Targeted Au-core-Ag-shell nanorods as a dual-functional contrast agent for photoacoustic imaging and photothermal therapy

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Abstract: Optimizing contrast enhancement is essential for producing specific signals in biomedical imaging and therapy. The potential of using Au@Ag NRs as a dual-functional theranostic contrast agent is demonstrated for effective cancer imaging and treatments. Due to its strong NIR absorption and high efficiency of photothermal conversion, effects of both photoacoustic tomography (PAT) and photothermal therapy (PTT) are enhanced significantly. The PAT signal grows by 45.3% and 82% in the phantom and in vivo experiments, respectively, when compared to those using Au NRs. In PTT, the maximum increase of tissue temperature treated with Au@Ag NRs is 22.8 °C, twice that with Au NRs. Results of the current study show the feasibility of using Au@Ag NRs for synergetic PAT with PTT. And it will enhance the potential application on real-time PAT guided PTT, which will greatly benefit the customized PTT treatment of cancer.

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1. Introduction

Photoacoustic tomography (PAT) is an emerging optical imaging modality that obtains functional and molecular information in real time [1, 2]. It is an innovation on the advantages of optical imaging method and cost-effective ultrasound imaging method. This approach utilizes pulsed laser light to generate ultrasound transients from optically absorbing materials through thermoelastic expansion [3]. Contrast in PAT comes from the natural variation in the optical absorption of tissue components, which has made it popular technique in recent years [2, 4]. Nonetheless, employing exogenous contrast in PAT will further expand its sensitivity and functionality in applications [5–7]. In addition, it offers the possibility of combining diagnosis with therapy, such as photothermal therapy (PTT) [8, 9]. PTT is a relatively noninvasive method and possibly becomes one of the alternatives for cancer treatment. It transfers optical energy into heat energy which results in the death of cancer cells [10]. To achieve better optical effectiveness, this method requires photoabsorbers and photothermal convectors to release heat production in a localized region [11]. Hence, both PAT and PTT call for an imaging contrast agent and an effectively therapeutic agent.

Requirements for such a dual-functional agent include: (i) easily synthesis and biocompatibility, (ii) smaller size for navigating the whole bloodstream, (iii) large absorption in the near-infrared (NI) wavelength region, (iv) conjugation with targeting moieties and long circulation time, (v) good stability in vivo [5]. Metal nanoparticles have been proved by several groups that they meet most of the demands above [12–14]. As is known to all, nano-sized structures made of metals exhibit surface plasmon resonance (SPR), allowing them to absorb and scatter far stronger light. Among these structures, those constructed of gold and silver are particularly suitable for biomedical imaging and PTT [15]. S. H. Yang et al. detected MCF7 cells using label-free gold nanorods with photoacoustic microscope (PAM) [16]. M. L. Li et al. used a high resolution PAM to image progressive extravasation and accumulation of nanoshells in a solid tumor in vivo [17]. K. Cheng et al. developed gold nano-architectures (Au-tripods) as a new generation of platform for in vivo PAI [18]. K.A.
Homan et al. used silver nanoplates as a new PA contrast agents for in vivo PAT [19]. S. C. Boca et al. explored silver nanoparticles as a PTT transducers for in vivo cancer cell therapy [20].

As a matter of fact, silver exhibits a lot of advantages over gold in the respect of optical properties, such as extinction coefficients and sharper extinction bands [21, 22]. However, it has been employed far less than gold in the fields of biomedical imaging and treatment because of the lower chemical stability. To solve the problem, Jang et al. managed to coat gold nanorods with silver and those Au_{core}-Ag_{shell} nanorods (Au@Ag NRs) showed much improved chemical stabilities than pure Ag nanorods. Furthermore, those Au@Ag NRs exhibited sharper, stronger and shorter-wavelengthed longitudinal plasmon absorption than Au NRs [23]. In addition, Au@Ag NRs possesses good biocompatibility, which was studied in our earlier work [24]. As a consequence, Au@Ag NRs may be an attractive alternative of contrast agent and therapeutic agent for PAT and PTT in biological tissue.

Moreover, conjugated with antibodies and natural property of enhanced permeability and retention (EPR) effect also make them ideal contrast and therapeutic agents for applications [19, 25–28]. Nanorods are especially attractive candidates since their per unit volume of absorption cross-section are much higher than most other types of nanoparticles, including nanoshells [29, 30].

