Mary Bird Perkins Cancer Center’s
CAMD Cancer Therapy Research Program

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Why High-Z Enhanced Radiation Therapy?

• Current radiation therapy practice targets a volume of tissue (PTV) quite accurately:
  – Intensity modulated radiation therapy (IMRT)
  – Proton therapy & heavy ion therapy
  – Image guided radiation therapy (IGRT)
  – Respiratory gated radiotherapy
  – Adaptive radiotherapy (Intrafraction and interfraction changes)

• Can we improve radiation therapy by targeting cancer at the cellular level?
Current Study
Properties of Iododeoxyuridine (IUdR)

- IUdR replaces thymidine in DNA during cell division.

- X-ray capture by I in IUdR results in tremendous local energy deposition in the DNA, enhancing the effectiveness to radiation dose.

Thymidine

IUdR

Kassis 2005

β⁻

Auger e⁻
CHO Cell Survival vs Dose to Water

- 16.6% thymidine replacement
- SER~2.7
- SER~4.3

- 12.0% thymidine replacement
- SER~2.3
- SER~3.1

- 9.2% thymidine replacement
- SER~1.6
- SER~2.1

- 0.001
- 0.01
- 0.1
- 1

- 0.0
- 0.5
- 1.0
- 1.5
- 2.0
- 2.5
- 3.0
- 3.5
- 4.0
- 4.5
- 5.0
- 5.5
- 6.0
- 6.5
- 7.0
- 7.5

- 35 keV + IUdR
- 4 MV + IUdR
- No IUdR
High-Z Enhanced Radiation Therapy
Requisites

• **Drug Properties**
  – Contains high-Z atom(s)
  – Preferentially targets cancer cells
  – Adequate concentration achievable (non-toxic)

• **Photoactivation**
  – Monochromatic X-ray Source ($E_\gamma > E_{K\text{-edge}}$)

• **Optimal Energy**
  – Treatment site
  – Drug location with respect to cell
    • DNA (IUdR, cis-platinum)
    • Intra-nuclear (oxine)
    • Intra-cellular or cell wall (antibodies)
    • Inter-cellular (iodine contrast, Au nanoparticles)
High-Z Enhanced Radiation Therapy with Monochromatic X-rays: Project Goals

• **Goal 1: Understand the Mechanism for IUdR Sensitization**
  – Measure cell survival curves as a function of %IUdR (9% & 18%) and energy (25-70 keV and 6 MV).
  – Develop cell survival model(s) as a function of E and %IUdR.

• **Goal 2: Predict cell survival in a patient-like phantom**
  – Use a Monte Carlo (MC) model for calculating differential dose in a cylindrical phantom for rotational therapy.
  – Develop models for calculating dose equivalent using MC-calculated differential dose.
  – Determine and verify optimal energies for rotational therapy for various planning target volumes by comparing measured cell survival curves with models.
MPBCC-LSU DOD Grant
High-Z Enhanced Radiation Therapy with Monochromatic X-rays: **Project Goals**

- **Goal 3: Construct User-Friendly Medical Radiology Beamline**
  - Specify, acquire, and install biomedical beamline components, hutch, and experimental apparatus on new multi-pole wiggler beamline.

- **Goal 4: Develop Treatment Planning System for High-Z Therapy**
  - Develop a treatment planning model for high-Z enhanced rotational delivery.
  - Integrate the model with a commercial treatment planning system and validate.

- **Goal 5: Develop Feedback for High-Z Drug Development**
  - Investigate dose to DNA versus monochromatic energy and cellular location.
  - Determine minimal drug concentrations and optimal beam E required for sensitization ratio of 2 as a function of tumor site and cellular location.