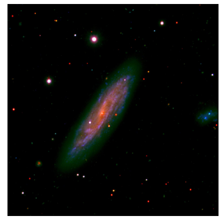
  LBT & Image

"X-RAY SPECTROSCOPY: FROM BLACK HOLES TO CANCER TREATMENT"

SULTANA N. NAHAR

Astronomy, The Ohio State University

Multidisciplinary Program:

Astronomy, Physics, Chemistry, Pathology, Radiation Oncology

Ohio State University, Thomas Jefferson U.

Department of Physics and Astronomy

Wayne State University, Detroit, Michigan

April 5, 2012

Support: DOE, NSF

Computations - Ohio Supercomputer Center (OSC)

STUDYING ASTRONOMICAL OBJECTS

ASTRONOMICAL objects are studied in 3 ways:

- **IMAGING: - Beautiful pictures or images of astronomical objects, Stars, Nebulae, Active Galactic Nuclei (AGN), Black hole Environments, etc**
  - Bands of Electromagnetic Colors ranging from X-ray to Radio waves $\rightarrow$ macroscopic information

- **PHOTOMETRY: - Low resolution spectroscopy - Examples: types of stars, abundances, general idea of physical conditions, etc**
  $\rightarrow$ macroscopic information

- **SPECTROSCOPY: - Provides most of the detailed knowledge: temperature, density, extent, chemical composition, etc. of astronomical objects. Brightness of the line indicates abundance of the element and width of the spectral lines indicate other effects such plasma broadening due to collisions, Stark effects etc.**

IMAGING: BLACK HOLE JET OF CENTAURUS A (Chandra space telescope)

• Imaging: red - low-energy X-rays, green - intermediate-energy X-rays, and blue - the highest-energy X-rays. The dark green and blue bands are dust lanes that absorb X-rays.

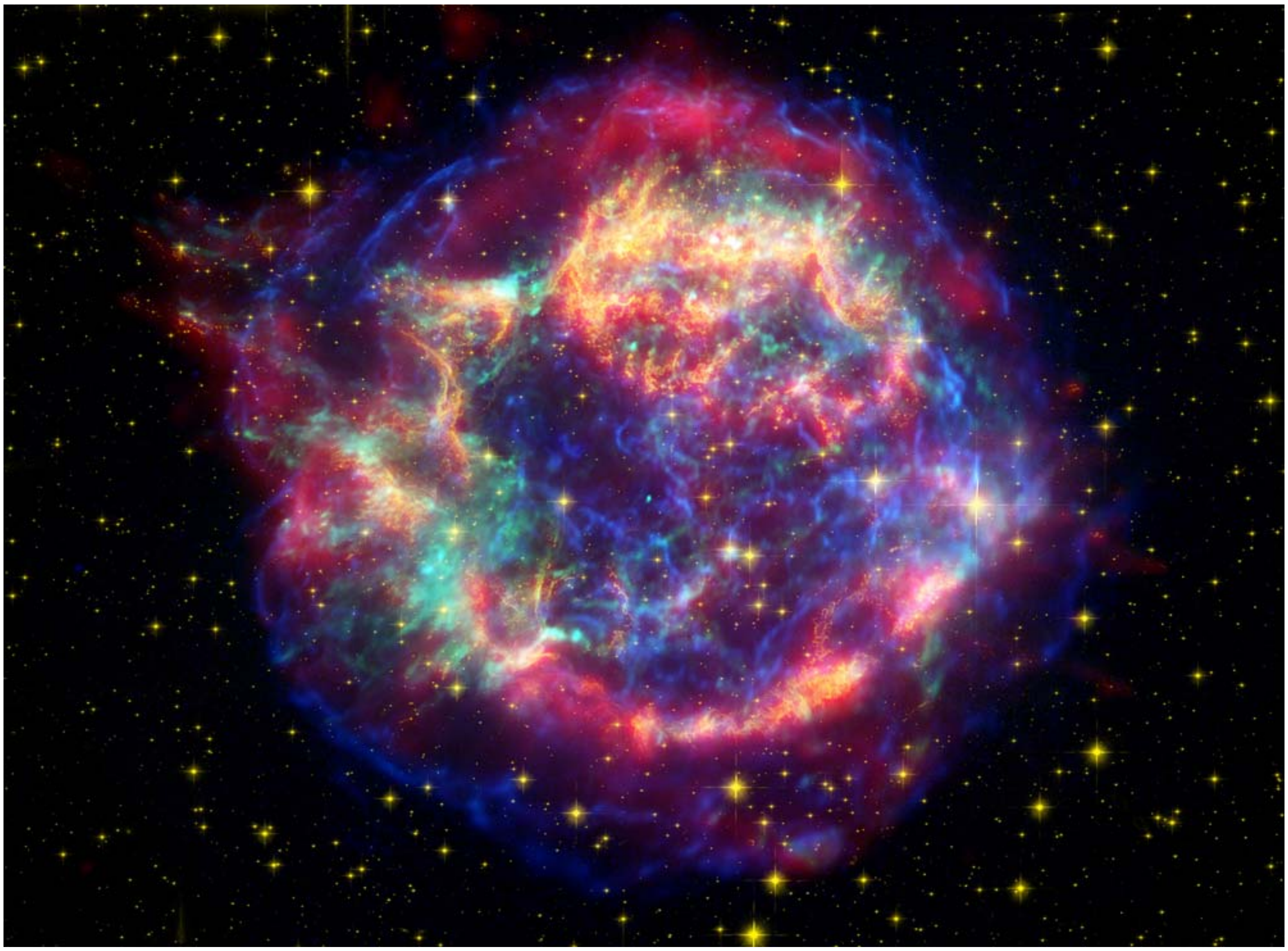
• The falling particles spiral around the blackhole, move faster close to it and release energy in the form of radiation - mainly X-rays

• The highly energetic SUPER HOT ATOMS near the blackhole are in a plasma state & emit bright K_α (1s-2p) X-rays

• Sucked materials are ejected as a jet (L & E conservation)

