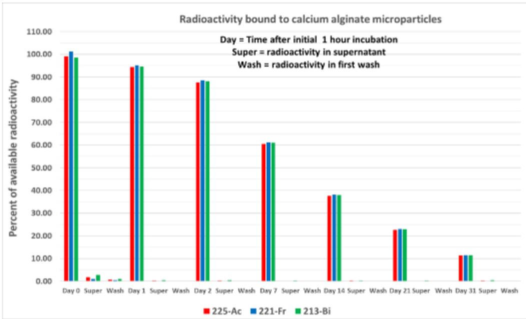
Do you know where your daughters are?
ARAspheres – Biopolymer nanoparticles with peptide targeting that chelate radionuclides and retain decay daughters

Michael Dornish[1] and Jostein Dahle[1,2]

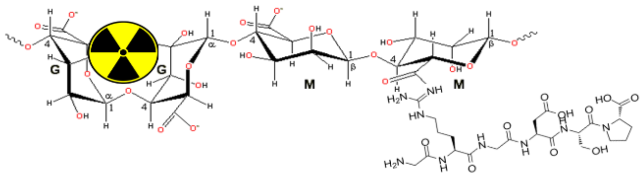
[1]Blue Wave Therapeutics AS, Industriveien 33, 1337 Sandvika, Norway; [2]Department of Oncology, Akershus University Hospital, Sykehusveien 25, 1478 Nordbyhagen, Norway

The challenge: Progress in targeted delivery using antibodies or peptides, in combination with alpha-particle emitting radionuclides, is demonstrating efficacy and reduced collateral damage to normal tissue. The 100 µm range α-particle radiation offers a unique mechanism of action, confining the radiation to the tumor cells to which the radiopharmaceuticals bind. Radionuclides are bound to the targeting vector by a chelator. However, the recoil energy from the alpha particle emission and the chemical differences between mother and daughter nuclides make it challenging to retain the daughters within a macrocyclic structure such as DOTA or MACROPA. A stable chelation of all decay chain daughters is crucial in targeted alpha therapy to prevent off-target toxicity from radionuclides released from the targeting molecule and to maximize the therapeutic efficacy.

The solution: A new type of micro- or nanoparticle has been developed that can stably chelate alpha-emitting radionuclides and retain decay daughters. The particles are produced from the natural biopolymer alginate, which is a straight-chain polysaccharide found in seaweed and kelp. We synthesized insoluble but biodegradable micrometer- or nanometer-sized alginate particles that can be functionalized by conjugating specific cell receptor targeting peptides to the particles. Additionally, these particles chelate many alpha- and beta-emitting radionuclides. RGD (Arginine-Glycine-Aspartic Acid) peptides were conjugated to the particles. RGD binds to cell surface integrins, particularly the αvß3 integrin. The alginate particles chelated the alpha-emitter actinium-225 (^{225}Ac) and were shown to retain decay daughters within the particle matrix.



The potential: Alginate micro- and nanoparticles have been developed that can stably chelate ^{225}Ac and its decay daughters for more than 30 days. The retention of ^{225}Ac decay daughters by the alginate micro- and nanoparticles results in a total of 4 α- and 2 β-emissions providing a greater radioactive dose delivered to the cancer cells to which the particles bind. This stable chelation represents a significant and innovative advancement over current radionuclide chelators, which cannot retain decay daughters. We know where the daughters are! Actinium-RGD-alginate nanoparticles (ARAspheres) are now undergoing pre-clinical testing in a rodent model of glioblastoma.



Radionuclide Alginate RGD

Supported by a grant 346303 ALPHAGLIO from the Research Council of Norway.

7th Targeted Radiopharmaceuticals Summit Europe, Amsterdam, 10-12 November 2025