each of the studied radionuclides were additionally quantified at each depletion step in EIRENE and Th-EIRENE. These were used to determine the maximum activity of each radionuclide available for harvest. Table 3 compares the maximum activity data for all of the radionuclides within the active fuel salt for the EIRENE and Th-EIRENE models, whereas Tables 4 and 5 present these data for the removed noble metals and radionuclides within the off-gas system, respectively.

Table 3. Maximum activity available for harvest in EIRENE and Th-EIRENE (active fuel salt nuclides).

Radionuclide	EIRENE Activity (Ci)	Th-EIRENE Activity (Ci)
^{89}Sr	2.2884×10^6	3.7651×10^6
^{90}Sr	1.2230×10^6	1.6773×10^6
^{131}I	8.4543×10^6	8.8093×10^6
^{143}Pr	1.7250×10^7	1.8586×10^7
^{225}Ac	1.4451×10^{-5}	0.62016
^{212}Bi	0.081146	1237.7
^{213}Bi	1.4304×10^{-5}	0.61550
^{223}Ra	2.0882×10^{-5}	0.20166
^{224}Ra	0.081415	1239.95
^{227}Th	2.1020×10^{-5}	0.20097
^{230}U	3.2272×10^{-7}	0.0028624
^{103}Ru	2.7421×10^4	1.9800×10^4
^{106}Ru	1480.9	841.53
^{99}Mo	4.9447×10^5	4.9447×10^5
^{111}Ag	4327.4	2488.66

Table 4. Maximum activity available for harvest in EIRENE and Th-EIRENE (removed noble metal fission product nuclides).

Radionuclide	EIRENE Activity (Ci)	Th-EIRENE Activity (Ci)
^{103}Ru	1.5924×10^7	1.1434×10^7
^{106}Ru	8.3159×10^6	4.4396×10^6
^{99}Mo	1.9827×10^7	1.9827×10^7
^{111}Ag	5.7699×10^5	2488.7

Table 5. Maximum activity available for harvest in EIRENE and Th-EIRENE (offgas system).

Radionuclide	EIRENE Activity (Ci)	Th-EIRENE Activity (Ci)
^{133}Xe	2.0196×10^7	2.0009×10^7
^{89}Sr	8.3274×10^6	1.0562×10^7
^{90}Sr	7.7433×10^5	8.6923×10^5

For further comparison of the EIRENE and Th-EIRENE designs, neutron flux spectra were obtained in the fuel salt of each model as a function of neutron energy in eV. Fluxes were sampled at the BOC and EOC with SCALE 6.3.1 KENO-VI and were normalized per unit lethargy. These results are presented in Figure 6 below, where the BOC and EOC fluxes

for both models are shown in the left and right plots, respectively. These data reveal that EIRENE is more thermal overall at both the BOC and EOC, whereas the Th-EIRENE model exhibits a harder neutron spectrum.

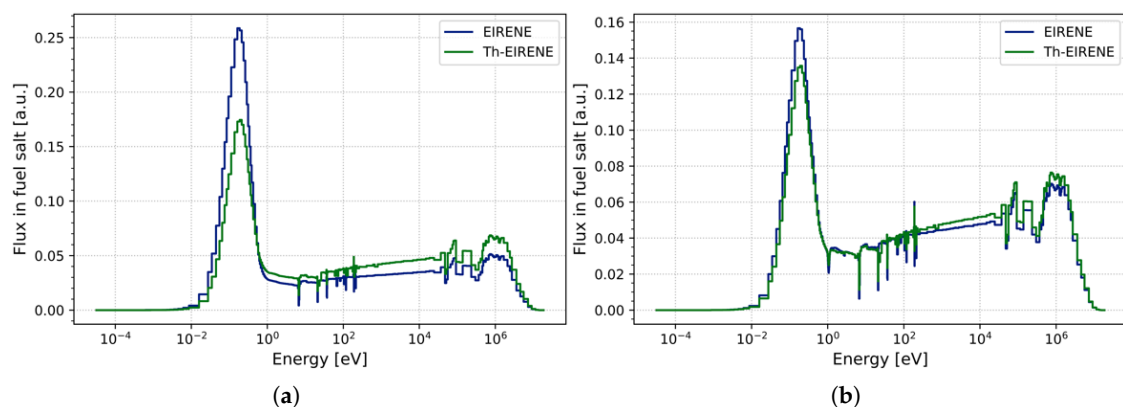


Figure 6. Neutron flux per unit lethargy for the EIRENE and Th-EIRENE models at: (a) BOC and (b) EOC.