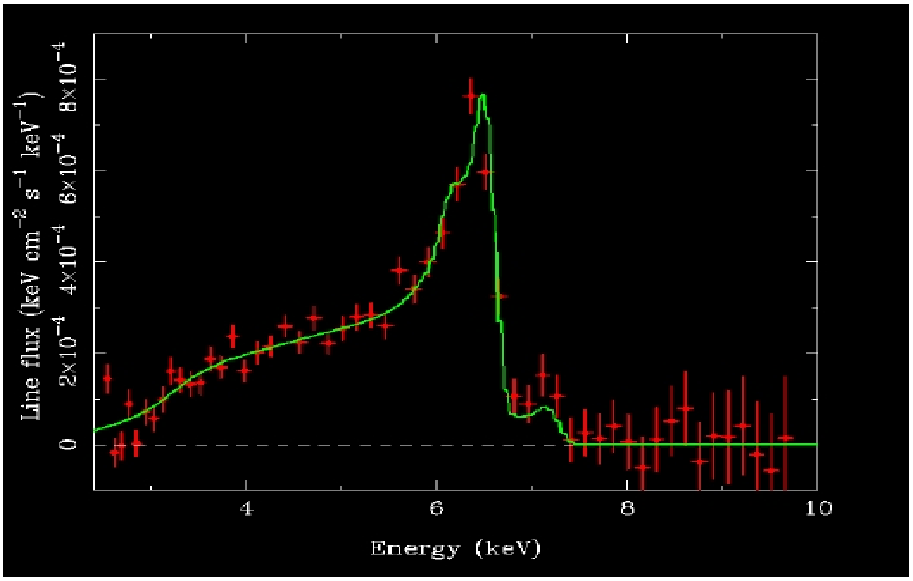
• Blasting from the black hole in the galaxy a jet of a billion solar-masses extending to 13,000 light years

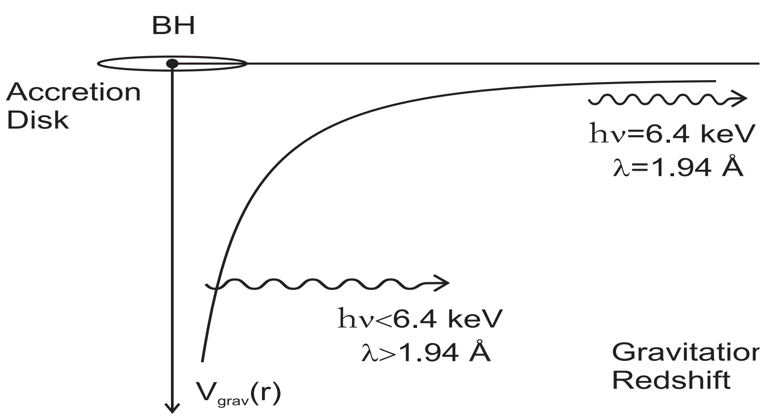
Photometry: Supernova Remnant CASSIOPIA A [Spitzer (Infrared - red), Hubble (Visible - yellow), Chandra (X-ray - green & blue)]



- Star elements: H, He, though Fe, some Ni
- Elements heavier than Fe created from nuclear fusion during supernova explosions are scattered into interstellar medium
- Our earth was created from supernova remnants (common for astronomical objects)
- Two pristine clouds of H & He discovered

Spectroscopy: Indication of a Black Hole (ASCA and Chandra)





- K_α (1s-2p) transition array lines of Fe in Seyfert I galaxy MCG-6-30-15 6
- Maximum ΔE = 6.4 keV for a 1s-2p transition
- The asymmetric stretching toward E $\sim$ 5 keV indicates presence of a black hole nearby
- K_α photons lose energy by the black hole's gravitational potential (AAS - Pradhan and Nahar)

X-RAY INTERACTION WITH ELEMENTS

1. Photoexcitation:

$$\mathbf{X^{+Z} + h\nu \rightleftharpoons X^{+Z*}}$$

- **Oscillator strength (f), Radiative decay rate (A-value)**
- **Form absorption and emission lines**

2. Direct Photoionization (PI) :

$$\mathbf{X^{+Z} + h\nu \rightleftharpoons X^{+Z+1} + \ e}$$

3. Photoionization via an Autoionizing State :

$$\mathbf{e + X^{+Z} \rightleftharpoons (X^{+Z-1})^{**}} \rightleftharpoons \begin{cases} e + X^{+Z} & \text{AI} \\ X^{+Z-1} + h\nu & \text{DR} \end{cases}$$

The intermediate doubly excited state - "autoionizing state" - introduces resonances

- 2 & 3. **Photoionization Cross Sections (σ_{PI})**
- **PI Resonances form absorption lines**

RESONANT NANO-PLASMA THERANOSTICS (RNPT)

(Pradhan, Nahar, Montenegro, Yu, Chem. Phys. 2009)

Physics of X-ray spectroscopy for a black hole similar to → X-ray sources in medical facilities.

- **Differences - heavier elements, high energy X-rays**
- **X-rays are absorbed by inner shell electrons for photoionization**
- **Produce low energy Auger electrons**
- **At the right Resonant energy production of electrons can be maximized (nano-plasma)**
- **A monochromatic X-ray source can be targeted at the resonant energy through spectroscopy and considerable reduce harmful effects**

RNPT is based on the above ideas

X-Rays: Cancer Treatment with Gold NP

N312 J F Hainfeld *et al*

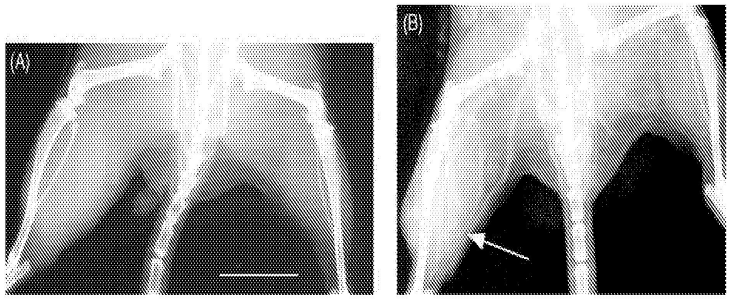


Figure 3. Radiographs of mouse hind legs before and after gold nanoparticle injection. (A) Before injection. (B) 2 min after i.v. gold injection (2.7 g Au/kg). Significant contrast (white) from the gold is seen in the leg with the tumour (arrow) compared with the normal contralateral leg. 6 s exposures at 22 kVp and 40 mA s. Bar = 1 cm.

- Top: Radiograph of mouse hind leg before and after injecting intravenously & accumulat-

Gold nanoparticles for radiotherapy in mice N311

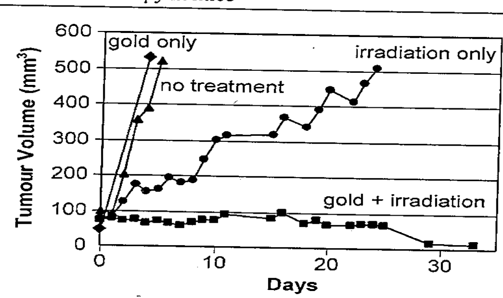


Figure 1. Average tumour volume after: (a) no treatment (triangles, $n = 12$); (b) gold only (diamonds, $n = 4$); (c) irradiation only (30 Gy, 250 kVp, circles, $n = 11$); (d) intravenous gold injection (1.35 g Au/kg) followed by irradiation (squares, $n = 10$).

