Dual-Modal Computed Tomography/Fluorescence Nanoemulsion Platform Composed of Iodinated Oil Injection and Indocyanine Green for Tumor Diagnosis

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A kind of X-ray computed tomography (CT)/fluorescence dual-modal nanoemulsion probe that combined both CT imaging and near-infrared fluorescent (NIRF) imaging abilities was developed for application in tumor diagnosis. In this study, NIRF molecule indocyanine green (ICG-Der-01), a kind of hydrophobic dye, was encapsulated in clinic CT contrast agent of iodinated oil injection based on oil-in-water nanoemulsion platform. The obtained ICG-iodinated oil nanoemulsion exhibited excellent CT and fluorescence capabilities. In vitro studies revealed that this nanoemulsion could serve as an effective dual-modal probe by Micro-CT and confocal microscopy imaging of murine macrophage cells and mouse breast tumor cells without obvious cytotoxicity. Then in vivo clinical CT and NIRF imaging results suggested the nanoemulsion could accumulate in tumor by the enhanced permeation and retention (EPR) effect and visualize tumor tissues in living body. All these results demonstrated the ICG-iodinated oil nanoemulsion had great potential in tumor diagnosis by dual-modal CT/fluorescence imaging in future.

Keywords: ICG-Iodinated Oil Nanoemulsion, Tumor, EPR Effect, CT Imaging, Fluorescence Imaging.

1. INTRODUCTION

Molecular imaging techniques such as positron emission tomography (PET), magnetic resonance imaging (MRI), X-ray computed tomography (CT) and optical near-infrared fluorescence (NIRF) imaging are more and more important in clinical diagnosis and therapeutics. However, different imaging modalities have their own advantages and disadvantages. A single imaging modality can’t provide comprehensive diagnostic information and meet all requirements in spatial and temporal resolution, sensitivity, noninvasive, 3D reconstruction, depth penetration, short imaging time and low cost.1,2 Therefore, a powerful way to combine two or more imaging modalities into single integrated multimodal imaging system or blend both therapeutic and diagnostic materials within a single nanoparticle arises.3,4 Meanwhile, the corresponding multimodal contrast agents are also aroused researchers’ concern.

The combination of nanotechnology and molecular imaging causes active development in multimodal nanoparticles that incorporate multiple imaging probes. Thus, numerous multimodal contrast agents are generated for early cancer detection, tumor-target drug delivery, as well as monitoring therapy. A theranostic nanoemulsion carrying iron oxide nanoparticle, fluorescent dye Cy7, and anti-cancer drug is developed for MRI/fluorescence imaging and therapy.5 FePt alloy nanoparticles conjugated with antibody can serve as a CT/MRI dual modality contrast agent for tumor targeting imaging.6 A conjugated polymer based on fluorescent-magnetic nanoparticle has been applied for in vivo NIRF and MRI.7

CT scanning with contrast agents remains routine imaging modality in terms of its efficiency and cost. Most present CT contrast agents are based on small iodinated molecules, due to its high X-ray absorption.8,9 Iodinated
oil injection (Lipiodol), an iodinated derivative of poppy seed oil, is a lipophilic agent for clinical use with iodine concentration of 480 mg/ml. Iodinated oil injection has been employed as a CT contrast agent, intravascular embolic agent and lymphographic contrast medium. But there are significant limitations, including short imaging time, rapid renal clearance, non-specific targeting.10–13 Nanotechnology is a good method to solve these problems. Previously, iodinated oil injection was used as a dispersion medium to deliver anti-cancer drug like styrenemaleic acid neocarzinostatin (SMANCS).12 And, iodinated oil injection was also applied to load materials for imaging such as Lipiodol-encapsulating Pluronic/PEG nanocapsules.11 Our previous studies also indicated that CdSe/ZnS quantum dots doped iodinated oil nanoemulsion could serve as a dual-modal CT/fluorescence contrast agent and specifically target to macrophages and thus visualize atherosclerotic plaques.14 However, the potential toxicity of the quantum dots may limit its further clinical application.

