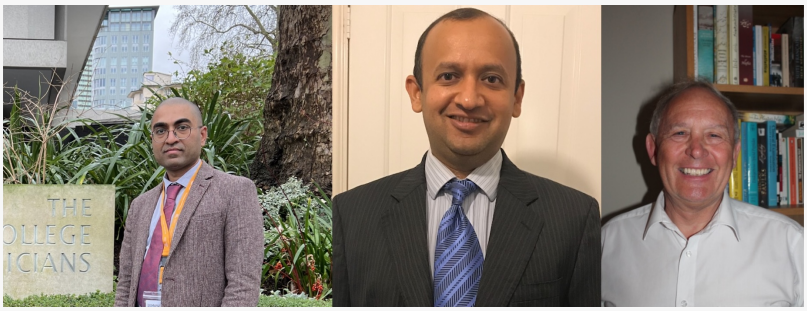
Alpha particle therapy emerges as a potent weapon against neuroendocrine tumours

Precision medicine breakthrough: Targeted alpha therapy delivers surgical-strike precision against resistant neuroendocrine tumors, offering new hope.



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LONDON, UNITED KINGDOM, March 4, 2025 /EINPresswire.com/ -- In a comprehensive Genomic Press Viewpoint (review) article, researchers are shining a spotlight on a revolutionary approach to tackling neuroendocrine tumours (NETs), a rare but increasingly prevalent cancer type. Published in Brain Medicine today, a peer-reviewed article titled "Alpha particle therapy for neuroendocrine tumours: A focused review" explores how targeted alpha therapy (TAT) redefines treatment when surgery is not an option. Authored by Drs. Kalyan Shekhda, Shaunak Navalkissoor, and Ashley Grossman, this work dives into the science behind TAT, its early successes, and the hurdles still ahead.

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>
> *Dr. Kalyan M. Shekhda*

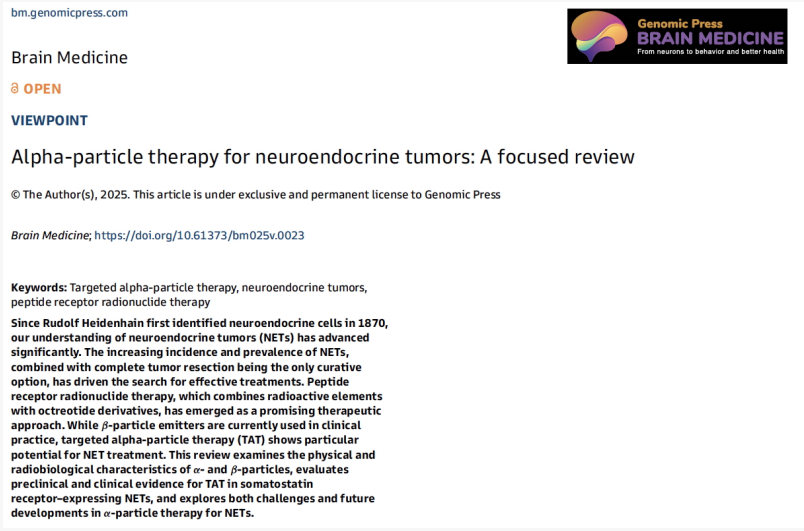
Since neuroendocrine cells were first identified over 150 years ago, NETs have posed a unique challenge to medical science. With complete tumour removal as the only cure, the rising incidence of NETs has fuelled a quest for innovative therapies. Peptide receptor radionuclide therapy (PRRT), which pairs radioactive particles with molecules like octreotide to target cancer cells. While beta-particle emitters like 177Lu-DOTATATE (Lutathera) have become standard as highly effective and well-tolerated therapy, their limitations - namely relapse within a few yearshave spurred interest in alpha particles. Why? Alpha particles pack a punch: they deliver high-energy bursts over a short range, shredding tumour DNA while sparing healthy tissue. Alpha particles are also more effective in hypoxic tumour micro-environments: a mechanism by which tumour cells can develop resistance to chemotherapy and conventional radiotherapy.

The Science of Precision

The Viewpoint review unpacks the physics and biology driving TAT's potential. Alpha particles, with their high linear energy transfer (LET), cause irreparable double-strand DNA breaks---far more lethal to cancer cells than the single-strand nicks from beta particles. Dr. Shekhda explains, "Alpha particles are like surgical strikes -short -range, high-impact, and devastating to tumours, even in low-oxygen environments where other therapies falter." Studies show their relative biological effectiveness outstrips beta emitters, raising a tantalizing question: could TAT turn the tide for patients with resistant NETs?

Dr. Navalkissoor, co-author and nuclear medicine specialist at Royal Free Hospital, adds, "What makes targeted alpha therapy particularly exciting is its potential as a precision tool for patients who have exhausted conventional treatment options. From our clinical experience, we're seeing that alpha particles can overcome resistance mechanisms that limit traditional therapies. The highly localized nature of alpha radiation means we can deliver potent treatment directly to tumour cells while minimizing collateral damage to healthy tissues."