- 30 days experiment: X-ray irradiation with gold NP reduced 85% tumor volume
- With Au NP, less radiation was needed to kill the defective cells than that in radiation therapy

Auger Electrons from Photoionzation

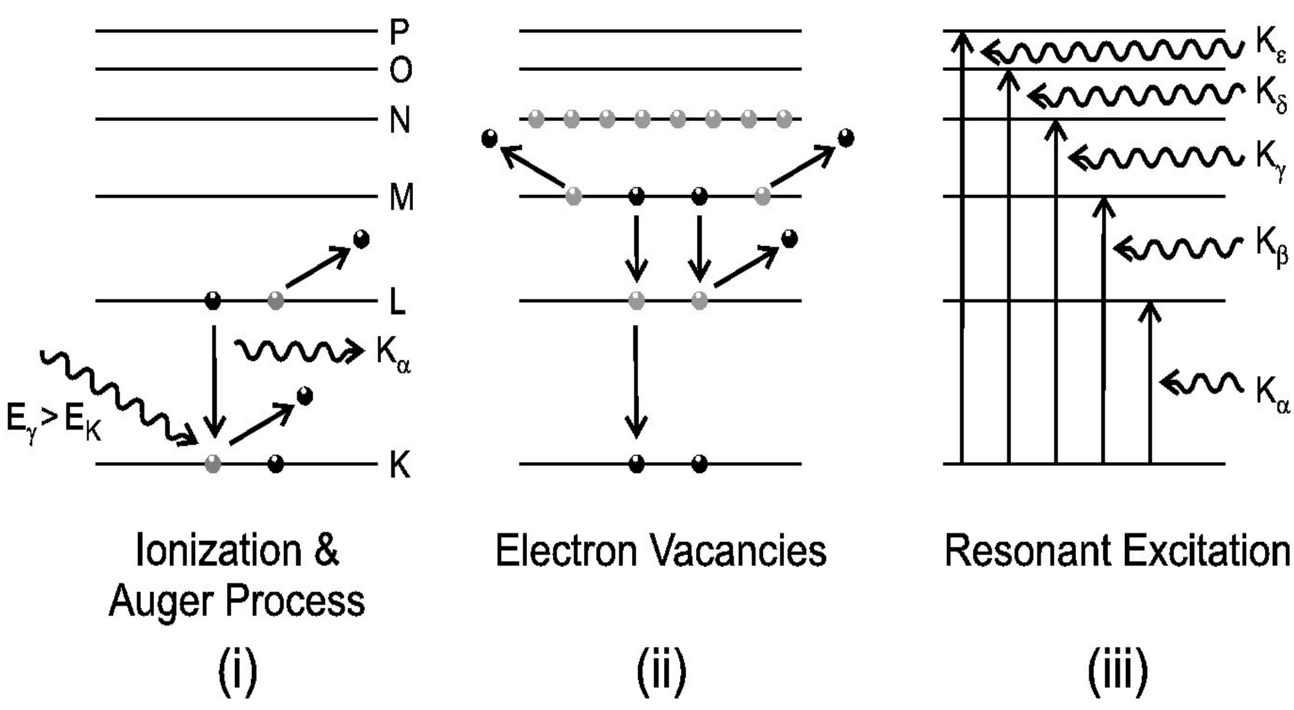
• Fig (i) K-shell ionization by an X-ray photon → Auger process - an inner shell hole is filled by an upper shell electron As a L-shell e^- drops to K-shell, a photon of excess energy is emitted which can knock out another L-shell e^-

• Fig (ii) Two vacancies created in L-shell are to be filled by M-shell e^-s. The process can lead to cascade of electron and photon emissions as multiple vacancies move upward

• Single ionization of 1s electron can lead to ejection of 20 or more electrons in an ion with occupied O and P shells

• Fig (iii) Inverse Auger - Resonant photo-excitation from 1s → 2p (with L-shell vacancy) by an external monoenergetic X-ray source with intensity above RNPT predicted critical flux

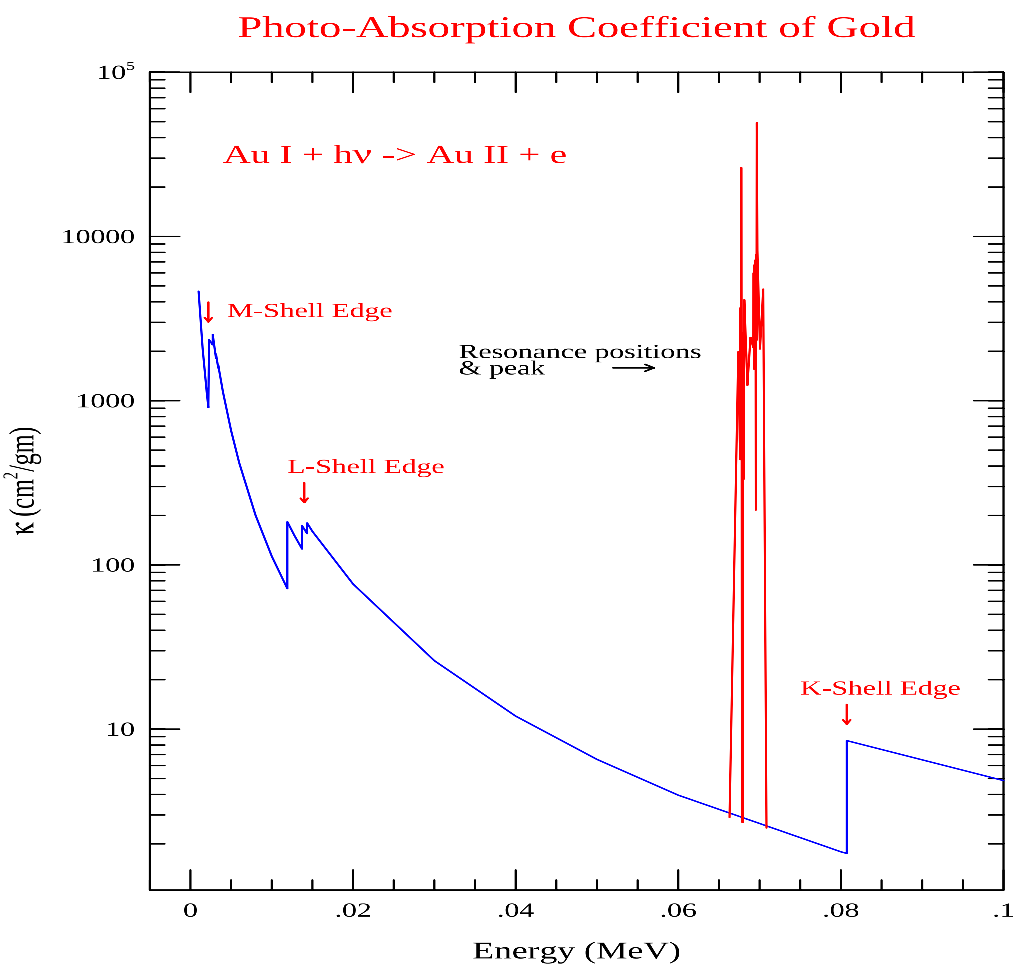
$$\Phi^c(\nu_{K\alpha}) = \frac{\sum_{n_i \geq 2} g_i A[n_i(S_i L_i J_i) \rightarrow 2(SLJ)]}{g_K B_{K\alpha}}. \quad (1)$$



