Gold nanoparticles designed for in vivo SRCT and MRI imaging and X-ray therapy

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The synthesis of gold nanoparticles functionalized by gadolinium chelates constitutes an attractive way for combining imaging and therapy. The presence of gadolinium chelates allows monitoring their biodistribution after intravenous injection in small animals by magnetic resonance imaging (MRI) while the gold core strongly absorbs the X-ray photons. This feature is exploited for X-ray imaging but also for radiotherapy.

Rationale and objectives

The intense research activities devoted to the nanotechnology led to the development of multifunctional nanoparticles which combine imaging and therapy. There is in fact a considerable need for new functionalized CAs for both imaging and therapy of cancer, in particular those that have adequate pharmacokinetic properties and low levels of non-specific accumulation in the body. The improvement of the sensitivity of magnetic resonance imaging (MRI), a non-invasive and powerful medical imaging technique, requires the development of original contrast agents with a higher efficiency than gadolinium chelates (DTPA:Gd), widely used for diagnosis. To achieve this goal, the strategy that we explored consists in the use of gold nanoparticles as a carrier for gadolinium chelates. Moreover these particles can be followed up by X ray imaging since gold have a high atomic number and a high density and can be used for X-ray therapy [1,2,3].

Methods

synthesis of multifunctional gold nanoparticles, in vivo imaging (magnetic resonance imaging (MRI), synchrotron radiation computed tomography (SRCT)), microbeam radiation therapy.

Results

The immobilization of Gd^{3+} ions onto gold nanoparticles requires the use of molecules which are able both to chelate Gd^{3+} ions and to anchor on gold surface. To achieve this goal, gold particles were synthesized by reducing gold salt in presence of dithiolated derivative of diethylenetriaminepentaacetic acid. The extensive characterization reveals that the resulting nanoparticles (Au@DTDTPA) are composed of a gold core (about 2.4 nm) embedded in a multilayered shell of DTDTPA [4]. After intravenous injection of

Au@DTDTPA-Gd (10 mg/mL, ~ 50 Gd per particle) in a tail of a mouse, these particles can be followed up by MRI since they induce a strong enhancement of the positive contrast of the MR images. They accumulated first in kidneys and then in the bladder and no undesirable uptake by liver, lungs, spleen or brain was observed. This biodistribution was confirmed by ICP analysis but also by in vivo X ray computed tomography imaging which was carried out at the ESRF (Grenoble, France) on the medical beamline [5]. In contrast to the case of healthy animals, Au@DTDTPA-Gd_{50} nanoparticles crossed the brain blood barrier (BBB) of rats bearing a tumor in brain (9L gliosarcoma). A moderate contrast enhancement (15%) was observed in the tumor zone until 20 minutes after the injection. The preferential accumulation of Au@DTDTPA-Gd nanoparticles was exploited for treating the tumor with X-ray beam. The irradiation of tumor bearing rats with X-ray microbeam 20 minutes after Au@DTDTPA-Gd injection led to a longer survival of the rats.

Conclusion

Owing to their peculiar design which confers them adequate pharmacokinetic properties and low levels of non-specific accumulation in the body, Au@DTDTPA-Gd nanoparticles appear very well suited for combining in vivo imaging and radiotherapy. The presence of gold element and gadolinium ions in Au@DTDTPA-Gd affords to the particles the ability to improve the survival of rats bearing tumor and to follow up them both by X-ray imaging and MRI.

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