Thermosensitive Liposomal Gold Nanoparticles as Radiosensitizers for Pancreatic Cancer Therapy

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Introduction

Less than 10% of all pancreatic cancer patients can truly undergo curative resection [1] and the high incidence of life threatening complications such as damage to liver and gallbladder is imminent. We therefore proposed an innovative delivery method; an antibody-conjugated thermosensitive liposomal loaded gold nanoparticles (TSLs-AuNps). These nanoparticles are incorporated with a conventional gadolinium (Gd) based MRI contrast agent for diagnostic capabilities. The liposomal complex (TSLs-AuNps-Gd) is capable of: i) surmounting biological barriers and release of their payloads deep into tumors [2-4], and ii) enhancing MRI sensitivity leading to early detection of cancer and visualization of metastatic disease [5]. These particles could support the novel use of MR-guided focus ultrasound (FUS) mediated mild temperature hyperthermia to locate tumor and trigger release of AuNps for optimal synergy between hyperthermia with AuNps and subsequent radiation dose enhancement [6, 7].

Experimental

To enhance AuNps transport into tumor core, AuNps and Gd (from Magnevist) are packed within pegylated thermosensitive liposomal nanoparticle-surface that is modified with epidermal growth factor receptor (EGFR) antibody which will facilitate the entry of AuNps-Gd-laden liposomes to the core of tumors (Fig. 1). The TSLs-AuNps-Gd are transported into tumor core by perturbing and adapting to each physiological barrier encountered. To improve tumor-specific accumulation of liposomes, their transport is enhanced across the vasculature/tumor interface using MR-FUS mediated hyperthermia before intravenous administration.

Results and Discussion

Fig. 1 shows a cartoon of the TSL nanoparticle with the Gd packed in the nanoparticle. Fig. 2 shows T_1-weighted images with regions-of-interest for relaxivity calculations (Table 1) using the molar concentrations (numbers below). When increasing the concentration of the Gd an increase in T_1 and T_2 contrast can be seen. In table 1 the measured T_1 and T_2 values are presented with the corresponding relaxivity.

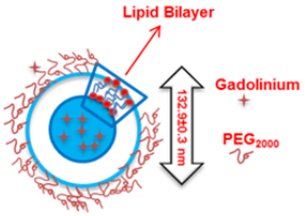

Fig.1 Cartoon of the TSL nanoparticle

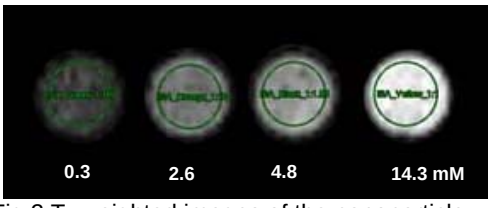

Fig.2 T_1 weighted images of the nanoparticle loaded with increasing mM concentration of Gd.

Table 1

Concentration Gd (mM)	T_1 (ms)	T_2 (ms)
14.3	503.1	25.6
4.8	970.9	36.1
2.6	1414.4	51.8
0.3	2638.5	55.3
Control (Agarose)	2849.0	36.1
Relaxivity ($s^{-1}mM^{-1}$)	0.11	1.53

Conclusions

These preliminary data show promising results for obtaining TSLs-AuNps-Gd with MRI contrast. Relaxation data in agarose phantoms show increasing T_1 contrast with increasing Gd concentration. Relaxivity have been determined based on ICP-MS results aimed at quantifying the amount of Gd on the particle. Future work is aimed at increasing the Gd payload to increase the MR contrast and to further investigate with *ex vivo* pancreatic tumor samples and *in vivo* with an animal model of pancreatic cancer.

Acknowledgements

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