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Locally targeted delivery of a therapeutic agents using temperature-sensitive hydrogel

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Purpose: To propose a novel radiation therapy (RT) delivery modality: locally targeted delivery of micron-size RT sources by using temperature-sensitive hydrogel (RT-GEL) as an injectable vehicle.

Methods & Materials: Hydrogel is a water-like liquid at room temperature but gels at body temperature. Two US Food and Drug Administration-approved polymers were synthesized. Indium-111 (In-111) was used as the radioactive RT-GEL source. The release characteristics of In-111 from polymerized RT-GEL were evaluated. The injectability and efficacy of RT-GEL delivery to human breast tumor were tested using animal models with control datasets of RT-saline injection. As proof-of-concept studies, a total of 6 nude mice were tested by injecting 4 million tumor cells into their upper backs after a week of acclimatization. Three mice were injected with RT-GEL and 3 with RT-saline. Single-photon emission computed tomography (SPECT) and CT scans were performed on each mouse at 0, 24, and 48 h after injection. The efficacy of RT-GEL was determined by comparison with that of the control datasets by measuring kidney In-111 accumulation (mean nCi/cc), representing the distant diffusion of In-111.

Results: RT-GEL was successfully injected into the tumor by using a 30-gauge needle. No difficulties due to polymerization of hydrogel during injection and intratumoral pressure were observed during RT-GEL injection. No back flow occurred for either RT-GEL or RT-saline. The residual tumor activities of In-111 were 49% at 24 h (44% at 48 h, respectively) for RT-GEL and 29% (22%, respectively) for RT-saline. Fused SPECT-CT images of RT-saline showed considerable kidney accumulation of In-111 (2886%, 261%, and 262% of RT-GEL at 0, 24, and 48 h, respectively).

Conclusions: RT-GEL was successfully injected and showed much higher residual tumor activity with a minimal accumulation of In-111 to the kidneys. Preliminary data of RT-GEL as a delivery modality of a radiation source to a local tumor are promising, 170% (200%, respectively), than that of RT-saline at 24 h (48 h, respectively) after injection.

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