With development of NIF probes, optical NIF imaging technology expands rapidly in tumor diagnosis, immunoassays and cell labeling, and even in vivo real-time tracing of biological signals with high sensitivity. The wavelength range of NIF is 700–1200 nm, which can penetrate the deeper tissue and possess relatively low auto-fluorescence compared to visible light. Moreover, it is relatively easy to operate, noninvasive, efficient and low cost. But it is still limited to the penetration of light, non-specific fluorescence interference and low spatial resolution.2, 15–17

Fluorescence dyes and quantum dots (QDs) act as two major classes of NIF probes and have been developed for disease detection in vitro and in vivo. Among the organic fluorescence dyes, indocyanine green (ICG) is one of the most important types used in biomedicine. ICG is the only NIF molecule approved by Food and Drug Administration (FDA) for human imaging. It is clinically used for retinal angiography, liver function tests, cardiac and hepatic blood flow measurement. Lipid nanoparticles loaded with ICG is used to label tumors and lymph nodes.18 Many research groups are focused on the synthesis of ICG derivatives for potential application. For example, ICG-Der-01 is a hydrophobic ICG derivatives with maximum absorption at 783 nm and emission peak at 813 nm.16, 17 Folate-PEG16 or Folate-decorated N-succinyl-N’-octyl chitosan (folate-SOC)17 conjugated ICG-Der-01 are successfully synthesized with high targeting affinity and sensitivity for in vivo early folate receptor (FR) over-expressed tumor diagnosis.

Hence, CT and NIF probes are particularly suitable to combine together to realize advantageous complementarities with both the high spatial resolution of CT and high sensitivity of NIF imaging. Here, a CT/fluorescence dual-modal nanoparticle platform is prepared based on oil-in-water nanoemulsion technique5, 14, 19 and carries iodinated oil injection for CT imaging and fluorescence dye ICG-Der-01 for NIRF imaging. For free ICG, the rapid clearance from the body and fluorescence quenching in physiological environments lead to the relatively short circulation time and thus low accumulation in tumor tissue. Encapsulating ICG into oil phase can prevent its degradation and rapid clearance and thus increase its stability and target capability. The CT/fluorescence potentialities are explored for the probe itself and the co-incubated cells. When injected intravenously, the enhanced permeation and retention (EPR) effect allows the penetration of the ICG-iodinated oil nanoemulsion to accumulate in tumor tissue, and the underdevelopment of lymph vessels prevents the excretion of nanoemulsion droplets, resulting thus in passive targeting to tumor and subsequent dual-modal CT/Fluorescence imaging for investigating tumor. The nanoemulsion is a very practical design with complementary imaging function and excellent druggability due to reasonable material selection acceptable in clinical application. So CT/fluorescence properties in vitro and in vivo are evaluated in the following exploration.

2. MATERIALS AND METHODS

2.1. Materials

Polyoxyethylene glycol monostearate (Aladdin), ICG-Der-01 of 805 nm emission wavelength (China Pharmaceutical University, China), Iodinated oil injection (Guerbet, France), Lipoid E-80 (Lipoid, German), Cell counting kit (CCK-8 or WST-8, KeyGEN Biotech, China), DMEM (Gibco, USA), RPMI-1640 (Gibco, USA), Fetal calf serum (Hangzhou SIJIQING Biotechnology Company, China), Apoptotic Cell DAPI Detection Kit (KeyGEN Biotech, China), Iodinated oil injection. The mixture was heated to 70°C using a tip (VCX750, Sonics, USA) to form a uniform nanoemulsion.

2.2. Preparation of Oil-in-Water ICG-Iodinated Oil Nanoemulsion

2 mg ICG-Der-01 of 805 nm emission wavelength was dissolved in 5 ml chloroform, and then mixed with 500 μl iodinated oil injection. The mixture was heated to 70°C to remove chloroform. 200 mg Lipoid E-80 was dissolved in 200 μl ethanol. 250 mg Polyoxyethylene glycol monostearate was dispersed in 20 ml distilled water. Subsequently, the Lipoid solution and the mixture were added into the above-mentioned boiling water dropwise under continuous stirring. The preparation was concentrated to 10 ml which named crude emulsion. Finally, the crude emulsion was homogenized for 15 min using a sonicator tip (VCX750, Sonics, USA) to form a uniform nanoemulsion. The ICG-iodinated oil nanoemulsion was stored in dark at 4°C.
2.3. Characterization of ICG-Iodinated Oil Nanoemulsion

The morphology of ICG-iodinated oil nanoemulsion was observed by transmission electron microscopy (TEM) (JEM-2100, JEOL, Japan) with a working voltage of 200 kV. TEM was performed on the ICG-iodinated oil nanoemulsion diluted 1:100 in distilled water after negatively stained by 2% sodium phosphotungstate (PH = 7.0).20 A dynamic light scattering (DLS) device (Brookhaven-Zetaplus, Brookhaven, UK) was used. After 1:100 diluted, 2 ml ICG-iodinated oil nanoemulsion was taken to measure the hydrodynamic size.