This article is part of a Festschrift commemorating Dr Seymour Reichlin. His work on neuroendocrinology laid the ground for theranostics–such as TAT that blend diagnostics and therapeutics. Now 100 years old and cognitively sharp, Dr Reichlin remains a living legend.



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VIEWPOINT

Alpha-particle therapy for neuroendocrine tumors: A focused review

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Since Rudolf Heidenhain first identified neuroendocrine cells in 1870, our understanding of neuroendocrine tumors (NETs) has advanced significantly. The increasing incidence and prevalence of NETs, combined with complete tumor resection being the only curative option, has driven the search for effective treatments. Peptide receptor radionuclide therapy, which combines radioactive elements with octreotide derivatives, has emerged as a promising therapeutic approach. While β-particle emitters are currently used in clinical practice, targeted alpha-particle therapy (TAT) shows particular potential for NET treatment. This review examines the physical and radiobiological characteristics of α- and β-particles, evaluates preclinical and clinical evidence for TAT in somatostatin receptor–expressing NETs, and explores both challenges and future developments in α-particle therapy for NETs.

Alpha-particle therapy for neuroendocrine tumors: A focused review

Preclinical trials in animal models have been promising. Experiments with alpha-emitters like 225Ac-DOTATATE and 212Pb-DOTAMTATE in mice and rats delayed tumour growth with minimal toxicity to kidneys or bone marrow. Clinical studies, while still very preliminary, echo this optimism. A phase I trial of

212Pb-DOTAMTATE reported an 80% disease control rate in PRRT-naïve patients, earning it a coveted FDA Breakthrough Therapy Designation. Meanwhile, 225Ac-DOTATATE has shown a disease control rate nearing 90% in some cohorts with progressive NETs. But how do these early wins translate to long-term outcomes? Future trials will explore the longer-term effects of these therapies, and their possible adverse events, although to date any untoward effects seem to be uncommon and possibly no greater than with conventional PRRT.

A Festschrift for a Living Legend

This article is published as part of a special Festschrift commemorating the centennial of Dr. Seymour Reichlin, a titan of neuroendocrinology who was born in 1924. Dr. Reichlin's pioneering work on the regulation of neuroendocrine cells in the pituitary, and then later on neuroendocrine-immune interactions, laid the groundwork for modern theranostics –therapies like TAT that blend diagnostics and treatment. Now 100 years old and still cognitively sharp, Dr. Reichlin remains a living legend whose mentorship shaped generations of researchers. His curiosity was sparked by tragedy – losing his sister to a pancreatic endocrine tumour-and fuelled his breakthroughs, from hypothalamic control of the pituitary to identifying hormone-releasing factors. This review's focus on NETs resonates with his legacy, asking: how might TAT build on his foundational insights to tackle endocrine cancers?

Challenges on the Horizon

Despite its promise, TAT is not without obstacles. Alpha-emitters like 213Bi decay rapidly, complicating production and delivery, and alpha emitters like 213Bi and 225Ac can be complex to source. Regulatory hurdles, high costs, and the need for precise dosimetry – measuring radiation doses to organs---pose further challenges. Yet, solutions are emerging. Companies are developing 212Pb generators, and advanced microdosimetry techniques could refine safety profiles. Professor Grossman notes, "We're at a tipping point. The technology is here, but scaling it sustainably is the next frontier." Could international collaboration or eco-friendly production methods unlock TAT's full potential?

Toxicity remains a concern, though rare. A meta-analysis pegs severe side effects at just 2-3%, but long-term data are scarce. Kidneys, vulnerable to alpha particles' intense energy, may prove a limiting factor. Researchers are exploring enhancers like chemotherapy or PARP inhibitors to boost TAT's efficacy---raising another question: could combination therapies amplify its impact without compromising safety?

Why This Matters Now

NETs, though rare, are on the rise, and TAT offers a lifeline where beta therapies fall short e.g. when tumours have developed resistance. Ongoing trials, like the ACTION-1 study of 225Ac-DOTATATE, are set to compare it against standard care, with results due in coming years. This is a story of innovation teetering on the edge of breakthrough. What will it take to bring TAT from

niche trials to widespread use? And how might it reshape our approach to other cancers?

The article, "Alpha particle therapy for neuroendocrine tumours: A focused review," is a testament to both cutting-edge science and Dr. Reichlin's enduring influence-a convergence of past inspiration and future hope. It appears online on 4 March 2025 in Brain Medicine (Genomic Press), where it is freely accessible at https://doi.org/10.61373/bm025v.0023.

About Brain Medicine: Brain Medicine (ISSN: 2997-2639) is a peer-reviewed medical research journal published by Genomic Press. Brain Medicine is a new home for the cross-disciplinary pathway from innovation in fundamental neuroscience to translational initiatives in brain medicine. It champions rigorous science with real-world impact. The journal's scope includes the underlying science, causes, outcomes, treatments, and societal impact of brain disorders across all clinical disciplines and their interface.

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