Here, we introduce the use of Au@Ag NRs as a new dual-functional agent for PAT and PTT. Arginine-glycine-aspartic acid peptides were conjugated to Au@Ag NRs (RGD-Au@Ag NRs) for actively targeting the breast tumor. To estimate the impact of different volume of Ag⁺ on PAT, three different thicknesses of the Ag shells were synthesized and performed under the same circumstances through all the studies. The performances of these RGD-Au@Ag NRs in PAT were compared directly with those of RGD-conjugated gold nanorods (RGD-Au NRs). The PAT signal amplitude of every material in the region of interests was extracted and investigated. Both in the phantom and in vivo imaging efficacy of Au@Ag NRs were radically enhanced relative to those of Au NRs. Moreover, due to the high energy conversion efficiency, the temperature of tumor site injected with Au@Ag NRs increased the most. Our results demonstrated that Au@Ag NRs could serve as an effectively dual-functional agent for both PAT and PTT. Benefits from using this contrast agent include high enhancement in PAT, reduction of side effects and less damage to healthy tissues. This may offer possibility to imaging-guided, customized cancer treatment.

2. Methods

2.1 Chemicals

Cetyltrimethylammonium bromide (CTAB), H₂SO₄, chloroaurosic acid, NaBH₄, AgNO₃, L-ascorbic acid (AA) and NaOH were purchased from Sinopharm Chemical Reagent Co., Ltd. (Shanghai, China). Thiolated polyethylene glycol (PEG, molecular weight 5000) was purchased from Shanghai Yare Biotech, Inc (Shanghai, China). The RGD peptides were purchased from China Peptides Co., Ltd (Shanghai, China). Deionized water (Millipore Milli-Q grade) with a resistivity of 18.2 MΩ was used in all experiments.

2.2 Optimized synthesis of Au NRs

The synthesis of Au NRs was prepared according to the seed-mediated method [31, 32]. The seed solution was synthesized first. Briefly, chloroaurosic acid (5mL, 0.5 mM) was slowly mixed with CTAB solution (5mL, 0.2 M). Then ice-cold NaBH₄ (0.6 mL, 10 mM) was quickly added to the mixture under vigorous stirring. Reaction of this mixture for 3 min resulted in the formation of a brownish-yellow seed solution. For the growth solution, CTAB solution (100 mL, 0.1 M) was first mixed with AgNO₃ (1.2 mL, 0.01 M), followed by chloroaurosic acid (5 mL, 0.01 M), AA (0.8 mL, 0.1 M), H₂SO₄ (2 mL, 0.5 M), and a portion of seed solution (250 μL). Finally, the resulting solution was allowed to incubate at 30°C
over a period of 20 h. The as-prepared Au NRs were used to prepare the Au@Ag NRs directly. Another kind of Au NRs, as the control solution, were obtained through the same way but changing the dosage of AgNO₃.

2.3 Synthesis of Au@Ag NRs

The preparation of Au@Ag NRs were based on the seed-mediated growth method [33, 34]. First, 36 mL of the as-prepared Au NRs solution was centrifuged twice at 9600 rpm for 25 min. The pellets were redispersed in 18 mL of deionized water and added to 90 mL of 0.04 M CTAB. After that, 650 μL of 0.1 M AA, various volumes (0 to 400 μL) of 0.01 M AgNO₃, 1.45 mL of 0.1 M NaOH solution were added to the mixture under strong stirring. The colour of the solution changed quickly from red to brown or green, suggesting the formation of Au@Ag NRs with varying thicknesses of Ag shell. The thicknesses of Ag shells were confirmed by TEM which was about 1.2 nm, 2.3 nm, 3.2 nm, respectively. To ensure the amount of Au@Ag NRs in each sample was the same to that of the initial Au NRs sample, all the Au@Ag NRs samples were concentrated to 18 mL before further use.

2.4 Preparation of RGD-conjugated Au@Ag NRs and Au NRs

All of the as-prepared Au@Ag NRs and Au NRs solutions were centrifuged twice at 9600 rpm for 25 min. The pellets were redispersed in 40 mL of deionized water and mixed with 10 mg mL⁻¹ of thiolated PEG for 2 h. Finally, the encapsulated nanoparticles were washed 2 times by centrifugation, resuspended in PBS, and stored at 4°C. The (ACDCRGDCFCG) RGD peptides were covalently attached to the outer ends of the PEG-GNRs via amide bonds, using the standard EDC-NHS reaction [35, 36]. A solution of RGD in deionized water was added to a volume of PEGylated Au@Ag NRs and Au NRs to react for 3 hours and excess RGD peptides were removed by centrifugation at 10000 rpm for 10 minutes. The RGD-GNRs were dispersed in PBS and stored at 4°C for further use.

