Plasmonic gold nanorods for laser thermal therapy of gliomas in vitro and in tissue-mimicking phantoms

Rebecca J. Johnson[1], Sumiao Pang[1], Nikhil Pandey[2,3], Carla Arnau del Valle[1], Anshika Kapur[2,3], Pavlos Anastasiadis[2,3], Pranjali Kanvinde[2,3], Emylee McFarland[2,3], Brian Schnoor[1], Jeffrey A. Winkles[2,3], Graeme F. Woodworth[1,2,3], Anthony J. Kim[1,2,3], Huang Chiao Huang[1,2,3]

[1]Fischell Department of Bioengineering, University of Maryland, College Park, Maryland, USA
[2]Department of Neurosurgery, University of Maryland School of Medicine, Baltimore, Maryland, USA
[3]University of Maryland Marlene and Stewart Greenebaum Cancer Center, Baltimore, Maryland, USA

Introduction

Glioblastoma (GBM) is a highly invasive and aggressive brain cancer, with a five-year survival rate of ~5%.[1] Recurrence is nearly universal, and the median survival is 14 months.[2] **MRI-guided Laser Interstitial Thermal Therapy (LITT)** is a minimally-invasive option that uses laser light to generate localized heat and induce hyperthermia in tumor.[3,4]

However, several challenges remain:

- **Non-specific heating** can lead to off-target tissue damage.
- Reaching therapeutic temperatures often demands **high laser power**, which elevates the risk of unintended thermal damage.

Fn14 is a cell surface receptor that is overexpressed in up to 85% of GBM, while showing minimal expression in healthy tissue, making it a great option for targeting.[5]

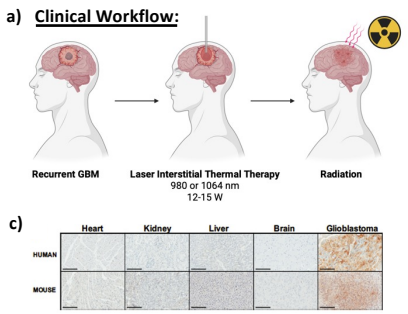


Figure 1. (a) Schematic of clinical LITT workflow.[6] **(b)** MRI demonstrating off-target toxicity of LITT treatment. **(c)** IHC stain showing minimal Fn14 expression in normal tissues and elevated expression in GBM. **(d)** Schematic of Fn14-targeted GNR after intratumoral administration. This allows for localized heating at lower laser power.[6]

Synthesis of Gold Nanorods (GNR)

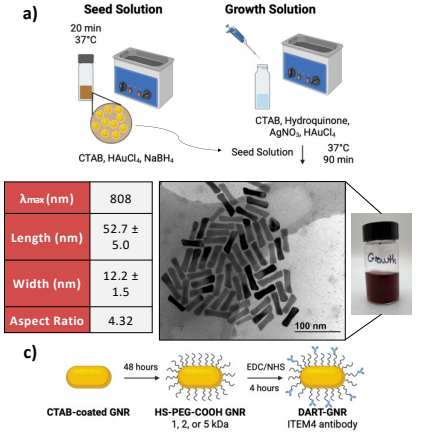


Figure 2. (a) GNRs are synthesized via seed-growth method.[6] The TEM image shows GNRs with absorption peak at 808 nm with further characterization in the table. **(b)** UV-Vis normalized absorbance of 690 and 808 nm excitable GNRs. **(c)** Schematic showing PEGylation and antibody conjugation reactions.[6] **(d)** Dot blot results demonstrating the ability to detect and quantify the amount of ITEM4 (Fn14 monoclonal antibody) on the GNRs.

Goal

Develop a Fn14-targeted gold nanorod (DART-GNR) to localize and improve tumor heating during laser interstitial thermal therapy and enable CT imaging.

Results

(1) DART-GNRs target the cell surface receptor Fn14 to enhance glioma cell photothermal therapy.