4. Discussion

4.1. Comparison of Radionuclide Yields with Uranium and Thorium Fuel Cycles

From examination of the results presented in Section 3, it is shown that the incorporation of ^{232}Th within the fuel salt has a significant impact on the production quantities observed for each radionuclide, most notably the alpha emitters, with their yields in Th-EIRENE far exceeding those observed in EIRENE for the same depletion length. This is due to the presence of ^{233}U in large quantities in Th-EIRENE, with its use of the $^{232}\text{Th}/^{233}\text{U}$ fuel cycle. The decay of ^{233}U allows for the production of valuable radionuclides within the neptunium decay chain which would otherwise not be generated from traditional uranium-based fuel cycles, with the valuable alpha-emitting TRT radionuclides ^{225}Ac and ^{213}Bi being decay products of ^{233}U [47]. Thus, the production of ^{233}U , which is fostered within thorium-fueled MSRs where ^{233}U acts as a primary fissile material, results in the generation of significant quantities of ^{225}Ac and ^{213}Bi . Other valuable alpha-emitting radionuclides such as ^{212}Bi and ^{224}Ra are members of the thorium decay chain, being produced from the decay series of ^{232}Th itself. The presence of large quantities of ^{232}Th within the active fuel salt of Th-EIRENE therefore allows for significant production of these radionuclides as decay products. On the other hand, due to the lack of ^{232}Th in the LEU-fueled EIRENE, which translates to low quantities of ^{233}U , radionuclides belonging to the neptunium and thorium decay series are generated only in very small quantities. Figures 7 and 8 provide a representation of the neptunium and thorium decay series, respectively, to further illustrate the production of these radionuclides with thorium-based fuel cycles. As indicated by the results in Section 3, inclusion of ^{232}Th within the active fuel salt is necessary for significant production of radionuclides like ^{225}Ac , ^{212}Bi , and ^{224}Ra .

In comparing the production mass yields in EIRENE versus Th-EIRENE for ^{131}I , ^{89}Sr , and ^{143}Pr in Figure 4, it is shown that, while larger quantities of both radionuclides are observed in Th-EIRENE overall, their production is still significant in EIRENE, with visible radionuclide yield quantities being observed with these data compared with the very small plotted mass quantities seen for ^{225}Ac and ^{212}Bi in EIRENE. For ^{131}I , in particular, production yields within EIRENE and Th-EIRENE are observed to be very similar. Although significant quantities of ^{89}Sr and ^{143}Pr are produced with EIRENE, which was previously observed by the authors in [58], greater production is shown to be possible through ^{232}Th incorporation. This is due to the lighter fission products, particularly those

close to $A = 90$, having a higher yield from thermal fission of ^{233}U compared to ^{235}U and ^{239}Pu . This phenomenon is illustrated in Figure 9, which includes on the left a plot of fractional thermal fission yields with respect to nuclide mass number for each of the three primary fissile nuclides: ^{235}U , ^{239}Pu , and ^{233}U . For plotting the individual thermal fission yields for each of these nuclides, the OpenMC ENDF/B-VII.1 depletion chain for a thermal neutron spectrum was utilized, with these data being publicly available for download on the official OpenMC website [97]. From these data, it can be seen that, for fission product nuclides around $A = 140$, differences in thermal fission yields are still observed for ^{233}U , ^{235}U , and ^{239}Pu , though these differences are significantly less pronounced. In the EIRENE model, larger quantities of ^{239}Pu are generated within the active fuel salt during reactor operation when compared with Th-EIRENE. For fission product radionuclides near $A = 100$, thermal fission yields are highest for ^{239}Pu , whereas significantly smaller yields are observed for ^{235}U and ^{233}U . This can be seen in the recorded maximum activity data for the radionuclides ^{103}Ru , ^{106}Ru , and ^{111}Ag in Tables 3 and 4, where higher production of these radionuclides is observed in EIRENE when compared with Th-EIRENE.