2.4. Optical Property and Stability of ICG-Iodinated Oil Nanoemulsion

UV-Vis Spectrophotometer (UV3000, Shimadzu, Japan) was used to measure the absorbance of ICG-iodinated oil nanoemulsion. Also, fluorescence spectrometer (F-7000, Hitachi, Japan) equipped with a xenon lamp was used to test fluorescence signals of the nanoemulsion with 400 V working voltage, the excitation wavelength was 725 nm. UV-Vis and fluorescence spectra were recorded on both ICG-iodinated oil nanoemulsion and free ICG-Der-01.

2.5. In Vitro Micro-CT Imaging

The ICG-iodinated oil nanoemulsion with different iodine concentration (24, 12, 6, 3, 0 mg/ml) were scanned by a micro-CT imaging system (Hiscan MCT-1108, HEJUN, Suzhou) with following parameters: tube voltage, 40 kV; working voltage, the excitation wavelength was 120 mA.

2.6. Fluorescence Imaging of the ICG-Iodinated Oil Nanoemulsion

In vitro fluorescence of ICG-iodinated oil nanoemulsion with 805 nm emission wavelength was detected by both near-infrared fluorescence imaging system (Maestro2.10.0, CRI, USA) and confocal laser scanning microscope (LSCM) (F1000, Olympus, Japan). After 1:10 diluted, 1 ml ICG-iodinated oil nanoemulsion was absorbed into 1.5 ml eppendorf tube, 1 ml distilled water was set as control. These two samples were put together under the near-infrared fluorescence imaging system using a 704 nm excitation filter and a NIR emission filter. A drop of the diluted nanoemulsion was taken to a clean glass slide. After the droplet dried, the glass slide was laid under the confocal microscope with a 647 nm excitation wavelength and the camera was chosen with a 688 nm filter.

2.7. Cell Culture

The PRMI-1640 and DEME medium supplemented with 10% FBS and 1% penicillin-streptomycin were used as cell culture medium. Mouse breast cancer cell line (4T1 cells) and murine macrophage cell line (RAW264.7 cells) were incubated in a humidified atmosphere with 5% CO₂ at 37 °C.

2.8. Cytotoxicity of ICG-Iodinated Oil Nanoemulsion

CCK-8 assay21 was conducted to assess the cytotoxicity of ICG-iodinated oil nanoemulsion. 4T1 cells in PRMI-1640 medium and RAW264.7 cells in DEME medium were seeded into 96-well plates (4 × 10³ cells/well) and incubated for 24 h. The culture medium was removed and added by 100 μl fresh medium containing ICG-iodinated oil with different concentration, iodine concentration ranged from 7.5 to 240 μg/ml. After 24 h incubation, 10 μl CCK-8 assay was added into each well, then the cells continued in incubator for 2 h. A microplate reader (Model 680, Bio-rad, USA) was used to measure the optical density (OD) at 450 nm.

2.9. In Vitro Micro-CT Imaging of Cells

4T1 cells and RAW264.7 cells were incubated with ICG-iodinated oil nanoemulsion with 600 μg/ml iodine concentration for 8 h at 37 °C. The cells were washed with PBS buffer three times to wash out unendocytosed nanoemulsion before trypsinization. After centrifuged at 1000–1500 rpm for 5 min, the cells were respectively transferred to 1.5 ml eppendorf tubes and centrifuged again. The tubes were put on the holder and imaged by Micro-CT with following parameters: tube voltage, 40 kV; current intensity, 120 mA. Using the 3D data analysis mode on the Micro-CT system workstation named Hiscan (HEJUN, Suzhou), images were reconstructed.

2.10. Fluorescence Confocal Imaging of Cells

4T1 cells and RAW264.7 cells were incubated with ICG-iodinated oil nanoemulsion containing 600 μg/ml iodine concentration for 4 h. Then the medium was replaced by 2 ml fresh medium with ICG-iodinated oil nanoemulsion (240 μg/ml of iodine concentration). The cells were then incubated again for 4 h. PBS solution was used to wash the ICG-iodinated oil nanoemulsion treated cells for three times to remove unendocytosed nanoemulsion. Then the cells were stained with DAPI (nuclei specific, blue, emission 460 nm) for 10 min. After washed thrice with PBS, cellular fluorescence was observed under 408 nm and 647 nm laser excitation.

