Low-Z linear accelerator targets
Options for image guidance and dose enhancement in radiotherapy

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Disclosures

Low-Z linear accelerator targets

1. Underlying physics
2. Beam characteristics
3. Imaging applications
   • Options with an MLC in the imaging beamline
4. Possibilities for therapy
   • Nanoparticle-aided radiotherapy
What is a low-Z target?

- A target with Z≤13, which is low in comparison to conventional tungsten (Z=74) or copper (Z=29) therapy target materials
  - Examples: beryllium, graphite, diamond, aluminum
- Used to recover a significant population of low-energy photons in a linac-generated beam
- Useful for imaging or dose enhancement

A look at the Truebeam target

Early days: Galbraith (1989)
Beryllium and graphite targets
Low-Z targets: physical rationale

1. While diagnostic energy bremsstrahlung photons are created in high-Z and low-Z targets, use of a low-Z target reduces the absorption of low-energy photons within the target itself.

2. Electron-electron bremsstrahlung is more significant in low-Z targets compared to high-Z targets. The spectrum produced has a lower peak energy than electron-nuclear bremsstrahlung [5].

3. With regard to efficiency, while higher-Z targets give a greater yield of bremsstrahlung overall, over the forward 0-15° angular range, i.e. that subtended by a typical linac primary collimator in a linac, the yield is roughly independent with Z.

Three modifications for a low-Z target beam

1. Reduce the Z of the target
2. Remove the flattening filtration
3. Lower the electron energy (optional)

Experimental targets
**Choice of target material**

**Reducing Z from 2 to 4 lowers peak energy from 50 to 20 keV**

<table>
<thead>
<tr>
<th>Author</th>
<th>Target thickness and material</th>
<th>Electron energy</th>
</tr>
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<tbody>
<tr>
<td>Galbraith (1989)</td>
<td>14.2 mm graphite</td>
<td>6 MeV</td>
</tr>
<tr>
<td>Tsechanski (1998)</td>
<td>5 mm aluminum</td>
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<tr>
<td>Ostapiak, O'Brien, and Faddegon (1998)</td>
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<td>1.65 to 2.35 MeV</td>
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**Target material, thickness and energy**

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**Lowering the electron beam energy**

| Graphite 2.25 MeV, Percent Deposition = 48.5% | Graphite 7.00 MeV, Percent Deposition = 46.5% | Aluminum 2.25 MeV, Percent Deposition = 46.5% | Aluminum 7.00 MeV, Percent Deposition = 46.5% | Aluminum 10.00 MeV, Percent Deposition = 46.5% |

**Patient dose deposition**

Lowering the electron beam energy... there are limits

Siemens low-Z target

Elekta low-Z target

... had a nickel vacuum window – this was the source of ~70% of the photons in the beamline!
Low-Z targets
Imaging applications

Improvement of image quality
CNR versus dose compared to 6MV

Improvement of CNR – BEV imaging

Factor of 2.2 to 9.7 improvement of CNR

Improvement of CNR – BEV imaging

Thin layer of Cu on exit side of target.
Detector considerations – remove Cu layer

Experimental imaging with low-Z beams

Volume Of Interest CBCT imaging
Spatially vary CNR with dynamic MLC sequences

Commission Eclipse with low-Z beam data

Compensate for imaging dose in treatment at planning time
Experimental high-Z / low-Z switching

- Prototype located in carousel of Varian Clinac platform
- ~ 250 ms switching between W/Cu and graphite targets
- Imaging application: periodic BEV imaging at high quality
- Imaging application – intrafractional BEV
- Therapy application: combination high-Z / low-Z treatment

Intra-fractional imaging paradigm

- 6 MV FFF treatment
- @ "imaging moment"
- Switch to 6 MV/Diamond beamline
- High CNR BEV image
- Switch to 6 MV FFF
- Resume treatment

Low-Z targets
Therapeutic applications
Au GNPs / HeLa cells with γH2AX staining

Berbeco et al., Radiation Research 178, 2012

Compelling evidence that photon energy will affect GNP dose enhancement in vitro

6 MV FFF beam more effective at cell kill compared to standard 6 MV beam (p=0.014 Wilcoxon)

Survival fraction

Dose [Gy]

Table 1. Dose enhancement factors in terms of BEG(AP2,ex), and BEG(Exc) for HeLa cells irradiated with 6 MV x-rays.

<table>
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<tr>
<th>Preparation</th>
<th>Dose Enhancement</th>
<th>BEG(AP2,ex)</th>
<th>BEG(Exc)</th>
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<tr>
<td>6 MV STD</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>6 MV FFF</td>
<td>1.05</td>
<td>1.10</td>
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p value: 0.014

6 MV FFF beam more effective at cell kill compared to standard 6 MV beam (p=0.014 Wilcoxon)

Low-Z targets for endothelial dose enhancement

Endothelial dose enhancement

Compared to a standard 6 MV beam, 6MV/Carbon provides

- 18.6 x dose at d=2 cm
- 7.7 x dose at d=10 cm
- 4.0 x dose at d= 20 cm

6 MV Cu/W FPF beam provides 1.5 to 2.0 x dose


To do NP dose enhancement experiments, we need sufficient dose rate!

Mark I
Mark II

A new experimental low-Z target for Truebeam

PDDs from new targets

High dose rate possible!

Dose rate is ~67% of that for 6MV clinical beam @ dmax
**Zebrafish as a model organism**

- *Danio rerio* is a tropical freshwater fish that has emerged as a useful model organism for studying vertebrate development and human cancers.
- Fully sequenced genome
- Embryos are produced in large numbers
- Develop rapidly outside the mother
- Optically clear
- Many useful transgenic lines.
- Established protocols for xenografting cancer cells into zebrafish embryos and assessing cell migration and proliferation.

![Image of zebrafish embryos and larvae]

**CURRENT WORK**

**Experiment 1: xenograft**

1. Label cells with GNP + fluorescent dye
2. Dissociate embryos to single cell suspensions and count fluorescent cells
3. B/A = Fold increase in cell number

4. 0 h
5. 72 h
6. No irradiation; OR
7. 6 MV standard; OR
8. 6 MV low-Z target

Modified from Corkery et al., 2011

**CURRENT WORK**

**Experiment 2: GNPs targeting endothelial cells**

- Inject GNP IV
- treatment
- confocal microscopy

- No irradiation; OR
- 6 MV standard; OR
- 6 MV low-Z target

Zhu et al., 2016

![Image of zebrafish embryos with fluorescent markers and confocal microscopy results]
Summary

• Low-Z target beams can contain up to 50% of photons in the diagnostic energy range

• Imaging
  • Factor of 2-9 increase in CNR per unit dose compared to 6MV
  • New options to localize dose using MLC
  • Switching target may allow rapid, high-quality BEV imaging

• Therapy
  • Compelling evidence that GNP-aided radiotherapy will be more effective with low-Z target beams
  • Much more work to do here, but we have the tools

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