Nuclear Isotopes Could Help Address Challenges in Oncology Clinical Trials

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Each year, 2 million patients are diagnosed with cancer in the US, and 10 million die from it around the globe.1 Every 2 minutes, someone in the US is diagnosed with lung cancer, and every day, more than 361 lives are lost to this disease.2 The race to cure cancer has spurred a surge in cancer trials, increasing from 19,211 in 2013 to an astounding 26,396 in 2022.3 Yet the failure rate of these trials remains stubbornly high at around 95%.4 Over the past 3 decades, remarkable advancements have been made in the fight against cancer, from integrating cutting-edge technologies to pioneering chimeric antigen receptor (CAR) T-cell therapies and even studying cancer cells in space. Despite these strides, the rising failure rate of cancer trials and the persistent toll of the disease remain sobering realities. Amid these challenges, a promising new contender is making its way into cancer trials: nuclear isotopes.

Nuclear Isotopes and Their Role in Cancer Cell Detection & Cure

It is important to first understand the foundational building block of nuclear isotopes: atoms. An atom is the basic building block of all matter—everything around us, from the air we breathe to the water we drink and the food we eat. Atoms are incredibly small, so small that millions of them can fit on the tip of a pin. Each atom is made up of 3 parts: protons and neutrons, which are located at the core of the atom (called the nucleus), and electrons, which orbit around the nucleus. Most atoms are stable, meaning the forces holding the protons and neutrons together in the nucleus are balanced. Because of this stability, their nuclei do not change or break apart over time, and hence they do not emit radiation.

Nuclear isotopes, on the other hand, have unstable nuclei. To achieve stability, they release energy in the form of radiation. This process is called radioactive decay, and atoms that undergo it are known as radioactive isotopes or nuclear isotopes. The radiation emerging from these isotopes can be used in 2 different ways in cancer trials: imaging (detection of tumors) and therapy (destruction of tumors).

For imaging, isotopes like Technetium-99m can be injected into the body, where they travel to tumors and emit signals that can be captured by special cameras, creating detailed scans to locate and assess cancerous growths. For therapy, isotopes such as Iodine-131 or Lutetium-177 can potentially deliver targeted radiation directly to cancer cells, damaging their DNA and stopping them from growing or spreading, while sparing surrounding healthy tissues. These isotopes are often attached to molecules that act like a GPS, ensuring precise delivery to cancer cells. This dual role in diagnosis and therapy positions nuclear isotopes as a powerful tool in modern oncology trials. Scientists and research teams worldwide are actively exploring the role of nuclear isotopes in cancer trials, leading to the emergence of radiopharmaceuticals (radioligands)—a new

class of cancer drugs that harness nuclear isotopes to precisely target cancer cells while sparing healthy ones.

Nuclear Isotopes Shaping Modern Cancer Trials

Although there are a range of nuclear isotopes that are being tested in these trials, Actinium-225 and Lutetium-177 have emerged as 2 of the most promising, each excelling in different therapeutic contexts. Actinium-225, an alpha-emitter, delivers highly concentrated radiation over an extremely short range, making it particularly effective for targeting small, localized clusters of cancer cells. Its high-energy emission causes irreparable damage to the DNA of tumor cells while sparing surrounding healthy tissues. This precision makes Actinium-225 ideal for cancers with well-defined targets, such as prostate cancers expressing prostate-specific membrane antigen (PSMA), where minimizing collateral damage is critical.5

In contrast, Lutetium-177 emits beta radiation, which travels farther than alpha particles, making it more suitable for addressing larger, less localized tumors or those with diffuse metastatic spread. The ability to deliver a lower-energy but broader radiation dose allows Lutetium-177 to effectively target cancers with more extensive involvement, such as advanced neuroendocrine tumors.6 Whereas Actinium-225 is favored for its precision and higher tumor-killing potential at smaller scales, Lutetium-177 offers versatility in treating cancers that require broader coverage, making the 2 isotopes complementary in the fight against cancer.

Cancer Trials Using Nuclear Isotopes

Several pharmaceutical leaders are driving innovation by incorporating these isotopes into trials for treatment-resistant cancers. Eli Lilly is utilizing both Actinium-225 and Lutetium-177 to advance therapies for metastatic prostate cancer and neuroendocrine tumors, demonstrating a strong commitment to isotope-based solutions.7,8 Bayer and Novartis are also at the forefront, conducting phase 1 trials focused on leveraging Actinium-225 to enhance precision and efficacy for prostate cancer patients with PSMA-positive tumors.9,10 Bristol Myers Squibb is using Actinium-225 in a phase-3 study to treat patients withgastroenteropancreatic neuroendocrine tumors.11 Adding to this global effort, the McGill University Health Centre is leading a pioneering phase 1 trial that evaluates Actinium-225's potential for patients with advanced, treatment-resistant prostate cancer.12 In November 2024, University College London initiated a new clinical trial to evaluate the effect of radioactive isotopes on patients with recurrent glioblastoma brain cancer.13 Although these isotopes offer promising avenues for improving cancer care, the challenges surrounding their supply and implementation in these trials remain significant hurdles.

Challenges in Integrating Nuclear Isotopes in Cancer Trials

Actinium-255, despite its remarkable therapeutic potential, is in critically short supply due to the scarcity of facilities equipped to produce it and the high costs associated with its synthesis. Scaling up production while maintaining consistent quality and purity is a daunting challenge that is yet to be fully addressed. Beyond production, ensuring precise delivery of these isotopes to

tumor cells presents another challenge.Variations in patient biology, tumor size, and tissue characteristics can lead to off-target radiation exposure, risking damage to healthy tissues.