2.11. Animal and Tumor Model

Female Balb/c mice (4–6 weeks) were purchased from Model Animal Research Center of Nanjing University (Nanjing, China). All animal experiments were carried out in accordance with the Animal Management Rules of Health of the People’s Republic of China and the guidelines for the Care and Use of the Southeast University Laboratory Animal Center. To setup the breast tumor model, 2 × 10⁶ 4T1 cells were subcutaneously injected into the
right hind flank of each mouse. When the tumor volume reached about 50–100 mm³ after a week, the mice were divided into two groups respectively for CT imaging and fluorescence imaging.²²

2.12. In Vivo Animal Studies of the ICG-Iodinated Oil Nanoemulsion by CT Imaging

A clinical CT-64 (SOMATOM Emotion Definition As, Siemens, German) was used to estimate in vivo CT efficacy of the nanoemulsion because macrophages in tumor could nonspecifically uptake the nanoparticles. After pre-scanned, 0.2 ml ICG-iodinated oil nanoemulsion (240 μg iodine/g body weight) was injected into each mouse of CT group (n = 5). The mice were labeled as Nos. 1–5. Then a series of images were taken at pre-injection and 10 min, 30 min, 1 h, 1.5 h, 2 h post-injection. Mouse No. 3 died in the experiment. The whole process was accomplished with following parameters: tube voltage, 110 kV; current intensity, 40 mAs.

2.13. In Vivo Distributing and Tumor Accumulation of ICG-Iodinated Oil Nanoemulsion

To trace in vivo fluorescence bio-distribution, ICG-iodinated oil nanoemulsion was injected into the fluorescence group (n = 3) via tail vein. Each mouse was injected 0.2 ml. Images were obtain at different time point (1 min, 2 h, 4 h and 6 h after injection) using the Maestro in vivo imaging system. 6 h after injection, the mice were killed the organs like heart, liver, spleen, lung, kidney and tumor were collected and analyzed by the Maestro. The parameters were as follows: a magnification of ×2, a wavelength of 704 nm and a NIR emission filter.

3. RESULTS AND DISCUSSION

3.1. Preparation and Characterization of the ICG-Iodinated Oil Nanoemulsion

ICG-iodinated oil nanoemulsion was prepared through stirring and ultrasonication emulsification as shown in Figure 1. Water phase consisted of distilled water and mixed surfactant including polyoxyethylene glycol monostearate and lipoid E-80. Oil phase was the mixture of ICG-Der-01 containing chloroform solution and iodinated oil injection. Under vigorous stirring, ICG-Der-01 was encapsulated into iodinated oil with chloroform evaporated and the surfactant formed a corona around the iodinated oil core. Subsequently, the significant step sonication was performed to make the nanoemulsion smaller and uniform. The mean hydrodynamic diameter of the ICG-iodinated oil nanoemulsion was 52.6 nm (Fig. 2(a)), which was small enough for uptake by cells.⁵ ¹⁄₂ TEM image (Fig. 2(b)) showed that the ICG-iodinated oil nanoemulsion was dispersed as individual spherical droplets and homogeneously distributed.

The ICG-iodinated oil nanoemulsion and the free ICG-Der-01 solution were also characterized by UV-Vis absorption spectrum and fluorescence spectrum analysis,
as shown in Figure 3. The UV-Vis absorption spectrum (Fig. 3(a)) of ICG-iodinated oil nanoemulsion and ICG-Der-01 was almost the same (absorption peaks at 795 nm and 780 nm). It was inferred that the ICG-Der-01 was included in the synthesized nanoemulsion. Then, the fluorescence intensity of ICG-iodinated oil nanoemulsion and ICG-Der-01 dye was compared (Fig. 3(b)). When excited with 725 nm light, the fluorescence signal of the nanoemulsion was observed with maximum emission wavelength of 802 nm, which was consistent with free ICG-Der-01 dye with emission wavelength at 805 nm.

3.2. Micro-CT and Fluorescence Imaging of the ICG-Iodinated Oil Nanoemulsion

The ability of ICG-iodinated oil nanoemulsion to serve as a CT contrast agent was investigated though five different iodine concentration (24, 12, 6, 3, 0 = distilled water mg/ml) samples. The CT contrast enhancement efficiency was iodine-dependent. With the increase of iodine concentration, images got brighter and brighter, the nanoemulsion showed gradual CT contrast enhancement (Fig. 4).

