Radiosensitisation by nanoparticles in Proton therapy

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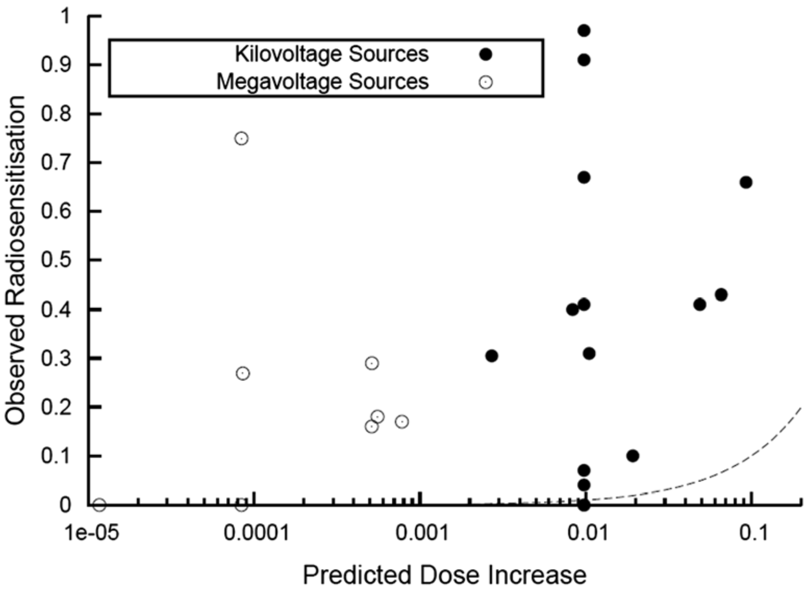
Justification

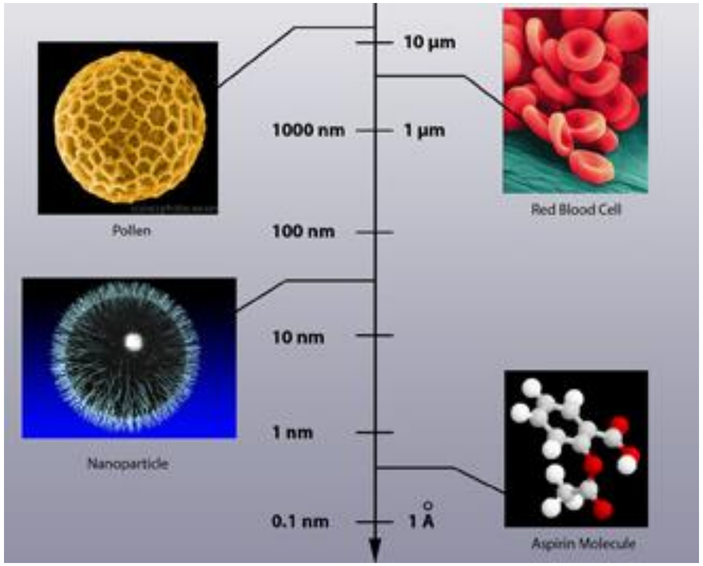
- High Z materials shown to create a radiosensitisation effect in x-ray radiotherapy
- Discrepancies between the Monte Carlo predicted dose enhancement and what was observed experimentally
- Mechanisms not fully understood



