Physical Bases for Gold Nanoparticle Applications in Radiation Oncology and X-Ray Imaging

AAPM 2015 Nanotechnology Symposium

July 15, 2015

Sang Hyun Cho, Ph.D.

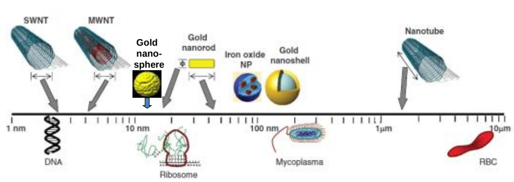
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History

Acknowledgment

- Georgia Tech:
  S.-K. Cheong, B. Jones, A. Siddiqi, N. Manohar
  F. Reynoso, F. Liu, K. Dextraze
- M. D. Anderson Cancer Center:
  S. Krishnan, P. Diagaradjane, J. Stafford, J. Hazle, J. Cho
- Univ. of Massachusetts Medical School:
  A. Karellas
- Support from Georgia Tech, Georgia Research Alliance, DOD/BCRP, DOD/PCRP, NIH/NCI, MDACC

Nanomaterials

- Fabricated in various shapes and sizes at the nanometer scale (~ 1-100 nm)



Adapted from Krishnan et al, *Int. J. Hyperthermia* 26(8), 2010

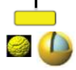
Applications of Gold Nanoparticles

Radiosensitization/Radiaiton Response Modulation

↑

Secondary electron production/Physical Dose Enhancement

↑

MR-visible Hybrid GNPs ←  → PET-visible Hybrid GNPs

Gold Nanoparticles (GNPs)

↙ ↘

Plasmonic Resonance

↓

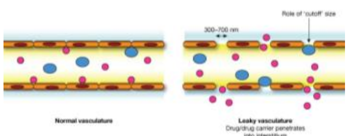
Thermal Therapy/Hyperthermia
Thermoradiotherapy
Optical imaging

X-ray fluorescence (XRF) Production

↓

XRF imaging (direct imaging, CT)
Molecular imaging with micro-CT/XFCT

Passive/Active Targeting using GNPs



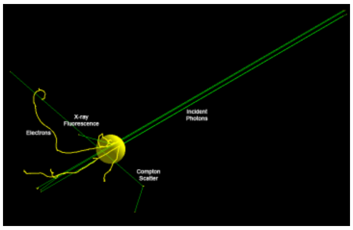
- Passive yet selective targeting - enhanced permeability and retention (EPR) effect
- Active targeting – conjugation with biomarkers
- GNPs are chemically inert, biologically non-reactive, and molecularly stable

Left image: Dembo, D., et. al. *Nanoparticulate delivery systems for antiviral drugs.* Antiviral Chemistry & Chemotherapy 2010; 21:53-70
Right image: Azonano.com

GNP-mediated Physical Dose Enhancement

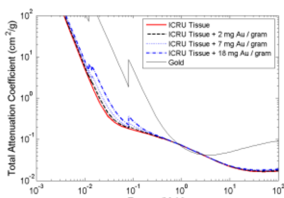
GNPs

- **Mediators for increased secondary electron production in tissue irradiated with hν, e-, p, etc.**



e.g., Interaction probability for photoelectric absorption ~ Z^4 to $Z^{4.8}$; *iodine (53), gadolinium (64), platinum (78), gold* (79)

Macroscopic Dose Enhancement in GNP-loaded Tissue



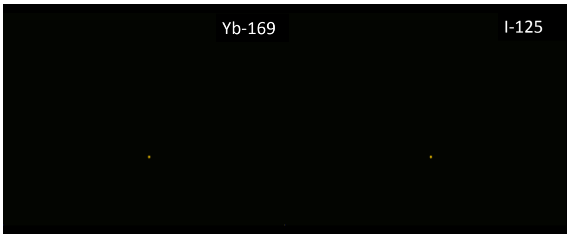
Cho, PMB., Vol 50, 2005 & Cho et. al., PMB Vol 54, 2009

- Unimpressive macroscopic (average) dose enhancement at very low GNP concentration (e.g., 6% at 0.07 wt.% vs. 60% at 0.7 wt.% with 250 kVp x-rays)

Microscopic Dose Enhancement around GNPs

Jones et al, Med. Phys., Vol 37(7), 2010

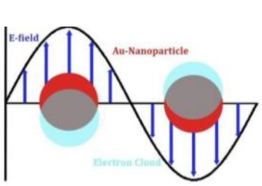
Microscopic Dose Enhancement around GNPs



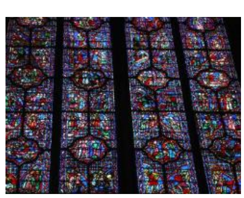
Jones et al, Med. Phys., Vol 37(7), 2010