2.5 Characterization

Au@Ag NRs and Au NRs samples were characterized by TEM (JEM-2100F, JEOL, Japan) operating at 200 kV. The samples were placed on carbon coated copper grids. UV–VIS absorbance spectra were measured with a UV-VIS spectrophotometer (Cary-100, Agilent, America) in the wavelength range from 400 to 900 nm. Fluorescence images were obtained using an IVIS Spectrum Pre-clinical in Vivo Imaging System (Hitachi, Tokyo, Japan).

2.6 Animal preparation

The mouse breast tumor model used in this study was developed on female nude mice purchased from Peking University Laboratory Animal Center. We used breast tumor cell line 4T1 in the PTT experiment and cell line 4T1-LUC in the fluorescent experiment. And 4T1 cells were cultured in Roswell Park Memorial Institute (RPMI) 1640 (HyClone, Thermo Scientific, USA) supplemented with 10% foetal calf serum (FCS; HyClone, Thermo Scientific) and were maintained at 37°C in 5% CO₂. The mice were 6 to 8 weeks of age and weighed an average of 18 g. When the tumors reached about 7 mm in diameter, these tumor-bearing mice were divided into 4 groups (3 mice each group) for PA imaging study. Mice in group 1 received a tail vein injection of 0.2 mL of 2 mg mL⁻¹ of Au@Ag NRs whose shell thickness was 1.2 nm. Mice in group 2 received a tail vein injection of 0.2 mL of 2 mg mL⁻¹ Au@Ag NRs whose shell thickness was 2.3 nm. Mice in group 3 received a tail vein injection of 0.2 mL of 2 mg mL⁻¹ Au@Ag NRs whose shell thickness was 3.2 nm. As control group, mice in group 4 received a tail vein injection of 0.2 mL of 0.2 mL of 2 mg mL⁻¹ of Au NRs. Three other groups of tumor-bearing mice (3 mice each group) were used for PTT study. In the treatment groups, mice were intravenously injected with 200 μL of Au@Ag NRs or Au NRs (2 mg mL⁻¹). After 24 h, they were irradiated with an 808 nm laser at a power...
density of 2.0 W cm$^{-2}$ for 8 min. In the control group, mice were subjected to an 808 nm laser irradiation with injection of PBS. After irradiation, all the tumors were effectively ablated and black scars were left at the original tumor sites. In vivo therapeutic efficacy of Au@Ag NRs and Au NRs was assessed by monitoring another two groups of mice, bearing tumors with luciferase. They received PTT 24 h after injection of Au@Ag NRs and Au NRs. The fluorescent scans were recorded on an IVIS Spectrum Pre-clinical in Vivo Imaging System. All animal experiments were in agreement with the guidelines of The National Regulation of China for Care and Use of Laboratory Animals.

2.7 PTT in vivo

Real-time thermal imaging of samples were recorded using a thermal camera (FLIR, Arlington, VA) and quantified by FLIR Examiner software (Examin IR image software, FLIR). These temperatures were measured at a single point where the cross icons in the FLIR images appeared. And the temperatures were recorded directly according to the thermal camera.

2.8 PAT in phantom and in vivo

All phantom and in vivo mouse imaging studies were carried on using a real-time multispectral PAT imaging system (in Vision 128, iThera Medical GmbH, Neuerberg, Germany) [37]. An optical parametric oscillator, operating from 680 nm to 980 nm, was used in PAT through all the experiments. It was pumped by a Q-switched Nd:YAG laser, with a 10-ns pulse duration and a 10-Hz repetition rate. Light was directed into a fiber bundle containing 10 individual fibers. PA signals were obtained using a 128-element concave transducer array spanning a circular arc of 270°. The phantom is made of polyurethane with a cylindrical shape. It is designed to mimic the shape, size and optical properties of the mouse. Besides, there are 2 inner cylindrical channels in the phantom, about 3 mm in diameter. As shown in Fig. 2(f), One was filled with deionized water while the other with dilute contrast agents. The 8 laser excitation wavelengths of 710 nm, 730 nm, 745 nm, 760 nm, 810 nm, 840 nm, 860 nm and 900 nm were selected for absorption spectra of the contrast agents in vitro and in vivo. As to in vitro imaging, the PAT images of each contrast agent were obtained under the nearest wavelength of their longitudinal absorption bands. As to in vivo imaging, ultrasound gel was applied onto the mouse skin. An animal holder with a thin plastic film was used to prevent the direct contact between the mouse and the water. The PAT imaging was recorded at the time point of pre-injection, 1 h, 3 h, 5 h, 7 h and 24 h after injection of the contrast agents, with a step size of 0.5 mm spanning from the chest to the lower limbs. After image reconstruction, multispectral processing of the images was carried on according to a model-based approach [37]. And the entire tumor site was selected for analyzing the intensity of PAT signal. For the selected region, the PAT signal was summed and averaged. Data analysis was performed by using Microsoft Excel 2010 and a p value of <0.01 was considered statistically significant. Difference of measurement data was compared with ANOVO.