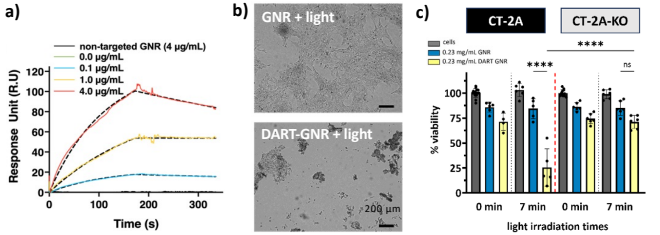


Figure 3. (a) DART-GNRs bind to Fn14 under SPR assay. **(b)** Bright field images of CT-2A glioma cells 24-hours post-treatment. **(c)** Cell viability for CT-2A (Fn14+) and Fn14- cell lines treated with GNRs and 2.5 W/cm^2 690 nm light.

(2) CT imaging of GNRs in tissue-mimicking phantoms and animal models.

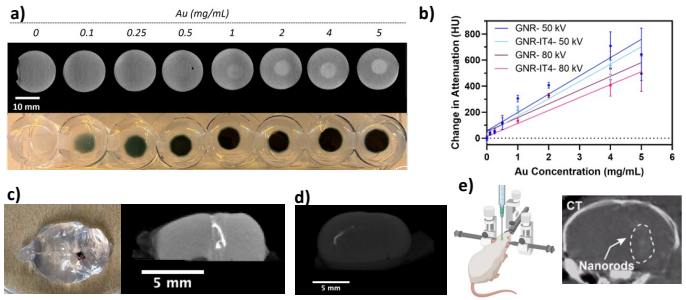


Figure 4. (a) MicroCT scan (80 kV, 200 μA) of GNRs in 0.6% agarose. **(b)** Quantification of GNR attenuation in Hounsfield units. **(c)** CT imaging of GNR (8 mg/mL, 5 μL) in brain phantom. **(d)** CT imaging of GNRs (4 mg/mL, 5 μL) in ex vivo mouse brain. **(e)** CT imaging of GNRs (8 mg/mL, 5 μL) in vivo 30 minutes post-injection.

(3) GNRs enhance spatiotemporal heating and thermal control in tissues.

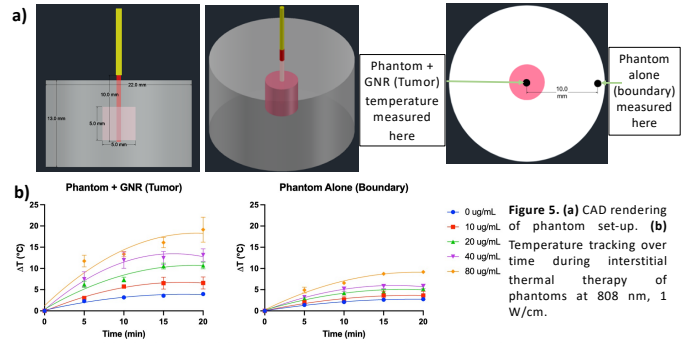
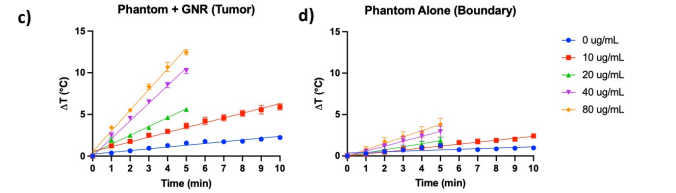


Figure 5. (a) CAD rendering of phantom set-up. **(b)** Temperature tracking over time during interstitial thermal therapy of phantoms at 808 nm, 1 W/cm.