GNP-mediated Plasmonic Resonance/Heating

Surface Plasmon Resonance (SPR)



Adapted from Kelly et al. *J. Phys. Chem. B, Vol. 107*, 2003

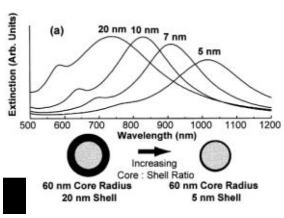


Stained glass at Sainte-Chapelle, Paris, France

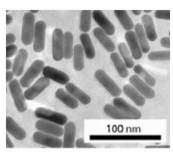
SPR

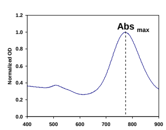
- The SPR frequency depends closely on size and shape of GNPs
- Allows for fabrication of optically-tunable GNPs
- Anisotropic nanoparticles possess multiple SPR modes (e.g., longitudinal and transverse modes for nanorods)

SPR Tuning

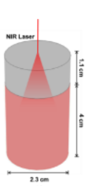


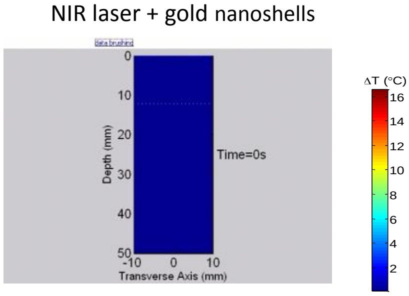
Oldenburg et al. Chemical Physics Letters 1998





GNP-mediated Plasmonic Heating
NIR laser + gold nanoshells





808 nm NIR laser (5 mm FWHM Gaussian), 1.5 Watts, 3 min (180 s), 7.2 x 10^9 GNPs/ml

Cheong et al, Med. Phys., Vol 36(10), 2009

GNP-based XRF Imaging

GNP-based XRF Imaging

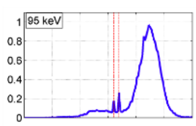
- Methods based on detection of gold K-shell x-ray fluorescence (XRF) photons (~67.0 and ~68.8 keV)
  - Higher energy allows imaging of larger objects
  - Can be used for tomographic reconstruction
- Methods based on detection of gold L-shell XRF photons (~9.71 and ~11.4 keV)
  - More suitable for direct 2D imaging with high resolution & high sensitivity

X-ray Fluorescence Computed Tomography (XFCT)

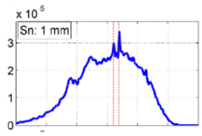
- Allows simultaneous determination of spatial distribution and concentration of metals present within imaging objects
- Issues with synchrotron XFCT
  - Accessibility, Dose, and Energy

Benchtop XFCT

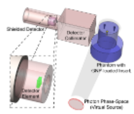
90° Scatter + gold XRF spectra



(Quasi-) Monochromatic photon beam



105 kVp x-rays filtered with 1 mm of tin

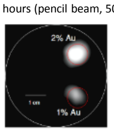


Manohar et al, Med. Phys., Vol 41(10), 2014

Benchtop XFCT

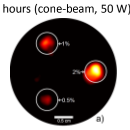
- Demonstrated first using GNPs and polychromatic pencil beam (110 kVp)
- Developed into the current cone beam XFCT
  - Decrease overall scanning time
  - Increase noise due to Compton scatter

~40 hours (pencil beam, 50 W)



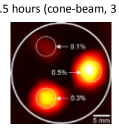
Cheong, *et al* PMB 2010

~6 hours (cone-beam, 50 W)



Jones, *et al* PMB 2012

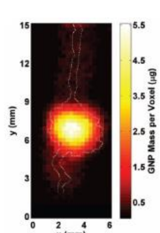
~1.5 hours (cone-beam, 3 kW)



Cho Group, 2015

Applications of Benchtop XFCT

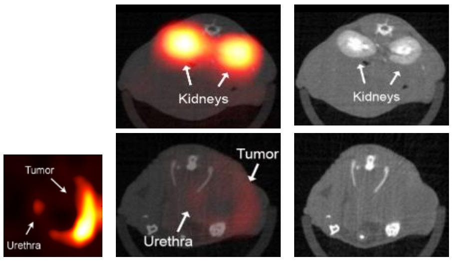
- Determination of GNP biodistribution via tomographic *in-vivo* imaging
- Combined CT/XFCT in the same platform for multimodal/multiplexed molecular imaging with bioconjugated GNPs and other metal NP probes



Manohar et al, Med. Phys., Vol 40(10), 2013

Benchtop XFCT: animal study

- First successful demonstration of GNP-based benchtop XFCT as applied to small animal imaging



Manohar et al. WMIC 2014

Thank you for your attention !