PHOTOIONIZATION: X(ion) + $h\nu \rightarrow X^{+}$ + e

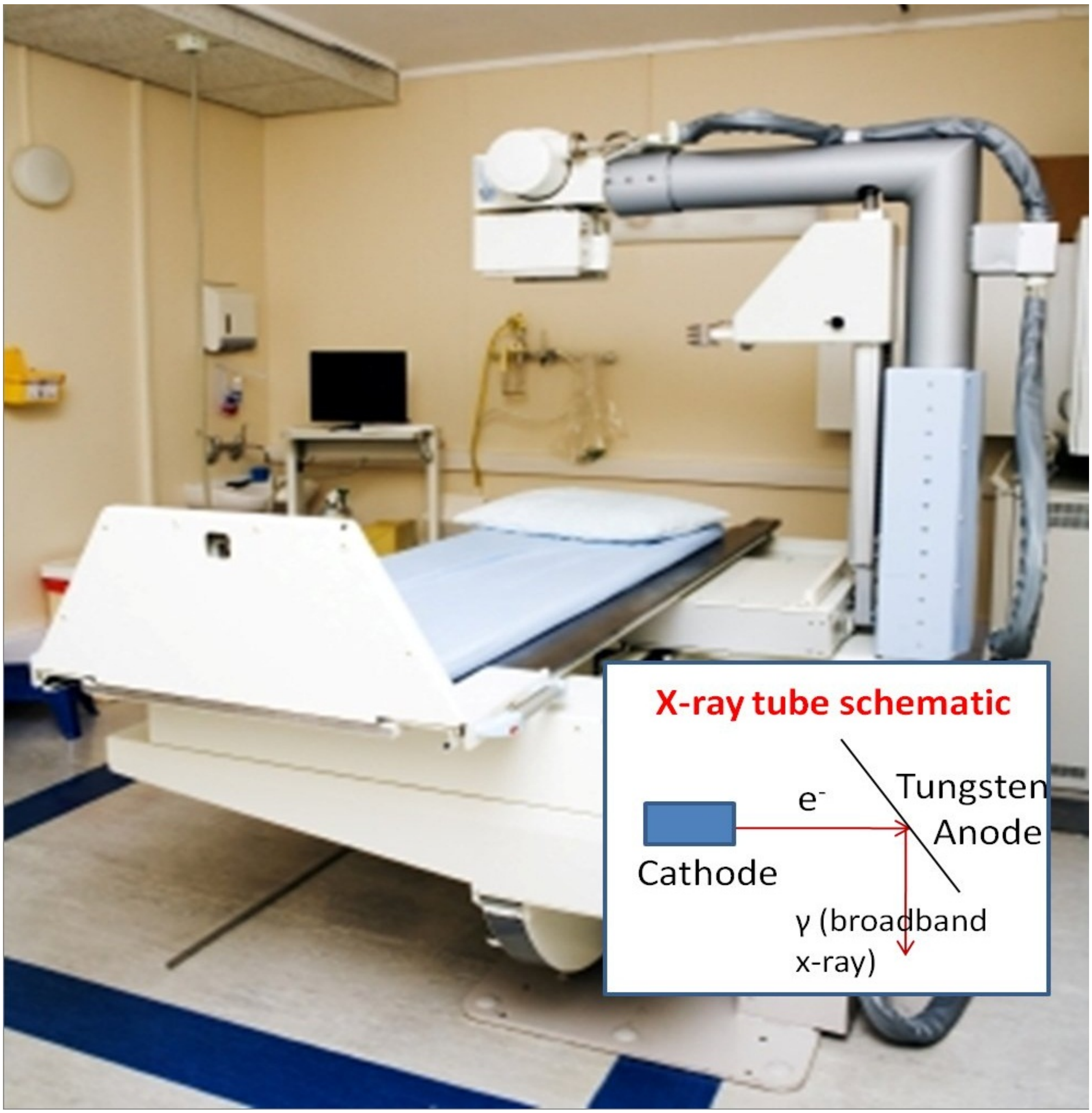
K-shell edge effect on X-ray absorption by gold nanoparticles

- Gold nanparticles absorb X-rays & photoionize
- Attachment of ejected electrons to the surrounding malignant cells breakdown the DNA
- OBJECTIVE: Increase number of electrons
- Fig: *background photoinization* σ_{PI} of Au
- σ_{PI} rises at various K, L, M (sub)-shells energies
- Rise in K-shell ionization edge $\sim$ 81 keV investigated with no evidence
- RNPT predicts resonant energy, below the K-edge, where probability of electrons production is orders of magnitude higher than that at K-edge (in red)



X-RAY SOURCES IN MEDICAL FACILITIES

- X-ray sources in medical facilities (Figure)
- Bremsstrahlung radiation is emitted as electrons accelerate between cathode & anode of a given ΔV and hit a high-Z target, e.g., tungsten (W) (Inset diagram)