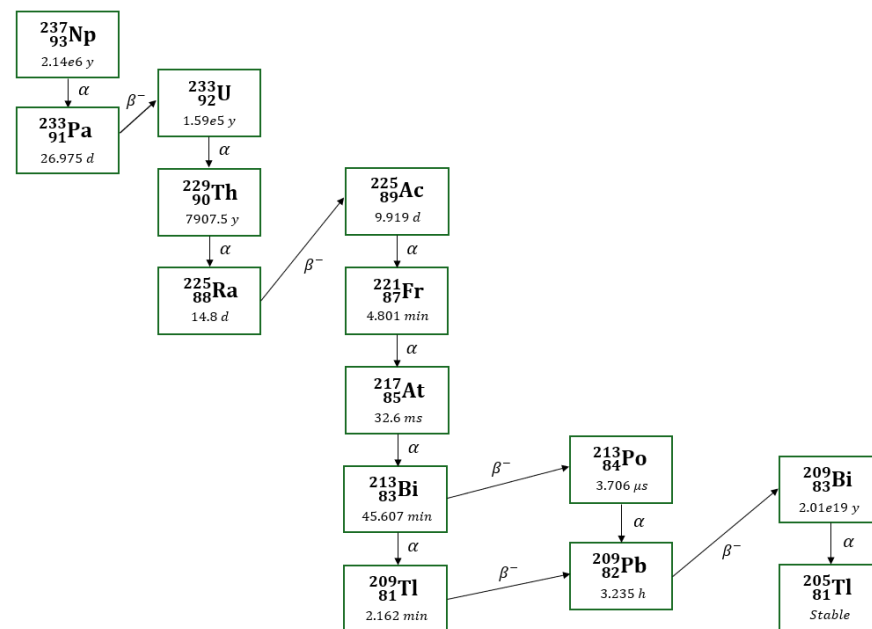


Figure 7. The neptunium decay series, beginning with ^{237}Np and ending with ^{205}Tl .

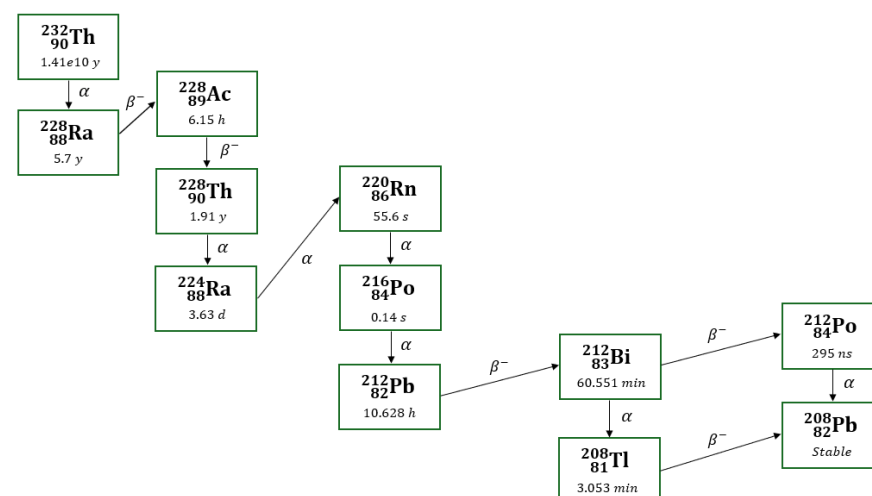


Figure 8. The thorium decay series, beginning with ^{232}Th and ending with ^{208}Pb .

To gain a greater understanding of the differences in the radionuclide yields observed in the EIRENE and Th-EIRENE models, total thermal fission yields were obtained for both models to include a sum of the yields from ^{235}U , ^{239}Pu , and ^{233}U at a fixed time period during simulated depletion. The thermal yields from each fissile nuclide were weighted using the macroscopic fission cross-section in cm^{-1} , with these cross-sections being obtained from the number density and microscopic fission cross-section of each nuclide. Microscopic fission cross-sections were obtained using the SCALE 6.3.1 OBIWAN command utility to analyze the .f33 ORIGEN library files generated for EIRENE and Th-EIRENE at a depletion time period of 1400 EFPD. The resulting weighted total thermal fission yields at 1400 EFPD are shown in plot (b) on the right in Figure 9 for EIRENE and Th-EIRENE. From this, it can be seen that significantly higher weighted total thermal fission yields are obtained with the Th-EIRENE model when compared with EIRENE, which corresponds with the overall higher production yields seen for most of the radionuclides studied in the Th-EIRENE versus the EIRENE model.