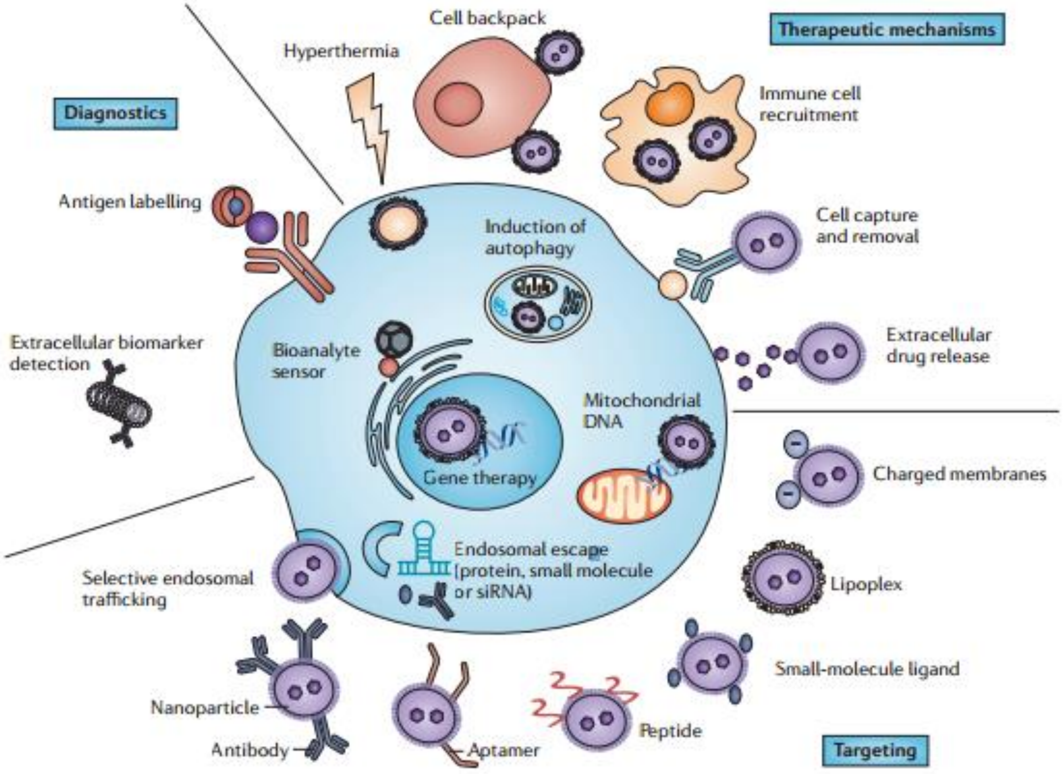
Butterworth et al. Physical basis and biological mechanisms of gold nanoparticle radiosensitization, Nanoscale 2012;4:4830–4838.

Perfect nanoparticle

- Highest cross-section
- Non-toxic
- High uptake
- Produces many secondary electrons



https://www.vet.purdue.edu/cpr/nanotechnology3.html



Schroeder et al. Treating metastatic cancer with nanotechnology, Nature Reviews Cancer 2012;12: 39--50

Mechanisms of dose enhancement

Physical

- Secondary electrons

Biological

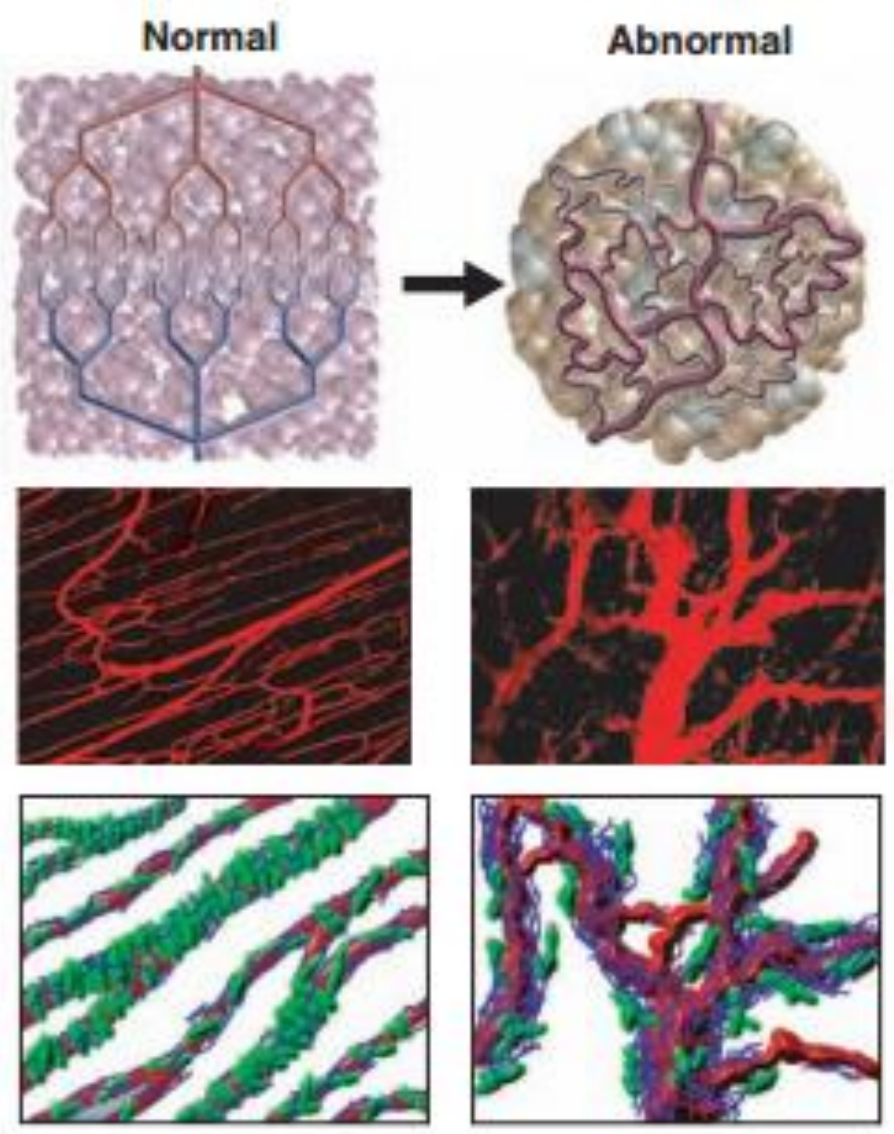
- Cell cycle effects
- Nanotoxicity
- Double strand breaks