3. Results and discussion

Au@Ag NRs with three different shell thicknesses were synthesized. The transmission electron microscope (TEM) analysis confirmed the thicknesses of Ag shells were about 1.2 nm (the length of Au@Ag NRs: about 58.1 nm; the width of Au@Ag NRs: about 18.1 nm), 2.3 nm (the length of Au@Ag NRs: about 60.0 nm; the width of Au@Ag NRs: about 21.1 nm) and 3.2 nm (the length of Au@Ag NRs: about 56.5 nm; the width of Au@Ag NRs: about 18.8 nm) (Fig. 1(b)-1(d)), while the length of Au NRs was about 59.4 nm and the width about 18 nm. With the help of TEM, elementary mapping was carried on the sample of Au@Ag NRs with the thickest shell. As can be seen in Fig. 1(e), the red curve represented...
the elementary of gold, while the cyanic curve represented the elementary of silver. The two peaks (white arrows) of the cyanic curve occurred at the two sides of the peak of the red curve, indicating that silver was around gold.

With the increasing amount of AgNO₃ and L-ascorbic acid (AA), the longitudinal absorption bands of Au@Ag NRs gradually blue-shifted. TEM images and measured UV-VIS spectrum of the synthesized Au@Ag NRs and Au NRs are shown in Fig. 1. As shown in Fig. 1(f), the localized surface plasmon resonance (LSPR) of Au@Ag NRs located at 736 nm (Au@Ag NRs / 3.2 nm), 770 nm (Au@Ag NRs / 2.3 nm) and 845 nm (Au@Ag NRs / 1.2 nm) for three different shell thicknesses, respectively. While the LSPR of Au NRs located at 770 nm.

To verify the PAT activity of these different contrast agents, we performed phantom experiments for all of them first. The phantom had a cylindrical body and a conical forepart (Fig. 2(a)). It contained 2 cylindrical channels in which contrast agents and a control agent could be injected to measure the PAT signal.

From Fig. 2(b)-2(e), all of the three Au@Ag NRs showed an enhanced brightness compared to Au NRs. It might be noted that, with increasing shell thickness, the brightness of the edge rose quickly while it attenuated rapidly around the center site. It is possibly due to the heterogeneous light fluence distributions in the PAT imaging [38, 39]. The relative PAT signal is a combination of the optical absorption coefficient and the fluence of local light. In this case, the absorption on the edge was too strong resulting in poor light fluence in the center site. And it resulted in fluence-related errors which can render in accurate photoacoustic spectroscopy both in terms of quantity and quality [38].

Since the problem of heterogeneous light fluence distributions, three different regions in the edge of the channels containing contrast agents were selected for analyzing the PAT signal intensity (Fig. 2(f)). Figure 2(f) is the enlarged picture of Fig. 2(d), showing the region of interests. As could be seen from Fig. 2(g), we found that the average PA signal amplitude were 2.65x10⁴ for Au NRs, 3.09x10⁴ for Au@Ag NRs / 1.2 nm, 3.47x10⁴ for Au@Ag NRs / 2.3 nm and 3.85x10⁴ for Au@Ag NRs / 3.2 nm. That means the PAT signal of Au@Ag NRs /
1.2 nm grew by 16.6% compared to that of Au NRs. This figure climbed to 30.9% and 45.3% for Au@Ag NRs / 2.3 nm and Au@Ag NRs / 3.2 nm, respectively. Through statistical analysis, there are significant difference between Au@Ag NRs groups and Au NRs group (p value < 0.05).