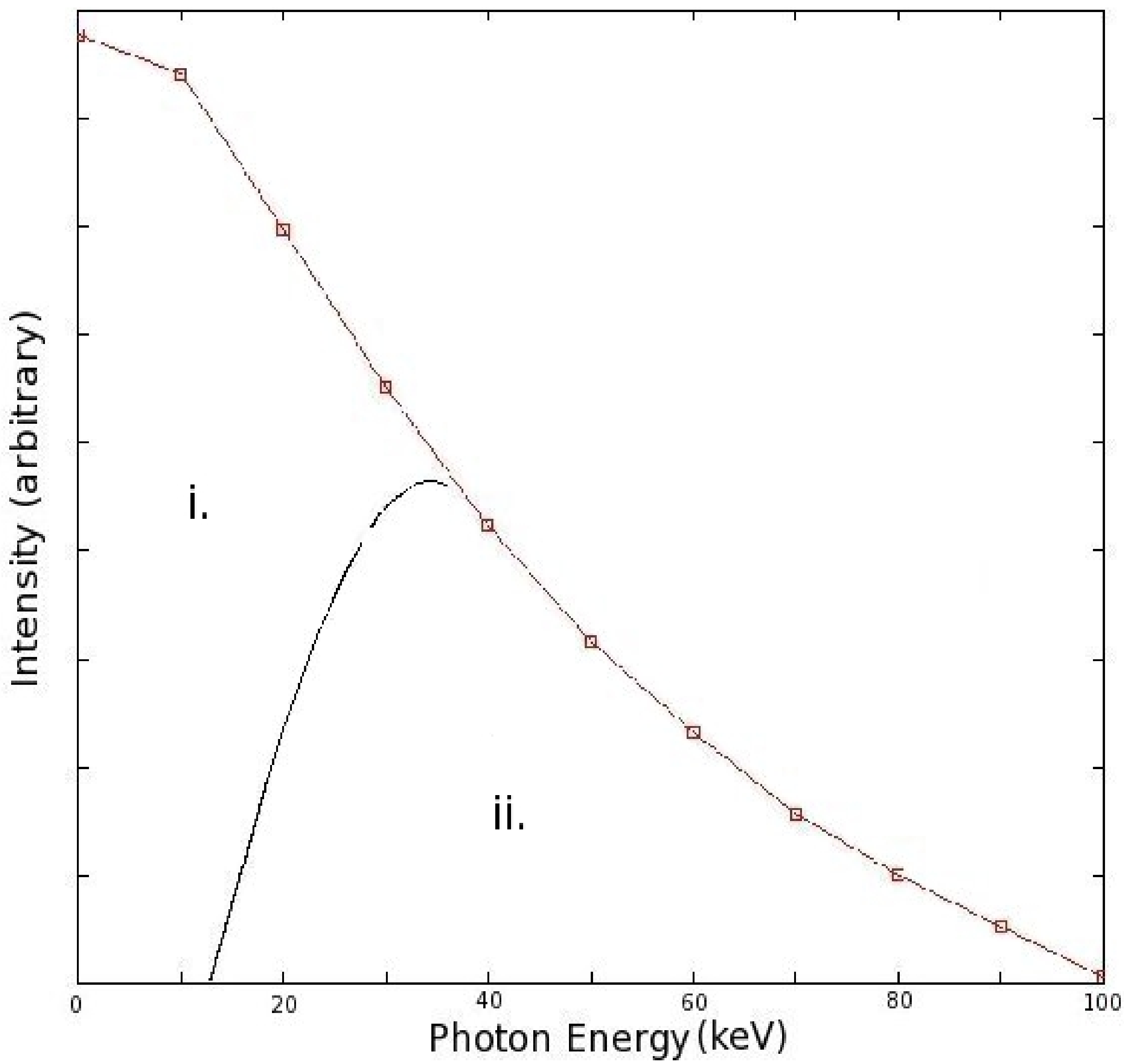


Typical Bremsstrahlung of an X-ray Machine

• The energy range of the BremsstrahlungI 0 - machine peak voltage (kVp). Fig: W Bremsstrahlung (square)

• A filter (e.g. Al, dotted) - reduces low energy radiation, harmful to body cells