Butterworth et al. Physical basis and biological mechanisms of gold nanoparticle radiosensitization, Nanoscale 2012;4:4830–4838.

Nanoparticle size

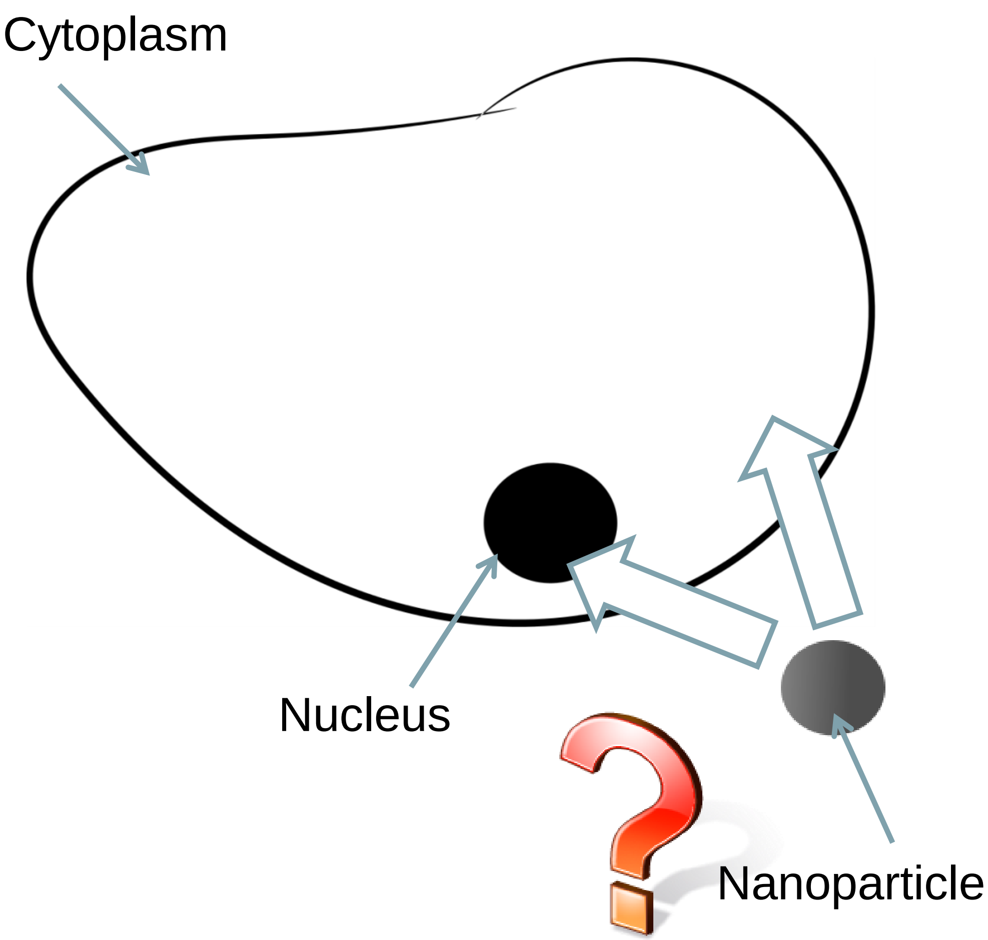
Factors to consider:

- Biological uptake
- Clearance pathways
- Nanotoxicity



Jain et al. Normalization of tumor vasculature: an emerging concept in antiangiogenic therapy, Science 2005: 58-62

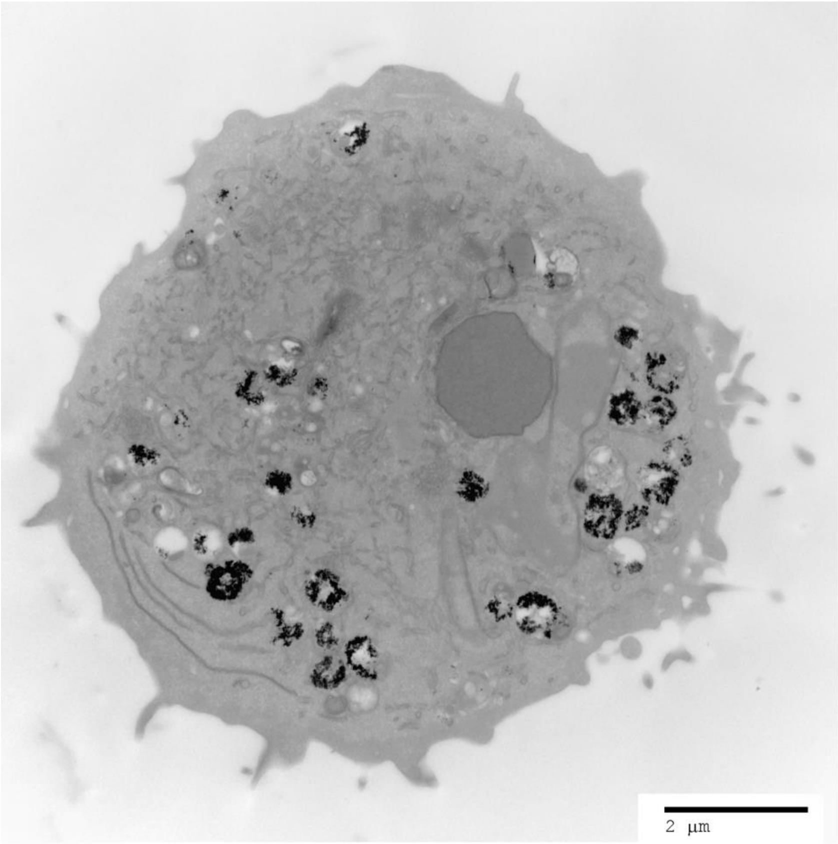
Location of nanoparticles

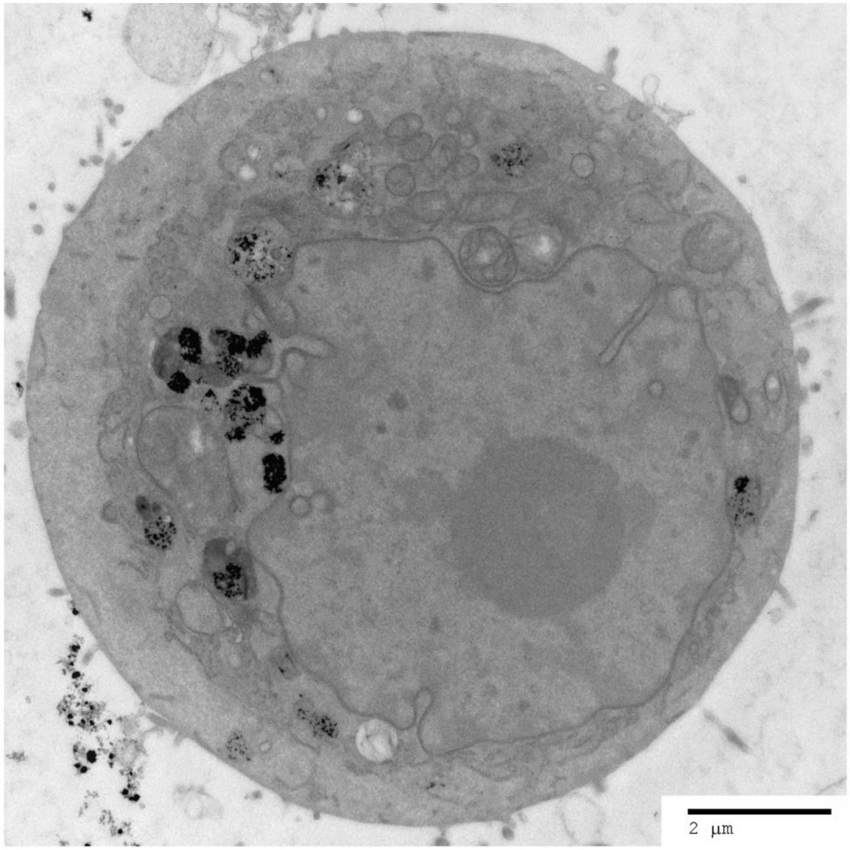


- Typical size of a cell is around 10 micrometres
- Using data of secondary particle tracklengths to determine the optimum location for the nanoparticles
