Impact of technology on Radiation Oncology

AAPM Symposium

Stephen M. Hahn

July 21, 2014

Disclosures

- No conflicts to disclose

http://www.med.upenn.edu/apps/my/index.php?_app_id=514c30e6e9b58Displays=1&_ Nat_Id=1&_ preserve=nt Panel]=%2Fread_public%2Fmain%2FCelID=

Cancer Statistics, 2013
Rebecca Siegel, MPH; Deepsa Nooruddin, MA, MS2;
Ahmedin Jemal, DVM, PhD

Overall, cancer death rates have declined 20% from their peak in 1991 (215.1 per 100,000 population) to 2009 (173.1 per 100,000 population).

Death rates continue to decline for all 4 major cancer sites (lung, colorectum, breast, and prostate).

The reduction in overall cancer death rates since 1990 in men and 1991 in women translates to the avoidance of approximately 1.18 million deaths from cancer, with 152,900 of these deaths averted in 2009 alone.

CACancerJClinc2013.63.11-30. VC 2013AmericanCancerSociety.
Are We At the Limits of What Technology Can Offer our patients?

IMRT Evolution
evolves to smaller and smaller subfields and high resolution IMRT along with the introduction of new imaging technologies

Computerized IMRT introduced which allowed escalation of dose and reduced complications

Computerized 3D CT Treatment Planning

High resolution IMRT

Functional Imaging

IMRT Cumulative Adoption

Mell et al, Cancer 2005

Study Aim

- To test the hypothesis that IMRT compared to CRT is associated with fewer post-treatment complications in elderly men with non-metastatic prostate cancer

Bekelman et al. ASTRO, 2010
Conclusions

- IMRT associated with moderate reduction in
  - composite measure of bowel complications, and
  - specific complications of proctitis/hemorrhage
- IMRT not significantly associated with
  reduction in urinary complications
- Erectile complications involving invasive
  procedures rare in both treatment groups
  - IMRT associated with a moderate increase in new
diagnoses of impotence compared to CRT

Bekelman et. al. ASTRO, 2010
Survival Outcomes for NSCLC patients after adoption of CT-Based Simulation

- Planning studies suggest that CT simulation improves the therapeutic ratio
- SEER-Medicare data 2000-2005 analyzed by Cox models & propensity score analysis
- CT simulation use increased from 2.4% (1994) to 34% (2000) & 77.6% (2005)
- CT simulation associated with a lower risk of death – hazard ratio 0.77

   – Chen AB et al J Clin Oncol 29(17) 2011

The Impact of Image Guidance

- Evaluation of multiple image-based modalities for image-guided radiation therapy (IGRT) of prostate carcinoma: A prospective study
- Essa Mayyas¹, Indrin J. Chetty¹, Mikhail Cheverakov¹, Ning Wen¹, Toni Necu¹, Teamor Nurushev¹, Lei Ren¹, Mei Lu², Hans Stricker³, Deepak Pradhan¹, Benjamin Movsas¹, and Mohamed A. Elshaikh¹
- Evaluated four 3D US, kV planar images, CBCT, & implanted electromagnetic transponders to assess inter- and intrafraction localization errors during intensity-modulated radiation therapy based treatment of prostate cancer
- Twenty-seven prostate cancer patients were enrolled in a prospective IRB-approved study and treated to a total dose of 75.6 Gy (1.8 Gy/fraction). Overall, 1100 fractions were evaluated.

The Impact of Image Guidance

- Analysis of interfraction setup errors were comparable (within 3–4 mm) among the 4 imaging modalities
- Evaluated four 3D US, kV planar images, CBCT, & implanted electromagnetic transponders to assess inter- and intrafraction localization errors during intensity-modulated radiation therapy based treatment of prostate cancer
- Interfraction planning margins, relative to setup based on skin marks, were generally within the 10 mm prostate-to-planning target volume margin
- With image guidance, interfraction residual planning margins were reduced to approximately less than 4 mm.

**Stereotactic Body Radiation Therapy**

- Not a machine, but a type of radiation delivery.
- Stereotactic = precise positioning of the target volume in 3 dimensions.
- Has become synonymous with high dose per fraction.
- Enabled by imaging & advances in delivery systems

---

**RTOG 0236: Local Control**

36 month local control = 94% (CI: 84-100%)

1 failure within PTV, 1 within same lobe

Timmerman et al.: JAMA 2010

---

**Dose Escalation, Not “New Biology,” Can Account for the Efficacy of Stereotactic Body Radiation Therapy With Non-Small Cell Lung Cancer**

J. Martin Brown, David J. Brenner, David J. Carlson


"Thus the higher TCPs for SBRT can be fully explained by the much higher tumor BEDs delivered. For NSCLC, then, it follows that there is no need to invoke a "new biology" to explain the high tumor control rates."