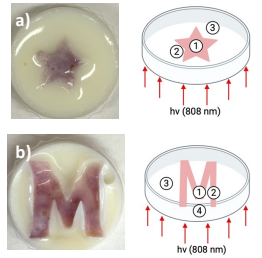


GNR conc. (μg/mL)	Heating rate at center (°C/min)	Heating rate at boundary (°C/min)
0	0.21	0.08
10	0.57	0.24
20	1.06	0.36
40	2.04	0.60
80	2.48	0.74

GNR conc. (μg/mL)	Time (min)	ΔT at center (°C)	ΔT at boundary (°C)
0	10	2.1	0.8
10	10	5.7	2.4
20	5	5.3	1.8
40	5	10.2	3
80	5	12.4	3.7

Figure 5 continued. Higher heating rate was observed at the **(c)** center (tumor) than **(d)** boundary (normal tissue) of the phantom during the linear heating range at 808 nm, 1 W/cm.

(4) Temperature increase was confined to regions containing GNRs with minimal to no heating observed in areas exposed to light alone.



GNR conc. (μg/mL)	Irradiance (W/cm^2)	Radiant Exposure (J/cm^2)	ΔT at different locations (°C) ①	②	③
0	2	1200	3.8 ± 0.8	3.3 ± 1.4	2.9 ± 0.4
10	1	600	7.7 ± 2.3	4.9 ± 1.1	2.4 ± 0.8
40	2	1200	27.9 ± 5.1	12 ± 1.4	7.9 ± 3.1
80	2	1200	29.4 ± 3.0	19.6 ± 2.8	9.4 ± 2.7

GNR conc. (μg/mL)	Irradiance (W/cm^2)	Radiant Exposure (J/cm^2)	ΔT at different locations (°C) ①	②	③	④
0	2	1200	3.8 ± 0.6	3.0 ± 0.5	2.9 ± 0.6	3.0 ± 0.9
10	1.15	690	5.8 ± 0.7	4.5 ± 0.6	1.5 ± 0.4	2.2 ± 0.2
40	2	1200	20.2 ± 2.2	17.1 ± 1.5	8.4 ± 1.8	9.9 ± 1.5
80	2	1200	22.1 ± 0.7	17.7 ± 0.8	7.9 ± 1.9	10.2 ± 0.7

Figure 6. (a) Image of phantoms (0.7% agarose + 160 mg/mL milk) with GNR in star-shape and **(b)** "M" (Maryland)-shape. Change in temperature at different locations labeled on schematic for star-shape and "M"-shape.

(5) Thermal imaging of GNR heating upon light activation in human GBM39 PDX cells injected intracranially into nude mice.

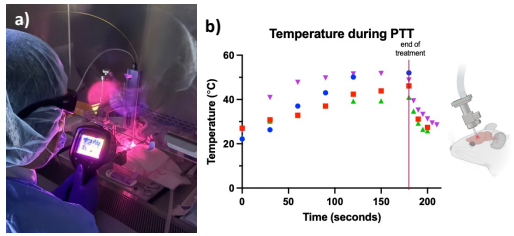


Figure 7. (a) Digital photo of thermal tracking during in vivo interstitial light activation of GNR. **(b)** Temperature tracking of GBM39 tumor-bearing mice that received 8 mg/mL intratumoral GNR injections. Light activation was performed at 808 nm, 1 W/cm. (N=4)

Future Directions

⇨ Investigate the safety and efficacy of DART-GNR-assisted LITT in vivo
⇨ Combination of DART-GNR-assisted LITT with radiation in vivo

[1] Tamimi and Juweid. Glioblastoma, Chapter 8 (2017), [2] Mohammed et al. Rep Pract Oncol Radiother, 27(6):1026–1036 (2022), [3] Salem et al. Cancer Imaging, 19(1):65 (2019), [4] Holste and Orringer. Neurooncol Adv, 2(1):vdz035 (2019) [5] Perez et al. Oncogene, 35(17):2145–2155 (2015), [6] Biorender images (2025)

Contact: Huang Chiao Huang, Ph.D. (hchuang@umd.edu)
This work is supported by the National Institute of Health