- May need to localise the NPs within the nucleus to cause damage to the DNA

Gold nanoparticles in a cell

Microscopy image showing passive uptake of gold nanoparticles in a mouse endothelial cell (left) and a colorectal cancer cell (right)

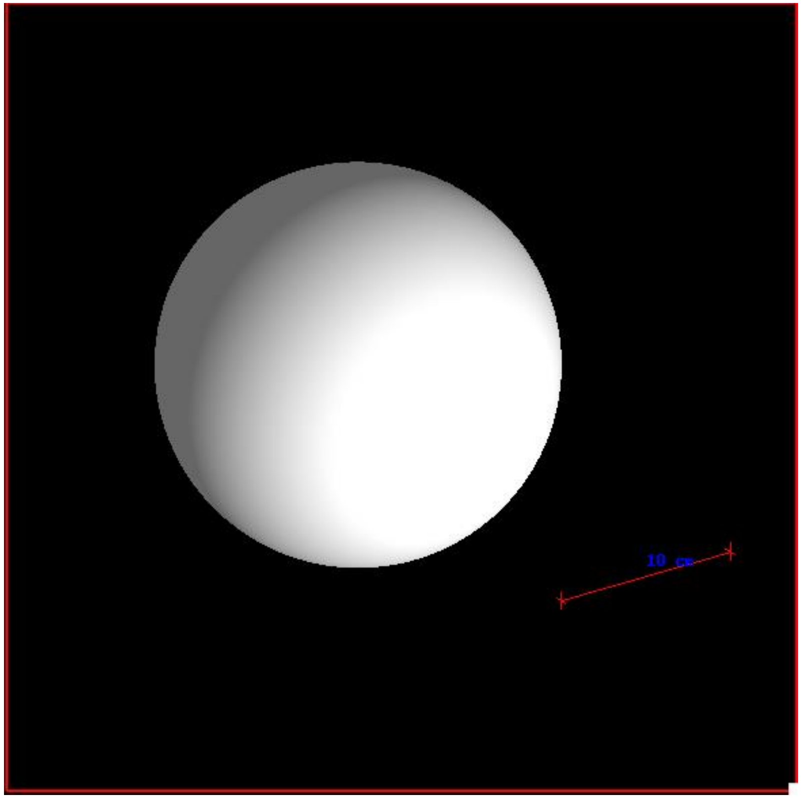




Images from Kate Ricketts - Dept of medical physics and bioengineering, University College London

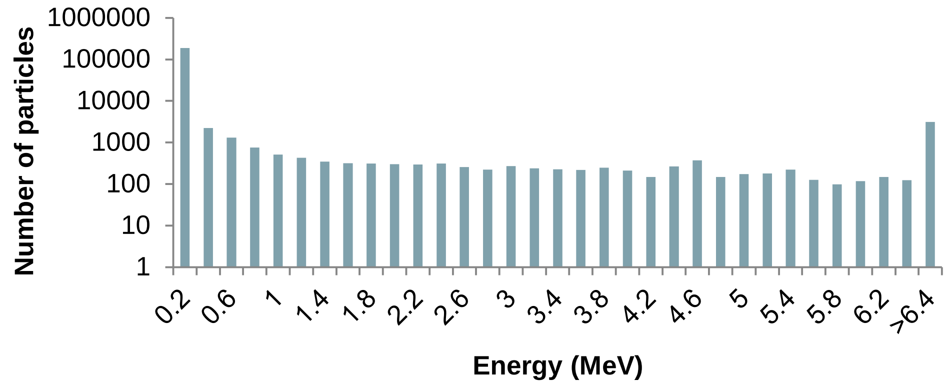
Monte Carlo simulations using Geant4 to choose the optimum material for the nanoparticle