• Bremsstrahlung- maximum at ~1/3 of kVP or MVp

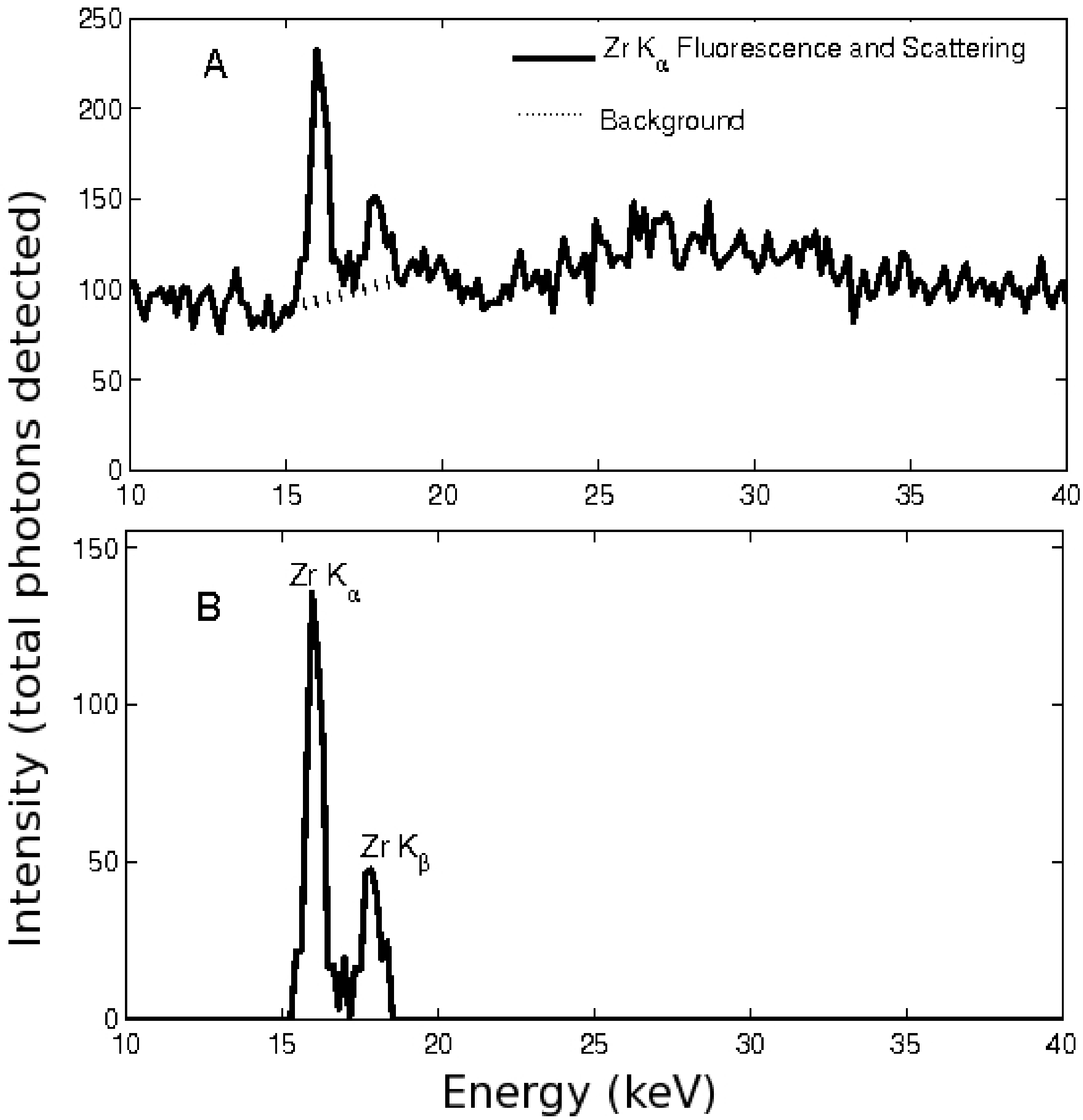


Production of Monochromatic X-rays

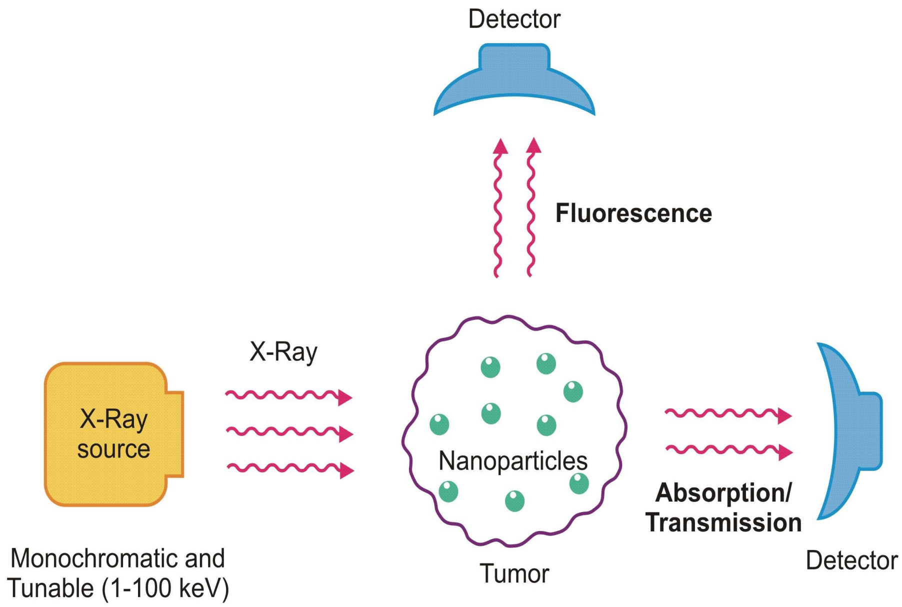
- Monochromatic X-rays can be produced by directing bremsstrahlung to a high-Z target rotated at a selective angle
- Inner K-shell ionization in the target followed by radiative decays by upper shell e^-s → X-ray fluorescence at monochromatic energies. Flourescence yield

$$\omega_{\mathbf{K}} = \mathbf{A_r(L-K)/[A_r(L-K) + A_a(L)]}$$

- Fig: Production of K_α X-rays from Zr (Pradhan et al 2010)



RNPT: NANOBIO-SPECTROSCOPY



- **With consideration of all points, RNPT is described above**
- **Nanoparticles of heavy elements are embedded in the tumor**
- **Direct X-rays at nanoparticle resonant energies from a tunable monochromatic source**
- **The heavy element absorbs/emits X-rays at higher energies where biogenic elements (H,C,N,O,CHON) are transparent**
- **Fluorescent emission and electron ejections due to inner-shell ionization and produce nano-plasma**
- **Electrons breakup the DNAs of tumor cells**
- **Spectroscopically targeted radiation should be far more efficient with reduced exposure**

Monte Carlo Simulation for Resonant K_α X-Ray Absorption by Au Nanoparticles

(Montenegro et al. 2009)

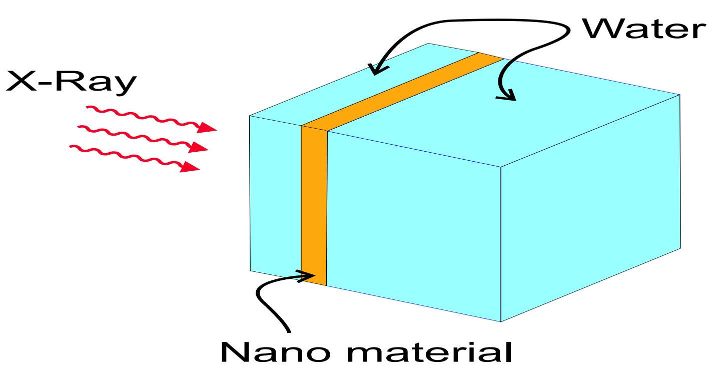
• We applied gold κ in Monte Carlo simulation to study X-ray absorptions and intensities of emitted photons and electrons by Auger process in tissues

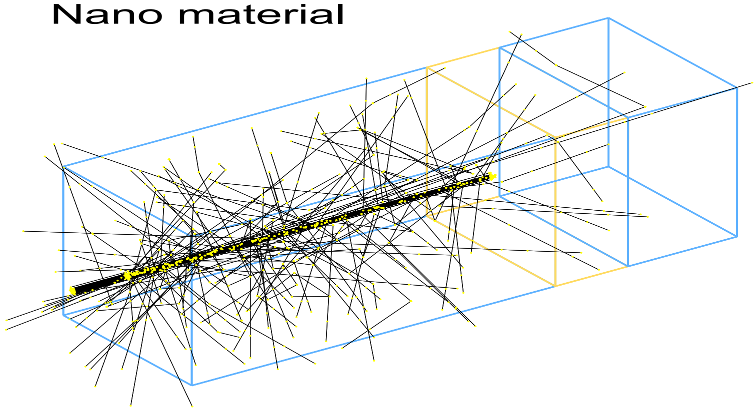
• Modifed the simulation code, GEANT4, to include the resonant cross sections

• **TOP:** Geomtry of the experiment - the phantom (15 x 5 x 5 cm) models a tumor embedded with gold nanoparticles (golden section 2 cm) 10 cm inside normal tissue (blue section)

• **BOTTOM:** Simulation - gold nanoparticles at 5 mg/ml, X-ray beam at resonant energy $\sim$ 68 keV

• **NOTE:** Because of Compton scattering only a few photons reach the region with gold nanoparticles

