MRI observation of the light-induced release of contrast agent from photo-controllable polymer micelles

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Introduction: The encapsulation of molecules into nanocarriers is studied for its potential in delivering a high dose of anticancer drugs to a tumor, while minimizing side effects. Most systems either release their content in a non-specific manner or under specific environmental conditions such as temperature or pH. We have synthesized a novel class of photo-controllable polymer micelles that can stably encapsulate a hydrophilic compound and subsequently release it upon absorption of UV light. Here, we describe an *in vitro* magnetic resonance imaging (MRI) assay that can evaluate the state of incorporation of a small Gd-based contrast agent.

Experimental Protocol: We have synthesized a shell-crosslinked reverse micelle (SCRM) as shown in Fig. 1. It was prepared based on an amphiphilic diblock copolymer composed of a hydrophilic block of poly(ethylene oxide) (PEO) and a hydrophobic block being a random copolymer of coumarin methacrylate and methyl methacrylate, referred to as PEO-*b*-P(CMA-co-MMA). The shell surface of the SCRM was grafted with hydrophobic poly (2-nitrobenzyl methacrylate (PNBMA). Details of the synthesis were reported elsewhere [1]. We also synthesized a contrast agent (Gd tetraphenylporphyrin, GdTPP), which was subsequently loaded into the SCRM. For this study, GdTPP-loaded PNBMA-grafted SCRM aqueous solution was divided into two containers, one was exposed to a UV lamp while the second remained intact. For comparison, a third container was filled with a solution of GdTPP, without any micelles. Samples were poured in a 0.5 mL filter tube (Slide-A-Lyzer MINI Dialysis Unit, Pierce Biotechnology) with molecular weight cutoff at 3,500, which was subsequently inserted into a 1.5 mL conical plastic tube filled with tap water. A feedback warm air system was used to keep the air around the samples at 27 °C throughout the experiments. A 7 T Varian animal scanner was used for imaging the filter tube and the surrounding water as a function of time using a T_1-weighted gradient-echo sequence.

Results and Discussion: Fig. 2 shows the signal intensity recorded in the solution outside the filter tube for the three samples. The results clearly indicate the contrast agent alone can diffuse through a filter but that the same agent incorporated into micelles cannot. After exposure to UV light, the micelles released the contrast agent, which could then diffuse through the filter [2].

Conclusions: We studied with MRI the diffusion of GdTPP through a filter in three different conditions. A comparable time constant was obtained for diffusion from a free GdTPP solution and from a solution with a photo-controllable micelle into which GdTPP was incorporated, after exposition to UV light. Conversely, only a negligible signal change was observed from the same photo-controllable micelle without exposition to UV light. The assay described is thus able to monitor the state of encapsulation of a contrast agent in photo-controllable micelles.

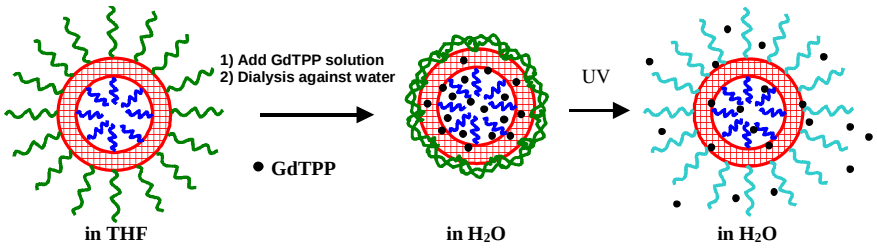

Fig. 1. Schematic illustration of the stable encapsulation of a hydrophilic MRI contrast agent and its release upon UV illumination.

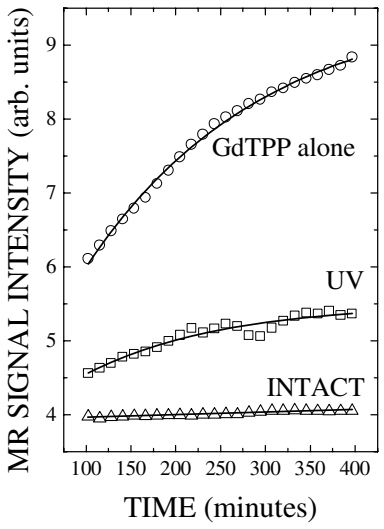

Fig. 2. MR signal intensity (arbitrary units) as a function of time in the solution outside the filter tube containing either GdTPP alone (top curve), micelles containing GdTPP after disruption from the exposition to UV light (middle curve) and intact micelles containing GdTPP (bottom curve). Monoexponential fits (top and middle) and a linear fit (bottom) are shown as solid lines.

References: 1- Jiang *et al*. Macromolecules 2007;40,790-2. 2- Lepage *et al.* Phys Med Biol 2007;52,N249-55.