- Simple geometry of a sphere in a box of water
- Needed to identify a suitable material for protons
- Used a bulk of material rather than a nanoparticle
- Ran simulations with platinum, gold and silver
- Used a proton beam of 62 MeV for 100,000 incident protons



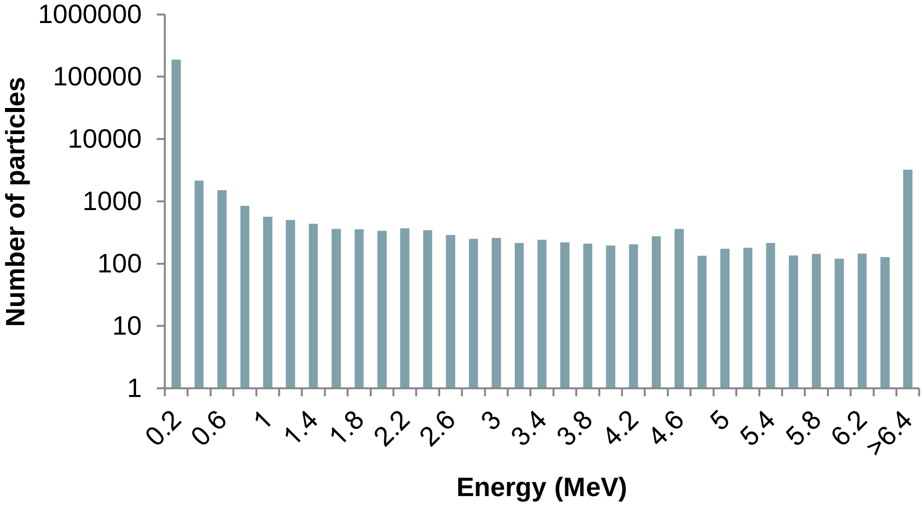
- The low energy secondary particles are mainly electrons
- We want a lot of electrons as these give a dose
- All 3 materials had the majority of secondary particles with an energy below 200 KeV