Fluorescence properties of the nanoemulsion was characterized by near-infrared fluorescence (NIRF) imaging system and confocal laser scanning microscopy (LSCM). Figure 5(a) showed that the 1:10 diluted ICG-iodinated oil nanoemulsion still had noticeable red fluorescence compared to the control distilled water. From LSCM image (Fig. 5(b)), there were lots of dispersive fluorescence dots owing to the ICG-Der-01’s fluorescence, demonstrating ICG-Der-01 dyes were imbedded in iodinated oil nanoemulsion droplets. Because point light would form an enlarged image due to diffraction when it passed through any optical system, known as the point spread function, the observed fluorescence dots were much larger than hydrodynamic size (1 μm vs. 52.6 nm). In brief, the ICG-iodinated oil nanoemulsion exhibited great potential for CT and optical dual-modal imaging.

3.3. In Vitro Cytotoxicity

Mouse breast cancer cell line (4T1 cells) and murine macrophage cell line (RAW264.7 cells) were co-incubated with ICG-iodinated oil nanoemulsion at different iodine concentration to assess the cytotoxicity of the nanoemulsion. The nanoemulsion could enter cells through endocytosis. After 24 h culture, cell survival was expressed as treatment over control (T/C) values by CCK-8 assay. As shown in Figure 6, when iodine concentration was below 60 μg/ml, the cell viability was above 80%, the nanoemulsion did not cause obvious cytotoxicity against these two cell lines. When the iodine concentration was above 60 μg/ml, the cell viability reduced with increase of iodine concentration, but was still above 70%. According to the result reported previously, the cell...
viable viability primarily depended on the iodine concentration. The nanoemulsion could be regarded as non-cytotoxic probe for potential imaging applications because ICG is FDA approved material and the iodine oil has low cytotoxicity.\textsuperscript{11,16}

3.4. Micro-CT Imaging and Fluorescence Imaging of Cells In Vitro

To prove that the ICG-iodinated oil nanoemulsion could be used to image cells efficiently via Micro-CT and confocal fluorescence microscope, 4T1 and RAW264.7 cells were selected. Micro-CT scanning was performed on both 4T1 and RAW264.7 cell mass incubated with or without the nanoemulsion for 8 h. Figure 7(b) revealed the transection CT images of the cell mass after incubation with the nanoemulsion. It was very evident that the treated cell mass was much brighter than untreated cell mass (Fig. 7(a)). The brighter CT images of cell mass should be associated with the more cellular uptake of ICG-iodinated oil nanoemulsion. Figure 7(c) also exhibited the image of 3D reconstructed cell mass incubated with the nanoemulsion by using a Micro-CT imaging software. Cell fluorescence imaging ability was investigated using LSCM for 4T1 and RAW264.7 cells treated with ICG-iodinated oil nanoemulsion for 4 h (Fig. 8). The nuclei were blue via DAPI-stained DNA. The red fluorescence from ICG-Der-01 in cells supported the result that the nanoemulsion was able to be efficiently internalized into both 4T1 and RAW264.7 cells and mainly gathered in cytoplasm. Meanwhile, RAW264.7 cells had stronger endocytosis and generated stronger intracellular red fluorescence than 4T1 cells. These results indicated that ICG-iodinated oil nanoemulsion possessed the potential as a CT/fluorescence dual-modal probe for cell imaging.

3.5. In Vivo CT and NIRF Imaging and Biodistribution

4T1 tumor model has several characteristics that makes it a suitable experimental animal. First, 4T1 tumor cells have active metabolism and strong capability of endocytosis. Second, the tumor is easy to grow and has a high tumor formation rate, which is almost 100\% only a week after inoculation. Third, a large number of macrophages exist in the tumor and are closely associated with tumor progression.\textsuperscript{26–28}

The hydrodynamic diameter of the nanoparticle is highly related to their capabilities for effectively overcoming the biological defense system and vascular barriers. When the diameter is greater than 100 nm, the nanoparticle will be taken up by phagocytes, but small nanoparticles of 1–100 nm can escape from phagocytes and circulate in blood vessels. And, the small-sized nanoparticles have enhanced permeability and retention (EPR) effects at the target tissues like tumor, infarction and inflammation, which have high porosity and large fenestrations (100 nm to several \( \mu \)m) of the blood vessels, so the nanoparticles can easily pass through the blood vessels in the vicinity of tumor tissues.\textsuperscript{29} The nanoemulsion of 52.6 nm and PEG-modified surface provide just a capability to avoid the phagocytosis by the reticuloendothelial system (RES) and then travel through the blood vessels for longer time. Because of increased vascular permeability of tumor tissues and limited lymph circulation, ICG-iodinated
oil nanoemulsion could easily pass through blood vessel wall of tumor tissues and increase the retention effect, that is EPR effect mentioned, then passively targeted to the tumor areas.