Encouraged by the promising results of in vitro effect of Au@Ag NRs, we then investigated the accumulation of these different contrast agents at the time point of pre-injection, 1 h, 3 h, 5 h, 7 h and 24 h after injection using PAT (Fig. 3(e)). The PA signal enhanced significantly at the time point of 1 h in all cases of Au@Ag NRs, meanwhile the highest signal level of Au NRs appeared on the 7th hour. As for Au@Ag NRs / 3.2 nm, the average PAT signal intensity had a 153%-increase as that observed before injection. When it comes to Au@Ag NRs / 2.3 nm and Au@Ag NRs / 1.2 nm, the figures were 61% and 59%. Figure 3(e) led to the conclusion that with the Au@Ag NRs treatment, significant contrast enhancement was observed about 1 h after application of nanoparticles, which was 6 h earlier than that in the Au NRs group.

The phenomenon is probably due to chemical instability of silver. There is a broad agreement that silver nanoparticles can be oxidized in aqueous solutions, resulting in the release of silver ions [40–42]. Several groups have reported the impact of size, surface conjugation, temperature, pH etc. on the dissolution behavior of silver nanoparticles [41–43]. They also found that a PEGylation coating on the nanoparticles did not protect them against...
these reactions [40]. We assume that after intravenously injected with Au@Ag NRs, silver ions were stimulated by lysosomes resulting in the dissolution of Ag shell. As shown in Fig. 3(e), the PAT signals of Au@Ag NRs / 1.2 nm and Au@Ag NRs / 2.3 nm plunged to almost the similar level as that of Au NRs 7 h after injection. It is probably that, at that time, part of the Ag shell had already been dissolved. Moreover, thinner shell thickness should dissolve faster than thicker one [42]. That’s why the PAT signal of Au@Ag NRs / 3.2 nm still maintain at a high level after 7 h of treatment. The in vivo degradation of the silver coating is a limitation of this construction of the nanoparticles.

Here we only show the images of tumor acquired at time points with the highest PAT signal level according to Fig. 3(e), that is, the images acquired at 1 h after injection for all Au@Ag NRs, and the images acquired at 7 h for Au NRs (Fig. 3(a)-3(d)). As can be seen from Fig. 3(d), Au@Ag NRs / 3.2 nm showed the strongest PAT signal in the tumor site. The entire tumor site was selected for analyzing the intensity of PAT signal. As for the maximum PAT signal intensity of Au NRs (at 7 h) and Au@Ag NRs (at 1 h), we found that the average PA amplitude were 6.76x10^3 for Au NRs, 7.487x10^3 for Au@Ag NRs / 1.2 nm, 8.90x10^3 for Au@Ag NRs / 2.3 nm and 1.2267x10^4 for Au@Ag NRs / 3.2 nm. From the illustration, it can be concluded that the value of Au@Ag NRs / 3.2 nm increased by 82.0%, Au@Ag NRs / 2.3 nm by 31.7% and Au@Ag NRs / 1.2 nm by 10.8% (Fig. 3(f)). Through statistical analysis, there are significant difference between Au@Ag NRs groups and Au NRs group (p value < 0.05).

RGD functionalized nanoparticles actually presented one of the successful examples for efficient tracking vascular cells inside tumor tissues. The RGD peptide used in this study has a restrained RGD sequence that binds specifically and with high affinity to αVβ3 integrin [44, 45]. Li et al found that the RGD-nanoparticle system could rapidly distribute into the whole body of mice with tumors through circulatory system, and then gradually accumulated in the tumor tissue [46]. Since the targeting specificity had been studied by several groups, we didn’t evaluate it in this study.

Both silver and gold nanoparticles are commonly employed in biomedical imaging and therapy. The plasmon excitation efficiency of silver nanoparticles is known to be even more pronounced than that of gold nanoparticles, as shown with their stronger, sharper plasmon resonance peaks at the same particle concentration [22, 47]. Silver nanoparticles thus can render better sensitivity for biomedical applications.