Histogram of secondary particle energy - Silver



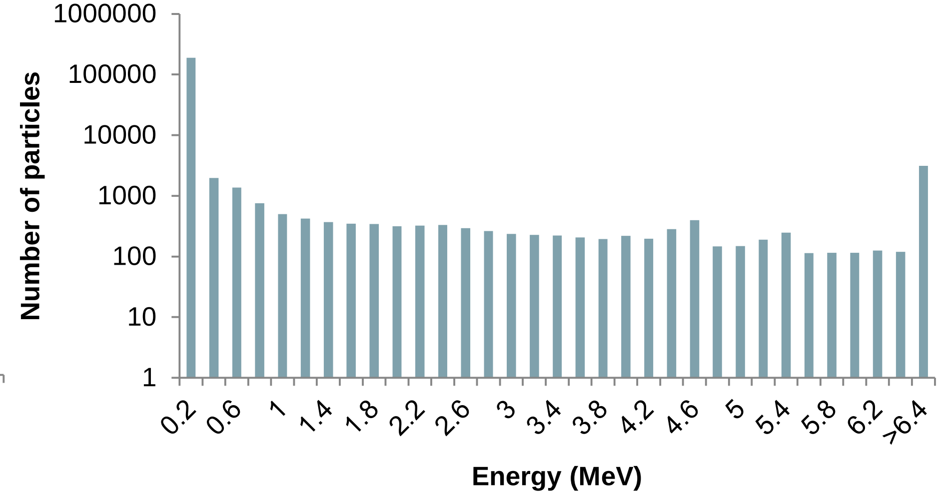
Produced 202,810 secondary particles

Histogram of secondary particle energy - Gold



Produced 203,463 secondary particles

Histogram of secondary particle energy - Platinum

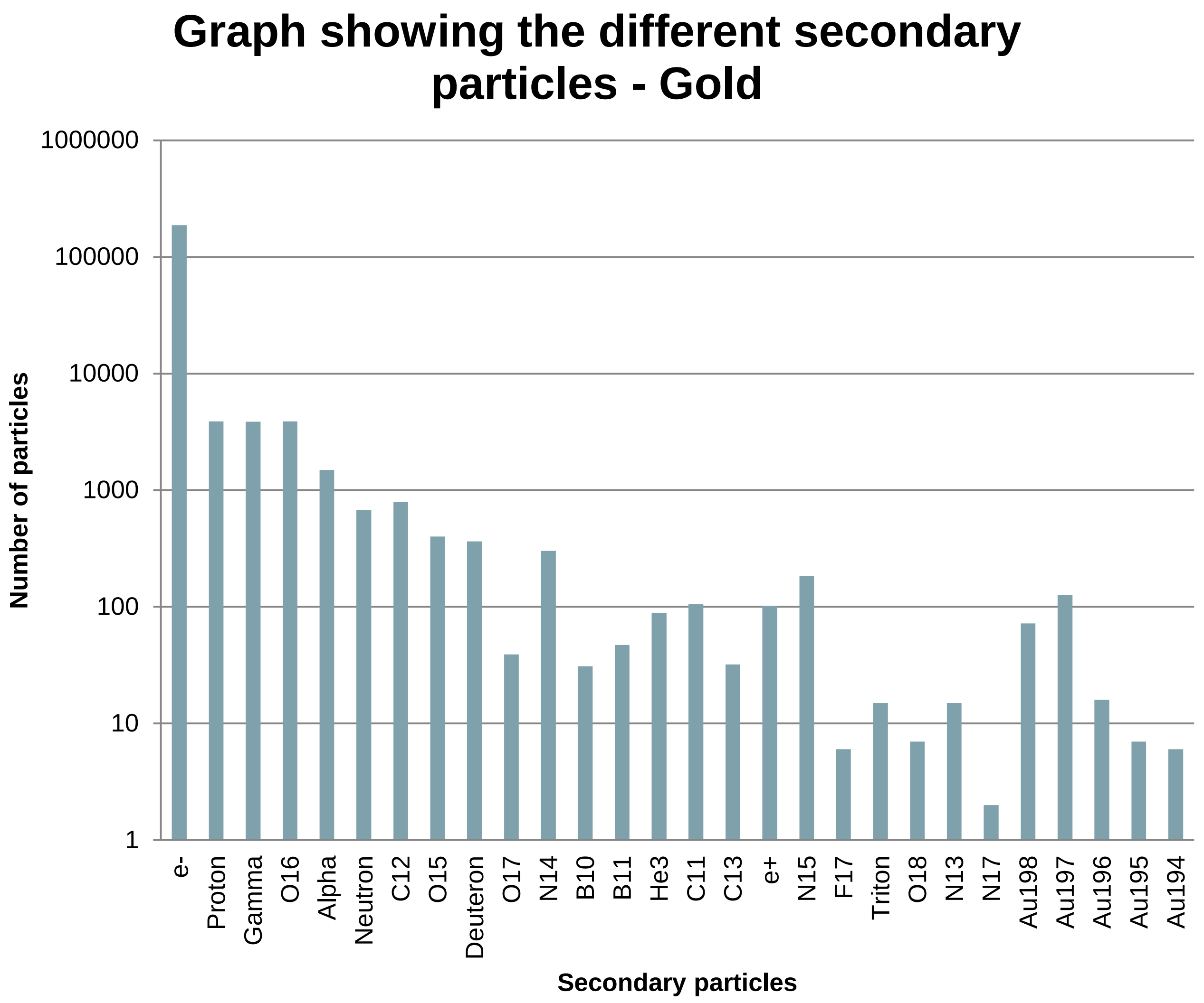


Produced 203,344 secondary particles

Prediction of where to place the nanoparticles

- The majority of the particles were electrons with an energy of approximately 200 KeV

- Using this information we can predict how far the electrons would travel



Future Work

- Determine the optimum location for the nanoparticles
- Expand the Monte Carlo simulations to consider the nanodosimetric effects
- Use nanoparticles as part of a bio-phantom
- Investigate the biological mechanisms that contribute to nanoparticle dose enhancement

Thank you

Questions?