High-sensitivity terahertz imaging technique using nanoparticle probes for medical applications

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***Abstract*-We present the principle and *in vivo* experimental results of high sensitivity terahertz imaging technique which enables the target specific sensing of cancers and the molecular imaging of drug delivery.**

I. Introduction

Recently, a new terahertz (THz) technique for cancer diagnosis has been invented using nanoparticle contrast agents [1]. The nanoparticles, in the forms of gold nanorods (GNRs) [1], gold nanoshells [2], or drug-loaded polymer gold nanoshells [3], induce surface plasma polaritons upon the irradiation of near infrared (NIR) laser beams. The hyperthermia effect due to the surface plasmon resonance raises the temperature of water in the cancer cell with nanoparticles. The THz electromagnetic waves are very sensitive to the variation of water temperature [4] and, thereby, the reflected THz signal from cancer cells with nanoparticles, which can be targeted only to cancer cells by antibody conjugation, is modulated upon the NIR illumination.

In this study, we demonstrate the principle of the high sensitivity THz imaging technique by differential irradiation of nanoparticle probes with NIR beams and present *in vivo* and *in vitro* experimental results.

II. Experiments

We have fabricated gold GNRs using the seed mediated growth technique. In the *in vitro* experiments, the GNRs were bound with epidermoid carcinoma A431 cell by electrostatic force between GNRs and the cells. The GNRs were coated with hetero bi-functionalized polyethylene glycol and conjugated with Cetuximab for *in vivo* experiments. In the *in vivo* experiments, the THz images were obtained 24 hours after injection of the GNRs in tumors of mice. All the images were measured using a reflection-mode THz time-domain spectroscopic system. Two laser systems were used for the experiments. One is the Ti:sapphire ultrashort pulse laser used to generate and detect the THz pulse. The other is the continuous wave Ti:sapphire laser which induce the surface plasmon resonance.

III. Results

The images of cells were acquired to demonstrate the principle of our technique *in vitro* as shown in Fig. 1. The image of the cell with GNRs became brighter upon IR laser beam irradiation than the THz-only image for the same sample, whereas there was almost no change in the cell without GNRs. When we subtracted the image with GNRs from that without GNRs, the image with GNRs was distinguished clearly. The reflected THz signal from the cancer cell with GNRs was 30 times higher than that from cancer cell without nanoparticles upon the differential irradiation of NIR beam as shown in Fig. 1(f). This result shows that highly sensitive THz imaging for

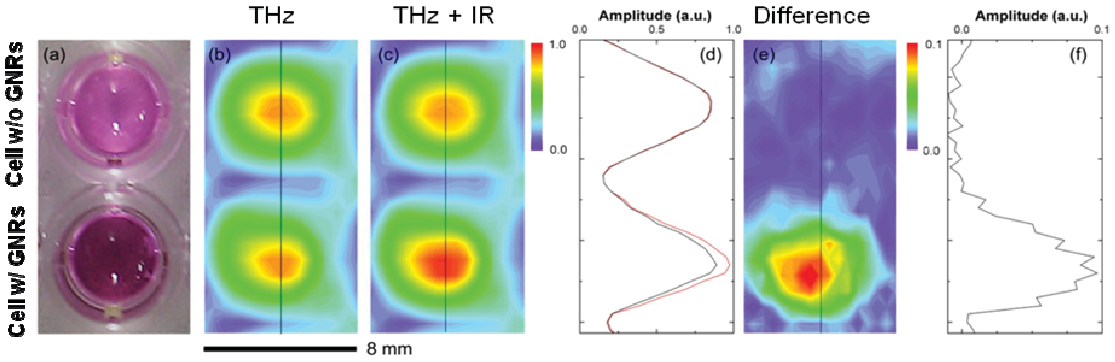

Fig. 1. Cancer cell images with and without GNRs. (a) Visible image; (b) THz image without IR irradiation; (c) THz image with IR irradiation; (d) amplitudes along the lines in (b) (black) and (c) (red); (e) subtraciton image between (b) and (c); and (f) amplitude along the line in (e).

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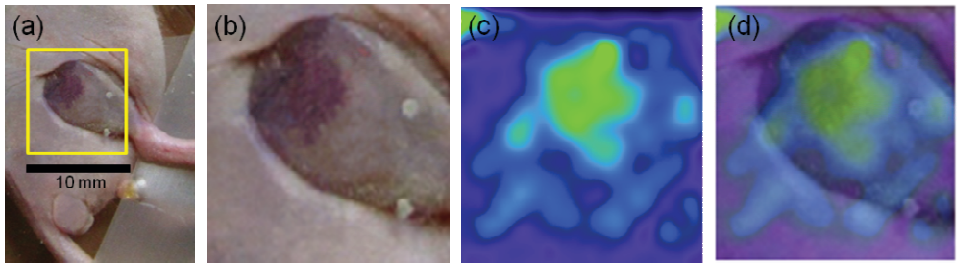

Fig. 2. *In vivo* cancer images with GNRs. (a), (b) Visible image of a mouse with cancer to where GNRs were targeted; (c) THz image under differential modulation of NIR beams; (d) overlap of images of (b) and (c).

cancer diagnosis can be achieved with nanoparticle probes such as GNRs.

The *in vivo* experimental results diagnosed by this high sensitivity differential technique are shown in Fig. 2, which clearly shows the area of cancer targeted with GNRs.

IV. Conclusion

This technique enables the molecular imaging of drug delivery as well as the target specific sensing of cancers due to its high sensitivity. The high sensitivity also makes THz endoscopy become more feasible.

The plasmonic nanoparticles can also be applied as hyperthermal therapeutic agents for the treatment of cancers simultaneously with the THz diagnosis. Therapeutic antibody, such as Erbitux, conjugated nanoparticles, combined with an NIR illumination, show an excellent therapeutic efficacy for the treatment of human epithelial cancers [2,3].

Acknowledgements

This work was undertaken with the support of the National Research Foundation of Korea under Grant Numbers 20090084187, 20090054519 and 20090093432.

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