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

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Nanomaterials

• Fabricated in various shapes and sizes at the nanometer scale (~ 1-100 nm)
Applications of Gold Nanoparticles

- Radiosensitization/Radiation Response Modulation
- Secondary electron production/Physical Dose Enhancement
- Plasmonic Resonance
- Therapeutic Hyperthermia
- Optical Imaging
- X-ray Fluorescence (XRF) Production
- Hybrid Gold Nanoparticles (GNPs)
- MR-visible Hybrid GNPs
- PET-visible Hybrid GNPs

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

GNP-mediated Physical Dose Enhancement
GNPs

- Mediators for increased secondary electron production in tissue irradiated with $h\nu$, $e^-$, $p$, etc.

  e.g., Interaction probability for photoelectric absorption $\sim Z^4$ to $Z^{1.8}$; iodine (53), gadolinium (64), platinum (78), gold (79)

Macroscopic Dose Enhancement in GNP-loaded Tissue

- 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
Microscopic Dose Enhancement around GNPs

Yb-169  I-125

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

GNP-mediated Plasmonic Resonance/Heating


Surface Plasmon Resonance (SPR)


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

![Graph showing SPR tuning](image)

GNP-mediated Plasmonic Heating

NIR laser + gold nanoshells

![Graph showing temperature change](image)
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


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]  ~6 hours [cone-beam, 50 W]  ~1.5 hours [cone-beam, 3 kW]


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

Benchtop XFCT: animal study

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

Thank you for your attention!