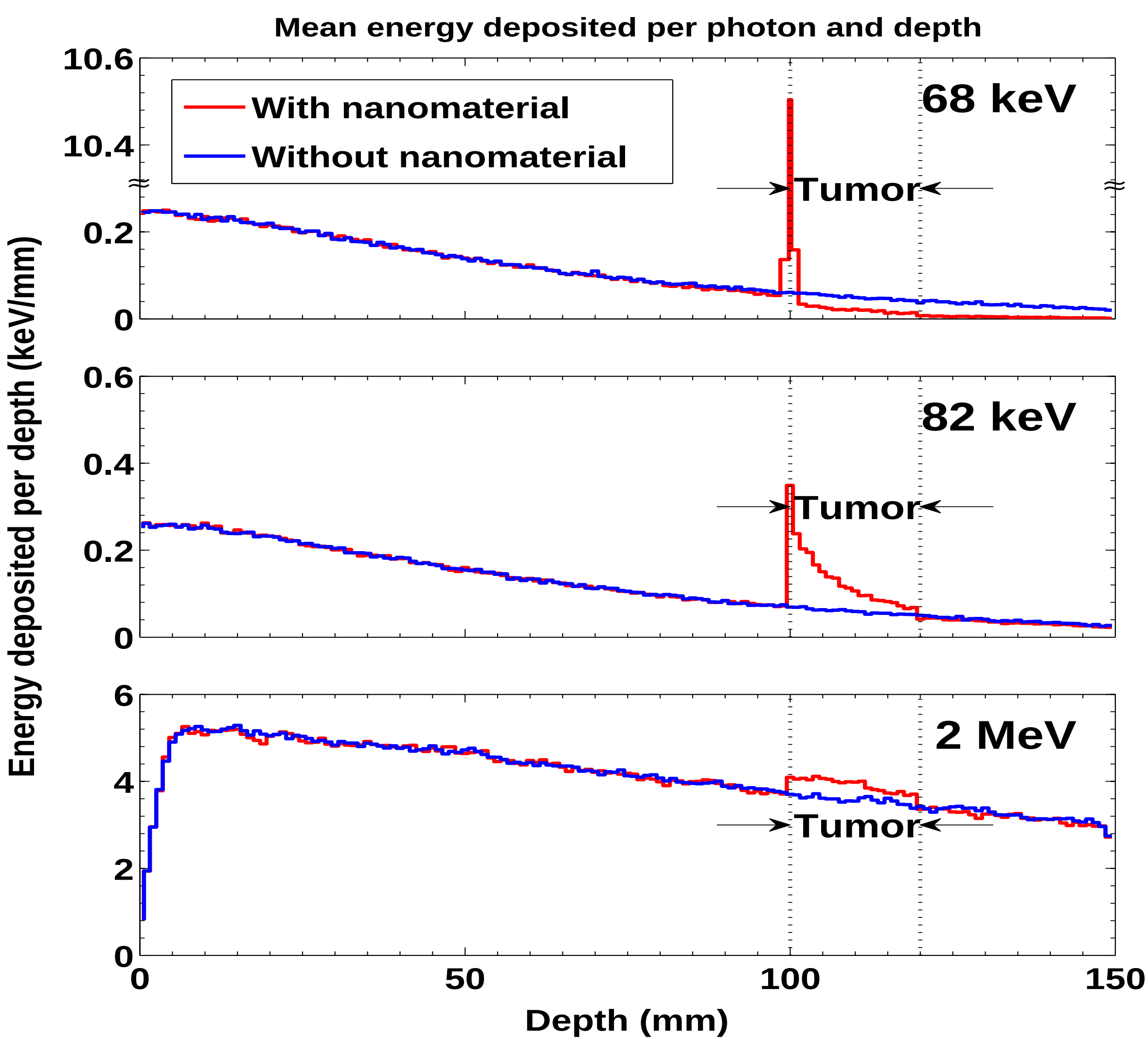




X-RAY ABSORPTION BY Au AT 68 keV, 82 keV, 2 MeV

Figure: X-ray energy deposited by depth in the phantom: Red curve - with tumor in region 100 to 120 mm embedded with gold nanoparticles at 5 mg/ml, Blue curve - only water

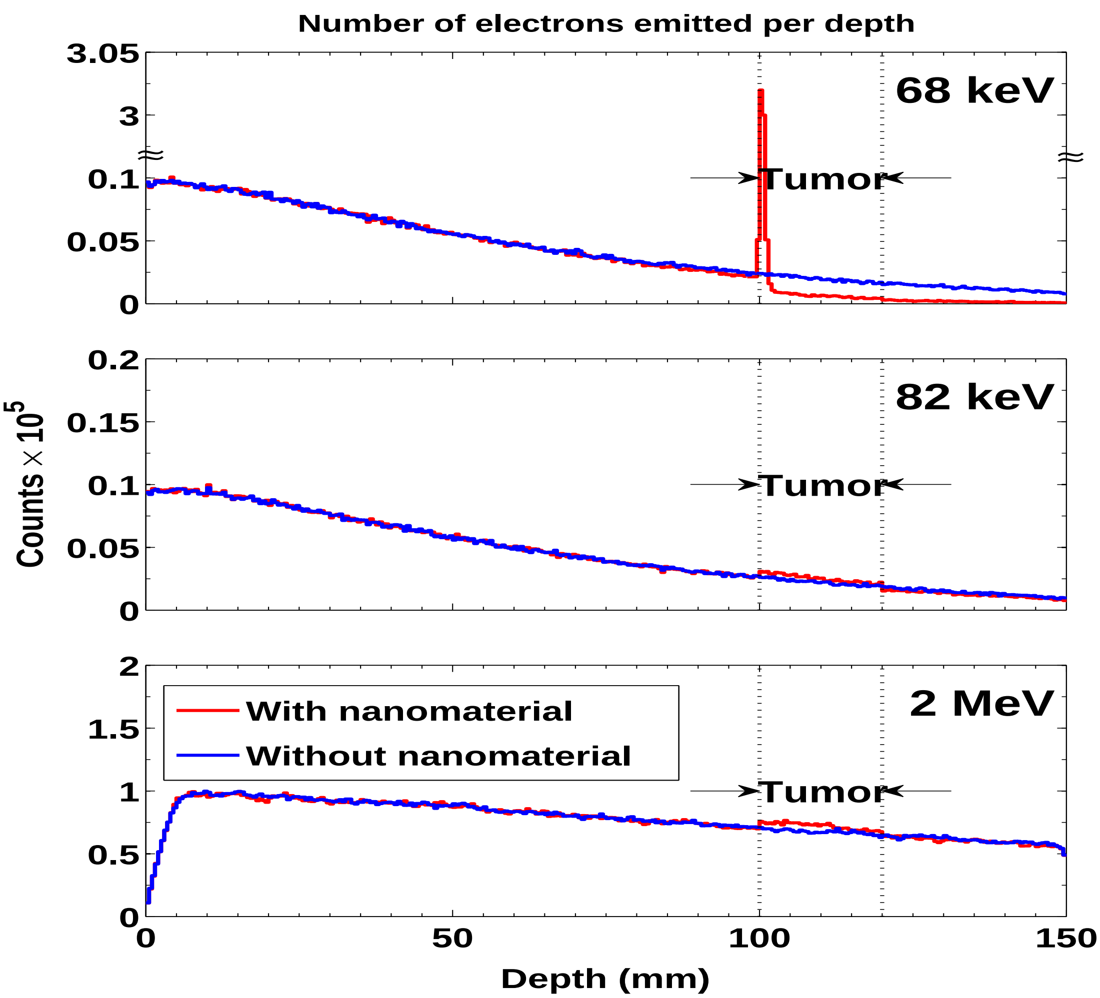
- **Top:** X-ray at 68 keV - averaged Kα resonant energy
- **Middle:** 82 keV - just above K-edge ionization energy
- **Bottom:** 2 MeV - high energy common in clinical usage
- The presence of gold nanoparticles has increased the energy deposited at the tumor
- The highest absorption, by more than 25 time that at 82 keV, is at the resonant energy 68 keV (top panel)



ELECTRON PRODUCTIONS AT 68 keV, 82 keV, 2 MeV

Figure: Number of Auger electrons produced with depth following X-ray absorptions: Red curve - tumor embedded with gold nanoparticles at 5 mg/ml in region 100 to 120 mm, Blue curve - only water