Throughout the whole experiment, Au@Ag NRs treated mice reveals stronger PAT signals when compared to the Au NRs group. In addition, the Au@Ag NRs with the thickest shell thickness gave the strongest signal enhancement of PAT. This is probably due to the better optical absorbing properties of silver. However, the shell thickness is a double-edged sword. Thicker shell made the LSPR extinction spectrum blue-shifted. One should make sure that the LSPR of Au@Ag NRs does not exceed the wavelength range of the PAT system. In conclusion, owing to the better optical properties of Ag shell, Au@Ag NRs are well suited as PAT contrast agents. In other words, Au@Ag NRs can render better images with shorter time.
Twenty-four hours after injection, the Au@Ag NRs-induced PTT effect in vivo was studied. To evaluate the efficiency of PTT treated with Au@Ag NRs and Au NRs, the mice injected with Au@Ag NRs /2.3nm and Au NRs which had the same LSPR absorption spectrum (Fig. 1(f)) were exposed to an 808 nm laser at 2.0 W cm$^{-2}$ for 8 min. The temperature of tumor tissue injected with Au@Ag NRs / 2.3nm rose rapidly over 57°C (Fig. 4(c)), which is more than the threshold of temperature of 54 °C needed for irreversible cell damage [8]. In contrast, the temperature of tumors with Au NRs or saline injection increased to 46.4 °C and 41.5 °C, respectively, which were insufficient to induce irreversible cell damage (Fig. 4(a)-4(b)).

Under the same laser intensity and exposure time, the efficiency of photothermal heating of Au@Ag NRs/2.3nm is much higher than that of Au NRs (Fig. 4(d)), producing an about 23 °C temperature rise. The temperature change of Au@Ag NRs/2.3nm was twice as that of Au NRs. This means that with less laser dosage and irradiation time, the normal tissue is well protected by using Au@Ag NRs. These results suggest that Au@Ag NRs can be used as more efficient photoabsorbers for PTT.
To assess the in vivo therapeutic efficacy of Au@Ag NRs and Au NRs, we monitored another two groups of mice bearing tumors with luciferase. They were received PTT after 24 h injection of Au@Ag NRs and Au NRs. The fluorescent scans were recorded on an IVIS Spectrum Pre-clinical in Vivo Imaging System. Before injection, intense fluorescence signal was observed in the tumor site (Fig. 5(a), 5(e)). One day after laser irradiation (Fig. 5(b), 5(f)), almost no fluorescent signal from the tumor sites was observed in both groups of mice. However, from the fourth day, weak fluorescence was detected in the tumor site again (Fig. 5(c), 5(g)). The fluorescent signal further enhanced on the seventh day (Fig. 5(d), 5(h)), implying the tumor reoccurrence.

It can be seen that using Au@Ag NRs have a better therapeutic effect on cancer treatment. In the same period of time, the fluorescent area and the severity of reoccurrence are always mild in the case of Au@Ag NRs (Fig. 5(b) and 5(f), 5(c) and 5(g)). The reoccurrence of tumor may come from several factors, e.g., single PTT treatment, non-optimization of the treating parameters, and/or contrast agents’ delivery. It is possible that repeated PTT or the optimization of treating and contrast agents’ parameters such as irradiation time, power density, concentration or size of Au@Ag NRs etc. may efficiently improve the therapy prognosis [48]. Furthermore, it is likely that if we performed PTT at the time point when Au@Ag NRs accumulated most in the tumor site, the therapeutic efficacy may be improved as well. We only discuss the feasibility of using Au@Ag NRs as therapeutic agents in this study. Many parameters in the photothermal experiment are still waiting for optimization. In general, these evidences could support that RGD-Au@Ag NRs can be used as a dual-functional contrast agent for PA imaging and PTT. This may further give chances to PA imaging-guided, customized tumor therapy. It should be further investigated.
Fig. 5. In vivo fluorescent images of tumor-bearing mice before and after PTT. Fluorescent images of tumor-bearing mice injected with Au@Ag NRs a) before laser irradiation. b) 1 day after laser irradiation. c) 4 days after laser irradiation. d) 7 days after laser irradiation. Fluorescent images of tumor-bearing mice injected with Au NRs e) before laser irradiation. f) 1 day after laser irradiation. g) 4 days after laser irradiation. h) 7 days after laser irradiation.

4. Conclusion

In summary, uniform and monodispersed Au@Ag NRs were successfully applied for PA imaging and PTT. We compared the contrast enhancement and heat absorption of Au@Ag NRs with Au NRs, and demonstrated that Au@Ag NRs could serve as an effective dual-model agent for both PA imaging and PTT. In addition, the biocompatibility of Au@Ag NRs were studied in our earlier work, thus making them promising candidates for use in biomedical applications. And it provides new possibility for image-guided customized treatment of cancer through the development and intervention of proper dual-functional agents.

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