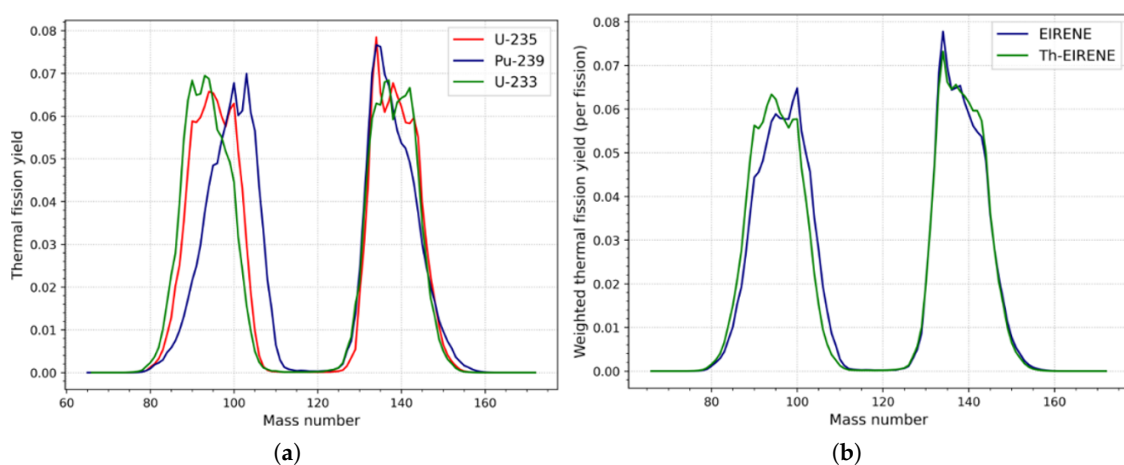


Figure 9. (a) Fractional thermal fission yields with respect to nuclide mass number for the three fissile fuels ^{235}U , ^{239}Pu , and ^{233}U . (b) Weighted fractional fission yields summed for ^{235}U , ^{239}Pu , and ^{233}U in EIRENE and Th-EIRENE.

For a more detailed analysis of the quantities of fissile nuclides present within the EIRENE and Th-EIRENE models during simulated depletion, atom fractions for ^{235}U , ^{239}Pu , and ^{233}U were calculated for both models with respect to burnup in EFPD. Each atom fraction represents the concentration of the given fissile nuclide over all three fissile fuels (e.g., ^{235}U over the sum of all ^{235}U , ^{239}Pu , and ^{233}U in the active fuel salt) at the current depletion step. Figure 10 illustrates the evolution of these atom fractions throughout simulated depletion in EIRENE and Th-EIRENE, with both ^{235}U and ^{239}Pu being shown to comprise a significantly larger portion of the fissile material within EIRENE compared to Th-EIRENE. Contrarily, in Th-EIRENE, limited ^{239}Pu exists in the active fuel salt, with large quantities of ^{233}U being present, whereas in EIRENE, ^{233}U exists in only very small quantities.

4.2. Current Study Limitations and Areas for Future Work

This study, with its primary objective being to compare radionuclide production based on fuel cycle type using the EIRENE and Th-EIRENE models, is significantly limited in its scope, with modeling only being performed for radionuclide production and without consideration of radionuclide recovery methods. With their capability to provide a stable supply of these highly valuable radionuclides as a byproduct of clean energy production, radiochemical separation strategies for MSRs is an active field of study which draws upon the extensive body of prior research on molten salt-based electrochemical techniques

for used fuel reprocessing [98]. Many recent works have been published on this topic which the reader is encouraged to review. Braatz et al. (2024) explore the promise and applications of electrolytic processes for directly extracting radionuclides of interest from fuel salts [99]. In their 2025 review, Choi and Lee discuss in detail the use of electrorefining and electrowinning, as well as the key technologies utilized in these processes and the significant advancements which have been made up until today [100]. Mirza et al. (2023) also examine in detail the design of electrochemical reactors to utilize electroreduction, electrowinning, and electrorefining technologies [98]. Specific to applications in medical radionuclide production, Moon et al. (2022) provide a comprehensive review of electrolytic processes for ^{99}Mo recovery in MSRs, noting current technological challenges and the value of further study to gain a greater understanding of ^{99}Mo behavior during reactor operation [101].

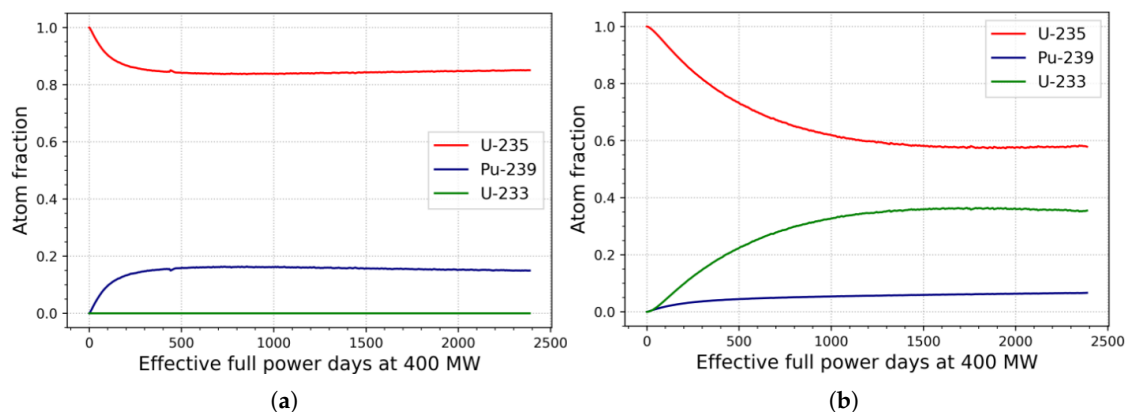


Figure 10. Atom fractions for the fissile nuclides ^{235}U , ^{239}Pu , and ^{233}U in: (a) The EIRENE model. (b) The Th-EIRENE model.