- **Top:** X-ray at 68 keV - averaged Kα resonant energy
- **Middle:** 82 keV - just above K-edge ionization energy
- **Bottom:** 2 MeV - high energy common in clinical usage
- A considerably large number of electrons, by more than an order of mangitude, were produced by 68 keV X-rays compared to those by 82 keV and 2 MeV

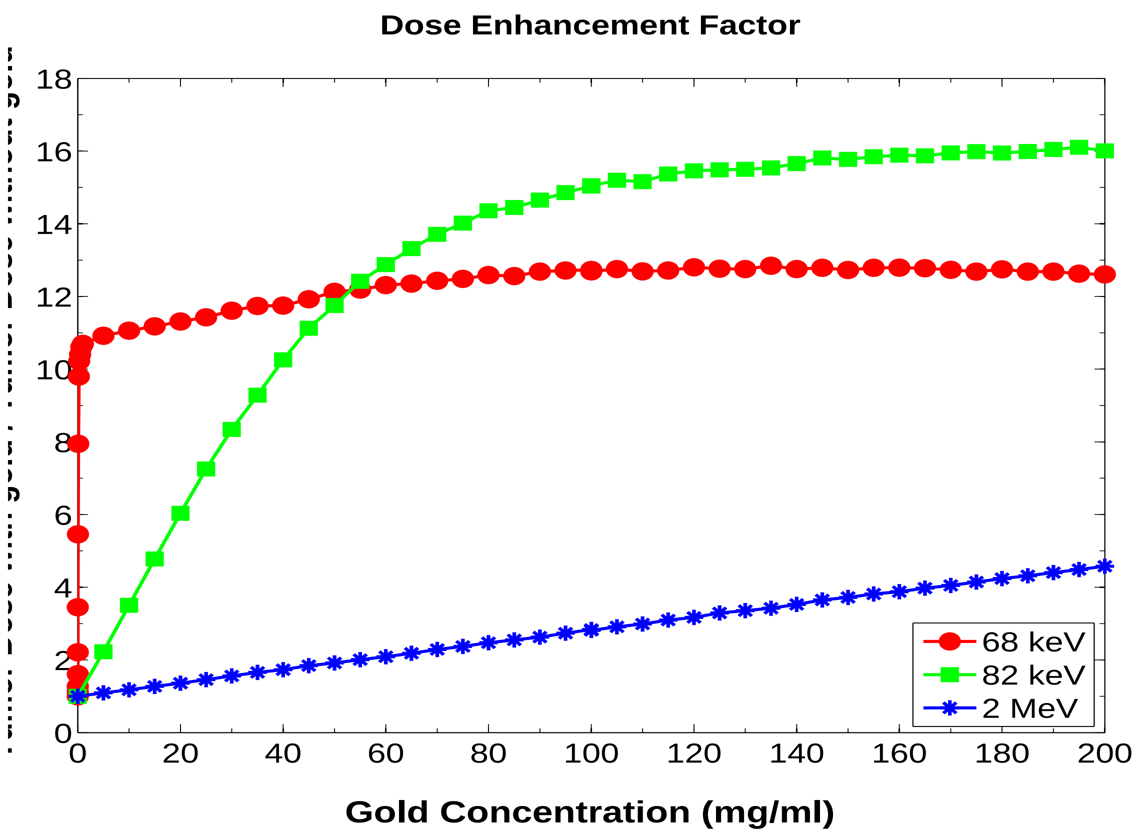


Radiation Dose Enhancement Factor (DEF)

DEF is the ratio of the average radiation dose absorbed by the tumor when it is loaded with a contrast medium or agent (viz. iodine) to the dose absorbed without that agent

Figure: DEFs with various gold nanoparticle concentration from 0 to 50 mg/ml

- **Red:** X-ray at 68 keV - averaged Kα resonant energy
- **Green:** 82 keV - just above K-edge ionization energy
- **Blue:** 2 MeV - high energy common in clinical usage
- The DEFs obtained for the resonant X-ray beam of 68 keV are one order of magnitude greater than those calculated at lower concentration using iodine as a contrast agent.



CONCLUSION

1. **RNPT is explained with X-ray spectroscopy of Au nanoparticles where we predict resonant energies below the K-shell ionization threshold for enhanced X-ray absorption**
2. **We obtained Auger resonant probabilities and cross sections to obtain total mass attenuation coefficients with resonant cross sections**
3. **We find that the attenuation coefficients for X-ray absorptions at resonant energies are much larger, over orders of magnitude, higher over the background cross section as well as to that at K-edge threshold**
4. **We have been able to produce monochromatic radiation from the Bremsstrahlung of a conventional X-ray tube machine**

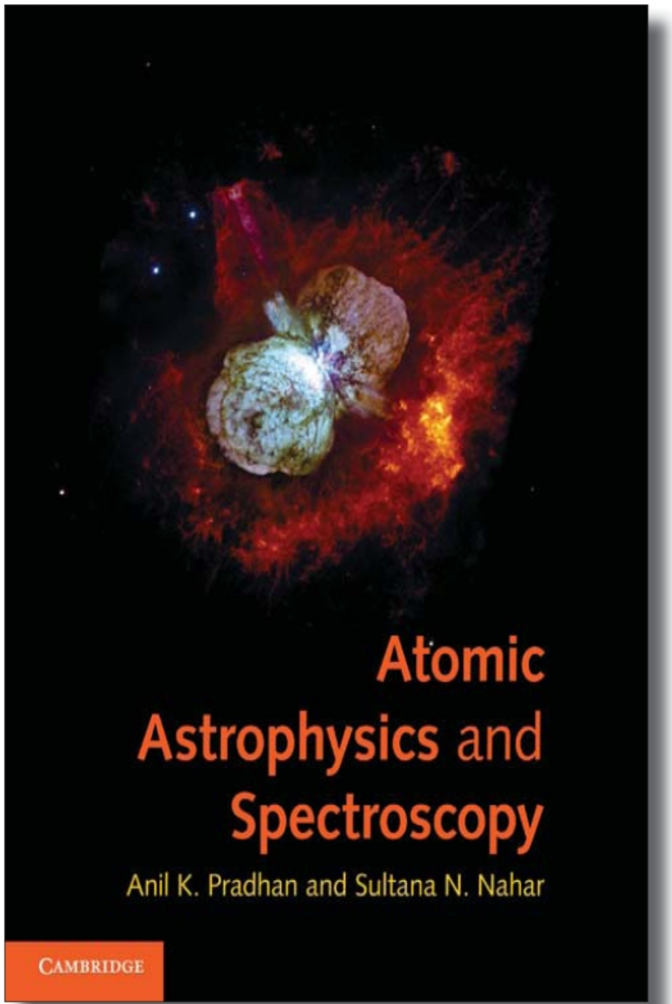


Table of Contents