What are Protons vs. CyberKnife

Protons:
- Charged particles (Bragg Peak)
- Deposits dose at certain depth in tissue
- No exit dose
- Treatment with 2 opposed lateral beams
- Standard fractionation over 8-9 weeks
- Doses identical to IMRT
- Used routinely in optic, CNS, BOS and pediatric tumors

CyberKnife:
- X-rays = photons (6MV)
- Robotically delivered
- Dose delivered continuously while transverse through tissue
- Exit dose
- Treatment with hundreds of beams
- Hypofractionated over 4-5 days
- Doses identical to HDR brachytherapy
- Used routinely for brain, spinal and some lung tumors

Dose Distribution Comparison
Photons vs. Protons

Effective Relative Dose*
True or False?
There are no randomized trials comparing protons to photons?

False (IJROBP 32:3-12, 1995)

Randomized trial of protons vs photons

- T3-T4 adeno ca prostate
- 50.4 Gy photons using 4 field box
- Randomized
  - 25.2 Gy protons
  - 16.8 Gy photons
- No difference in:
  - Overall survival
  - Disease-free survival
  - Local control
- Rectal bleeding
  - 32% (protons) p=0.002
  - 12% (photons) p=0.07
- Urethral stricture
  - 19% (protons)
  - 8% (photons)

IJROBP 32:3-12, 1995
True or False?
Protons are better at hitting the prostate than photons?

True and False

What are the problems with protons?

- Highly sensitive to uncertainties

Dosimetric uncertainty in prostate cancer proton radiotherapy

Li Yong Lin, Carla Vega, Wei Hua, Daniel Indelicato, Rolf Eklund, Zuo Fang Li, Daniel Yeung, Dave Horne, and Joelender Patra

University of Florida Proton Therapy Institute, Jacksonville, Florida 32286

- “The DVHs of rectal and bladder walls vary due to the uncertainty in the position of the rectal and bladder walls relative to the sharp dose falloff gradients produced by proton radiation therapy.”
- Locally translated: Protons are good at putting dose in the prostate, but if the prostate moves, protons will put dose in the rectal or bladder wall.


True or False?
The dosimetry of protons is better than IMRT?

The dosimetry of protons is better than IMRT?

True and False

Clinical Investigation

Radiotherapy treatment of early-stage prostate cancer with IMRT and protons: A treatment planning comparison


Department of Radiation Oncology, Massachusetts General Hospital and Harvard Medical School, Boston, MA.

- “In the range higher than 60 Gy, IMRT achieves significantly better sparing of the bladder whereas rectal sparing was similar with protons and IMRT.”
- “Dose the healthy tissue in the range lower than 50% of the target prescription (<40 Gy) was substantially lower with proton therapy.”

UROBP 69:444-453, 2007
Dosimetry of protons vs IMRT?

Clinical results: Protons vs Photons

- PROG (Harvard and Loma Linda)
  - 70.2 Gy vs 79.2 Gy
  - First 50.4 Gy delivered with photons
  - Only boost protons (19.8 or 28.8 Gy)
  - 5-yr bNED 79% vs 91%

- MD Anderson
  - 70 Gy vs 78 Gy
  - 5-yr bNED 85% vs 78%

Clinical results: Protons vs Brachytherapy

- UCSF
- Analysis of patients treated with PPI
- All risk groups

- Jabbari IJROBP in press

CyberKnife

- X-rays = photons (6MV)
- Hundreds of non-coplanar beams
- Robot controlled linac
- Hypofractionated over 4-5 days
- “Experimental” because the dose per fraction is higher than traditional IMRT or protons and there is no long term follow-up.
- “Not experimental” because dose delivered is identical to HDR brachytherapy, which is a standard therapy for prostate cancer with long-term follow-up.

Years from PPI Cumulative Proportion
0.00 0.25 0.50 0.75 1.00
5 Year Est.
PPI: Low Risk                         94%
PPI: Increased Risk               90%
CPBRT: Low Risk                  97%
CPBRT: Inreased Risk          82%

Nadir PSA (ng/mL)
25% 50% 75% 100%
Percent of Patients

PPI
CPBRT
Analogy to HDR brachytherapy

- Delivers high-dose radiation in a single fraction
- Allows for hypofractionated treatment
- Treatment can be completed in 2-5 fractions
- CyberKnife compared to HDR
  - Less invasive
  - Less anesthesia
  - Less risk of bleeding and infection
  - Less requirement for pain medication
  - No overnight stay in the hospital

HDR brachytherapy as boost

- High dose group
- Less biochemical failures
- Less distant mets
- Improved DFS, CSS and OS

HDR brachytherapy as boost is a standard therapy

- RTOG 0321 (PI: I.C. Hsu)
  - Phase II clinical trial of EBXRT + HDR boost
  - EBXRT 45 Gy
  - HDR boost 9.5 Gy × 2
  - Closed to accrual
HDR brachytherapy monotherapy

• N = 149
• T1c/T2a, PSA < 10, GS < 7
• $^{103}$Pd (120 Gy) vs HDR 9.5 Gy x 4
• Median follow-up 35 m
• Similar biochemical control at 3 yrs
  • HDR (98%) vs Pd (97%)

J Urol 171: 1098-1104, 2004

Dosimetric Comparison between HDR and CK

J UROBP 70: 1588, 2008

Dosimetric comparison of CyberKnife and IMRT

Hossain unpublished data

CK for Prostate: Stanford experience

41 patients
7.25 Gy x 5 fractions over 10 days
T1c-T2b, GS <=6, PSA <=10
Treatment volume = prostate + 5mm (3mm posterior)
Median follow-up 33 m
2 patient with late grade 3 GU toxicity
No patients with grade 3 GI toxicity
No PSA failures
PSA nadir < 0.4 (78%)
CK for Prostate: UCSF experience

- 47 patients (24 monotherapy, 23 as boost)
- Low-risk patients treated with monotherapy
- Int/high-risk patients treated as a boost to whole pelvic XRT
- One patient treated post-prostatectomy (HRPCa)
- One patient treated post-EBXRT (HRPCa)
- One patient treated post-RP and salvage RT (HRPCa)
- Treatment volume = prostate (first 15 patients) prostate + 2 mm (after)
- One patient with grade 3 GU toxicity
- No patients with grade 3 GI toxicity
- No PSA failures

Conclusions

Protons

- Physical advantage due to charged particle
- Results similar to 3DRT and brachytherapy
- Dose to normal tissue
  - Bladder receives more than IMRT
  - Rectum similar to IMRT
  - Femoral heads and penile bulb receive more than IMRT
- Less low dose regions than IMRT
- Implies less risk of secondary malignancies

CyberKnife

- Robotic RT
- Up and coming modality
- Low toxicity
- Short treatment time (4-5 days)
- Analogous dosing to HDR brachytherapy
- Less invasive than brachytherapy
- No long term follow-up