“The old paradigm, that successful radiation therapy involves putting as much dose into the tumor while depositing as little dose as possible to surrounding normal tissue, seems to remain unchanged. Stereotactic body radiation therapy of NSCLC has taken this to its logical extreme, with dose distributions that are so good that normal tissue sequelae play a much smaller role in determining the maximum tumor dose that can be delivered."
Summary - Rationale for Particles

- Dose distribution – less normal tissue dose relative to the dose deposited in tumors. Dose conformality is key, however. The dose distribution advantage will be most critical in those clinical situations where toxicities are of greatest concern
  - Pediatrics
  - Combined modality setting
  - Proximity to critical structures
  - Second malignancies

- Biological advantage for some tumors with higher LET particles. Fractionation, dose, dose rate are key factors. The LET advantage will be important in
  - Hypoxic Tumors (oxygen effect)
  - Slowly growing tumors

Phase III Randomized Clinical Trial of Proton Therapy vs IMRT

Study Schema

Randomize
400 men

Proton Beam Therapy (PBT)
versus
Intensity Modulated Radiotherapy (IMRT)

Follow
Months 1, 3, 6, 9, 12, 18, 24, 36, 48, 60

Primary Endpoint
- Bowel function at 24 mo (EPIC)

Secondary Outcomes
- Urinary and erectile function
- HRQOL and Utilities
- Perceptions of care
- Adverse events
- Efficacy endpoints
- Direct and indirect costs
**The Promise of Molecularly Targeted Therapy and Radiation**


---

**Prescribing Radiation Dose to Lung Cancer Patients Based on Personalized Toxicity Estimates**

Vinogradskiy et al., JTO, 7(11), 2012
Slide courtesy of King Lee, MD
MDACC
Valuation of High Technology

- Higher Health Care Value

Challenges

- How do we demonstrate the benefit of proton therapy and other high technology (HT) treatments?
- The theoretical benefits are significant
- Yet, cost containment pressures are real
- Technological changes are rapid and high technology therapies tomorrow are likely to look different from those today
- Value = benefit divided by cost
- The difficulties in assessing cost effectiveness

Comparative Effectiveness

The essence of comparative effectiveness research (CER) is to understand what health interventions work, for which patients, and under what conditions.

In the US, attention has focused on radiotherapy technological advances, including IMRT, proton therapy, and SBRT, that have been quickly adopted with few studies investigating whether they represent an incremental improvement in patient outcomes, the defining evaluation threshold of CER.
Coronary Intervention for Persistent Occlusion after Myocardial Infarction

```
Many doctors were so convinced of the value of this procedure...that they thought it would be unethical to assign any patients to the control group, which would get all the best medicines for this condition but not the artery-reopening procedure.”
  • Boston Globe, December 9, 2006
```
The Evolution of Conformal Radiotherapy

Localized Prostate Cancer

Are Protons Better?

Hazard ratio, 1.16; 95% CI, 0.92–1.45; P=0.20
Are Protons Better?

Proton Versus Intensity-Modulated Radiotherapy for Prostate Cancer: Patterns of Care and Early Toxicity
Manuscript received May 16, 2012, revised September 14, 2012, accepted September 15, 2012.

Although PRT is substantially more costly than IMRT, there was no difference in toxicity in a comprehensive cohort of Medicare beneficiaries with prostate cancer at 12 months post-treatment. J Natl Cancer Inst 2013;105:25–32.

The Value of Cancer Care Expenditures in the US

- Philipson and colleagues University of Chicago
- Study to assess the value of cancer care expenditures in the US compared to the European Union
- Standard health services metrics were evaluated — value of additional years of life in dollar terms

Philipson, T. et al Health Affairs, April 2012

Cost of Cancer Care Higher in the US

Cost of cancer care was higher in the US compared to the European Union. (Philipson, T. et al Health Affairs, April 2012)
The Value of Cancer Care Expenditures in the US

- Cancer patients in US lived – 11.1 years vs. 9.3 years after diagnosis
- Extra years of life worth $598 Billion or $61,000 per cancer patient
- Value highest in prostate cancer & breast cancer patients
- US cancer care was more expensive but achieved better outcomes & therefore, the additional costs may be justified

Philipson, T. et al Health Affairs, April 2012

While we cannot afford to pay for expensive therapies that provide little benefit to patients, we also cannot afford to stifle evidence development for innovative treatments that may lead to better health outcomes.

SOURCE: Bekelman and Hahn, 2014, in review

Conclusions

- There has been a substantial increase in the technological complexity of radiotherapy driven by advances in computing power, imaging and more efficient methods for delivering radiation
- IMRT, Image guidance, CT simulation, SBRT, and particle therapies have shown benefit to patients in defined situations
- It is unlikely that we have reached the limits of what high technologies can offer patients
- The intersection of biology and physics will also likely yield additional advances in therapy and imaging
- Is the cumulative effect of incremental advances of high technology greater than that observed with each individual therapy & if so, how do we justify the cost?