Balb/c mice bearing 4T1 mouse breast tumor were intravenously injected with ICG-iodinated oil nanoemulsion for each mouse (a dose of 240 µg/g). Figure 9 displayed CT images obtained at different time point. Every coronal image of the whole body from a representative mouse was shown along with a corresponding transverse image of the tumor. Tumor accumulation of the ICG-iodinated oil nanoemulsion led to an enhancement in brightness, especially for tumor edge, compared with pre-injection, but this enhancement is less obvious due to the fact that CT imaging possesses low sensitivity and thus needs high contrast agent concentration. CT values measured in tumor, liver, spleen and kidney were shown in Figure 10. 10 min after administration, the CT values

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**Fig. 7.** Transection Micro-CT images of RAW264.7 cells and 4T1 cells after 8 h incubation (a) without and (b) with the ICG-iodinated oil nanoemulsion. (c) 3D images of (b).

**Fig. 8.** Confocal images of RAW264.7 cells and 4T1 cells after 4 h incubation with the ICG-iodinated oil nanoemulsion (Iodine concentration was 240 µg/ml). (a) Showed nuclei stained by DAPI (blue), (b) showed fluorescence of the nanoemulsion (red) and (c) showed the overlap of the two images. All images have the same scale bars of 80 µm.
of tumor started to increase continually until it reached the maximum at 90 min post-injection, then the enhancement decreased (Fig. 10(a)). Though the CT sensitivity of the nanoemulsion was not so high, the achieved enhancement was about 20 Hu, attributed to that our nanoemulsion had smaller size through surface modification. Compared to iodinated nanoparticulate contrast agent N1177 of 259 nm, which had a 14 Hu enhancement with the injection dose of 250 μg/g body weight in the literature,30 the ICG-iodinated oil nanoemulsion can still reach a little higher signal enhancement at lower dose we used. At this time, the nanoemulsion had distributed to organs containing macrophages (Figs. 10(b), (c)). Hence CT values in liver and spleen were significantly higher
90 min post-injection than pre-injection value. And CT value in liver was detected to be still high at 2 h after administration. CT values measured in the kidney showed an initial increase, followed by a decrease (Fig. 10(d)), due to the rich blood vessels of renal tissue.

The NIR dye included in the established oil-in-water nanoemulsion enabled us to perform in vivo fluorescence imaging to determine the dynamic biodistribution in 4T1 tumor mice. Figure 11 showed that the fluorescence signal was located in the liver just 1 min after tail vein administration of ICG-iodinated oil nanoemulsion. At 2 h post-injection, there was apparent fluorescence signal around the tumor and kidney. The nanoemulsion started to accumulate in tumor tissue and a little was excreted through kidney metabolism. Afterwards, the fluorescence intensity in tumor persistently enhanced at 4 h and reached the maximum at 6 h. No detectable signal was recorded from liver and kidney. Thus ICG-iodinated oil nanoemulsion clearly displayed the tumor against surrounding tissues by passive targeting. It is further demonstrated the ICG-iodinated oil nanoemulsion had remarkable potential to target macrophage-rich 4T1 tumor with CT/fluorescence imaging. The efficient combination of high sensitivity of fluorescence imaging with high spatial resolution of CT imaging for tumor and its surrounding tissues would provide a powerful tool for tumor diagnosis. Moreover, fluorescence imaging could continue 6 h, which is beneficial to guide tumor excision in future.

4. CONCLUSIONS

A dual-modal and biocompatible contrast agent composed of ICG-Der-01 in iodinated oil was synthesized based on oil-in-water nanoemulsion platform. The CT and fluorescence properties were characterized and evaluated by in vitro and in vivo imaging. Results indicated that ICG-iodinated oil nanoemulsion was a promising CT/fluorescence dual-modal imaging agent for cell imaging and tumor diagnosis. Due to the excellent druggability for ICG and iodinated oil we used, the nanoemulsion would have great potential in practical clinical application. And the established preparation method may also be extended to design multimodal contrast agent for the delivery of hydrophobic materials or drugs.

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References and Notes


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