The investigation of radiochemical separation techniques such as these in the EIRENE and Th-EIRENE reactor designs is beyond the scope of the present work, though it represents a significant area of future study which would be valuable to provide a more complete understanding of the ability of these designs, and liquid-fueled MSRs in general, to be used in a commercial setting for radionuclide production to meet global clinical demand.

In addition to radiochemical separation strategies, radionuclide production yields observed in the EIRENE and Th-EIRENE designs, and their anticipated costs, are not directly compared with other production methods which are currently utilized, such as cyclotrons and research reactors. This is due to the limited nature of this study, with final production yields and costs being highly dependent upon the chosen method of extraction for a given radionuclide, as well as its desired purity. To perform a true comparison between the EIRENE and Th-EIRENE yields and current production methods, methods of radiochemical separation must first be studied. Cost analyses would additionally need to be performed separately for each radionuclide of interest to fully capture the impacts of purity requirements specific to their applications, which will also be a significant factor impacting the anticipated cost of production. For further details on current production routes for ^{225}Ac and reported yields, Rahman et al. (2024) provide a valuable overview in their work [102].

Furthermore, as previously discussed, the current implementation of refueling in the Th-EIRENE model, with the refuel salt containing only HALEU and no fertile ^{232}Th , significantly limits the production of neptunium-chain radionuclides such as ^{225}Ac , and is a limitation of the present study. The inclusion of ^{232}Th in the refuel salt would significantly bolster the production yields for neptunium chain radionuclides such as ^{225}Ac , as well as

yields for radionuclides belonging to the thorium decay series. In future work, implementing an active thorium feed, such as what was done by Rykhlevskii et al. (2019) in their MSBR model in [103], would be highly valuable to gain a greater understanding of the full potential of the Th-EIRENE model and other thorium-utilizing MSRs of similar design in producing sufficient quantities of ^{225}Ac and other valuable radionuclides.

5. Conclusions

Radionuclides play a vital role in nuclear diagnostic and therapeutic procedures for patients with cancer, with TRT being a powerful form of targeted therapy expected to see increased clinical usage in the coming years. With the limited supply and availability of these radionuclides currently hindering the widespread usage of TRT, developing new production routes is essential for ensuring patient care. In this study, the production of therapeutic beta- and alpha-emitting radionuclides for TRT, as well as radionuclides valuable for diagnostic procedures and palliative therapy, was studied in two geometrically identical MSR models, each operating with a different nuclear fuel form: the uranium-fueled EIRENE, and the mixed uranium- and thorium-fueled Th-EIRENE.

In comparing isotope production in the EIRENE and Th-EIRENE models, it was shown that Th-EIRENE produced greater mass quantities of the radionuclides studied overall, with only ^{131}I being observed to have a slightly larger production mass in EIRENE early on in the depletion simulations before being exceeded by Th-EIRENE. In a prior study by the authors examining the production of ^{89}Sr , ^{90}Sr , ^{131}I , and ^{143}Pr in the EIRENE SCALE 6.3.1 model [58], it was shown that significant quantities of these beta-emitting radionuclides were produced within the active fuel salt during simulated depletion. The results of the present study confirm this finding; however, the alpha-emitting radionuclides ^{225}Ac , ^{212}Bi , ^{213}Bi , ^{223}Ra , ^{224}Ra , ^{227}Th , and ^{230}U were shown to be produced in only very small quantities in EIRENE. The incorporation of fertile ^{232}Th within the active fuel salt in the Th-EIRENE model facilitated the production of significant quantities of these radionuclides, as indicated both in the mass quantities produced and the calculated maximum activities available for harvest. Further research into radionuclide production in liquid-fueled MSRs with uranium- and thorium-based fuel cycles is desirable, notably in chemical separation and purification processes which were not explored in the current work.

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Abbreviations

The following abbreviations are used in this manuscript:

MSR	Molten salt reactor
TRT	Targeted radionuclide therapy
TAT	Targeted alpha therapy
TBT	Targeted beta therapy
PET	Positron Emission Tomography
SPECT	Single Photon Emission Computed Tomography

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