The challenges don't stop there. Optimizing the dose for each patient—which demands a delicate balance of tumor eradication and side effects minimization—is hard to accomplish using current labor-intensive trial-and-error methods. Compounding this issue is the challenge in tracking how isotopes behave in real time once administered in the human body. Current imaging technologies, while advanced, are often unable to provide dynamic, detailed insights into isotope distribution within the body. This limitation increases the risk of radiation exposure to healthy tissues, particularly in cases where tumors are located near vital organs.

On top of these technical barriers, the logistical demands of clinical trials compound the challenges. Managing the fragile supply chain of isotopes, identifying suitable patient cohorts, and processing the immense volume of data—from imaging scans to molecular analyses—are daunting tasks that can easily overwhelm traditional approaches in oncology trials, drastically slowing down their pace. This raises a pressing question: Can modern advanced technologies help us address these time-sensitive barriers? Could artificial intelligence (AI) provide the breakthrough we need in nuclear oncology trials? The potential is worth exploring.

Harnessing AI to Transform Isotope Production & Delivery to Cancer Cells

AI is essentially a set of mathematical (probabilistic) functions generated by computers that are capable of analyzing and contextualizing large volumes of diverse datasets, including visual, textual, and audio. This unique capability of AI models makes them especially suitable to address barriers in nuclear oncology trials.

To begin with, bottlenecks in isotope production capacity and purity can be addressed by leveraging AI models to analyze geological data and identify regions with the highest concentration and quality of resources, ensuring safe and ethical extraction. For isotopes produced synthetically using cyclotrons and reactors, machine learning models—particularly those utilizing reinforcement learning—can optimize reactor and cyclotron parameters, such as beam energy, irradiation time, and target material composition, to enhance the synthesis of isotopes like Actinium-225 with higher purity and efficiency while minimizing waste. Additionally, anomaly detection algorithms, such as those based on unsupervised learning, can identify inconsistencies in production processes, improving quality control and ensuring the isotopes meet therapeutic-grade standards. These streamline isotope production, addressing one of the most critical barriers in expanding nuclear medicine's reach.

For delivering isotopes effectively, advanced AI systems can be used to transform how we approach medical imaging and treatment planning in these trials. For example, convolutional neural networks—a type of machine learning algorithm designed for image analysis—can be integrated with imaging tools like positron emission tomography or single photon emission computed tomography. This integrated approach can help us enable real-time analysis of imaging data at scale and with extremely high precision to track isotope accumulation in tumor regions.

This ensures targeted destruction of cancer cells while sparing healthy tissues. But precision doesn't end with imaging—it extends to tailoring treatments for individual patients. This raises an important question: How can oncologists and oncology pharmacists ensure that radiation dosage and treatment plans are personalized to suit each patient's unique needs? This is where AI-based radiomics might play a vital role.

AI-Driven Precision in Radiation Dosing and Patient Selection

AI-based radiomics is an advanced application of AI, focused on extracting quantitative features from imaging data. This process goes beyond traditional imaging by analyzing complex patterns and metrics within tumor scans, providing clinicians with a detailed understanding of how isotopes are distributed throughout the body. These insights enable oncologists to fine-tune treatment plans tailored to each patient's unique anatomy and tumor profile, maximizing efficacy while minimizing adverse effects. Another challenging aspect of these trials is determining the optimal radiation dose. Here, Bayesian optimization methods can simulate how isotopes interact with tumors, helping calculate the safest and most effective dose for each patient.

Finally, ensuring these trials start with the right set of patients is critical. This is where large language models (LLMs) can come to our rescue. LLMs, a cutting-edge class of AI models, can analyze unstructured patient data such as clinical notes, medical histories, and genomic profiles to identify individuals most likely to benefit from isotope therapies. While modern AI models can help us address some of these risks in nuclear oncology trials, there are those thatcannot be fully addressed through technology alone.

Navigating Risks in Nuclear Oncology Trials

The performance of modern AI models is dependent on the quality, volume, and diversity of data fed to these models. Given that nuclear oncology is an emerging field, there is not enough data available today that might cover all the scenarios and edge cases. This means we may not be able to fully realize the potential of AI in this domain. Beyond technology, the cost of producing these isotopes is staggering and it is unclearhow these expenses will be distributed among pharmaceutical companies, health care providers, insurers, and patients. Moreover, working with nuclear isotopes introduces a unique and delicate risk profile that requires oncology trials to operate with unmatched precision and safety. Addressing these challenges goes beyond technological innovation—it demands collaboration, standardization, and transparency across industries and institutions.

To move these therapies from cutting-edge trials into everyday clinical practice, we need a multi-pronged approach. Investing in scalable and sustainable isotope manufacturing technologies is crucial to addressing supply shortages. Equally important is fostering partnerships between pharmaceutical companies, nuclear facilities, and research institutions to innovate collectively. On the regulatory front, there's a need for streamlined approval pathways that maintain safety standards while expediting access to these nuclear isotopes. Governments and private

organizations must also step up to provide funding for infrastructure and research, ensuring that radiopharmaceutical breakthroughs are both developed and delivered responsibly.

The promise of nuclear isotopes isn't just in their precision—it's in the collaborative, forward-thinking efforts required to transform them into a lifeline for the next 10 million people courageously battling cancer, waiting for the breakthrough that could change their fate.

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