Panel discussion: Randomized trials vs. Prospective registry

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Disclosures

- Andre Konski, MD, MBA, MA, FACR
  - Institute for Clinical and Economic Review (ICER)
    - Evaluation of the brachytherapy/proton beam in the management of localized low-risk prostate cancer
  - Center for Medical Technology Policy (CMTP)
    - Registry trial comparing protons beam therapy and IMRT in the treatment of Low and Intermediate-risk prostate cancer
  - ASTRO Emerging Technology Committee (ETC) co-chair
    - Technology evaluation of Proton Beam Therapy

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Disclosures

- Andre Konski, MD, MBA, MA, FACR
  - Involved in Fox Chase Cancer Center's evaluation of building a Proton Beam Therapy Center

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The For-Profit Side of Cancer Treatment

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By ANDREW POLLACK
Published: December 26, 2007

Cancer Fight Goes Nuclear, With Heavy Price Tag

By ANDREW POLLACKPublished: December 26, 2007

States Limit Costly Sites for Cancer Radiation

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By ANDREW POLLACK
Published: May 1, 2008

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JOURNAL OF CLINICAL ONCOLOGY | COMMENTS AND CONTROVERSIES

Should Randomized Clinical Trials Be Required for Proton Radiotherapy?

Michael Goitein, *Department of Radiation Oncology, Harvard Medical School, Boston, MA*
James D. Cox, *Division of Radiation Oncology, The University of Texas M.D. Anderson Cancer Center, Houston, TX*

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VOLUME 26 · NUMBER 15 · MAY 20 2008

JOURNAL OF CLINICAL ONCOLOGY | COMMENTS AND CONTROVERSIES

Protons and Parachutes

Joel E. Tepper, *Department of Radiation Oncology, UNC Lineberger Comprehensive Cancer Center, University of North Carolina School of Medicine, Chapel Hill, NC*

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JOURNAL OF CLINICAL ONCOLOGY | COMMENTS AND CONTROVERSIES

Should Randomized Clinical Trials Be Required for Proton Radiotherapy? An Alternative View

Eli Glatstein, *Department of Radiation Oncology, University of Pennsylvania School of Medicine, Philadelphia, PA*
John Glick, *Department of Medicine, University of Pennsylvania School of Medicine, Philadelphia, PA*
Larry Kaiser, *Department of Surgery, University of Pennsylvania School of Medicine, Philadelphia, PA*
Stephen M. Hahn, *Abramson Cancer Center, University of Pennsylvania School of Medicine, Philadelphia, PA*

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Why the Controversy

- “It’s about the economy stupid”
  - James Carville
- “It’s about the reimbursement”

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- Data from a vendor of a national claims database with information from 90 or so health plans across the country was accessed.
- Identification of 50 prostate cancer patients with proton beam monotherapy (2001-2007) from this database
- Average health plan payments for a course of therapy were approximately $85,000 (billed charges were approximately $150,000); payments per fraction were about $2100.

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- …”proton therapy will generate about $100 million in clinical revenue out of a system that spends $2 trillion on healthcare” Mr. Slater ONI April 2008
- 5 centers currently, impact will be higher when additional centers become operational in 2011

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Concern over Increasing Radiation Oncology Reimbursement

Part B Physician/Supplier National Data - CY 2006
Top 200 Level 1 Current Procedural Terminology (HCPCS/CPT) Codes
Note: Codes Copyrighted by the American Medical Association

Ranked By Charges	Procedure Code	Allowed Charges	Allowed Services
1	99213	$5,460,970,768	106,538,566
2	99214	$5,047,731,967	62,475,261
3	99232	$2,871,461,441	51,278,959
4	66984	$2,226,103,213	3,251,386
5	99233	$1,509,285,311	18,809,743
6	78465	$1,159,131,442	3,274,533
7	88305	$1,107,245,309	19,896,780
8	99285	$1,098,872,842	7,254,456
9	99244	$1,021,733,370	5,999,858
10	92014	$932,325,854	9,939,661
11	99215	$908,685,473	7,658,242
12	99223	$884,137,916	5,638,210
13	99212	$856,876,715	23,112,300
14	93307	$856,047,109	7,359,069
15	99254	$831,861,541	5,786,926
16	97110	$814,147,762	28,877,316
17	99291	$741,603,194	3,513,679
18	99243	$607,546,405	5,075,530
19	99231	$601,866,239	17,768,897
20	77418	$581,612,048	870,083

Was #38 in 2004, and #26 in 2005

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Concern over Increasing Radiation Oncology Reimbursement

Table 9.9—Continued
Services, Submitted and Allowed Charges, and Program Payments for Medicare Physician and Supplier Services, by Leading HCPCS Codes: Calendar Year 2006

Description	Code	Persons Served[1]	Services: Number in Thousands	Services: Percent	Allowed Charges: Amount In Thousands	Allowed Charges: Per Person Served[1]	Program Payments: Amount In Thousands	Program Payments: Per Person Served[1]
Rituximab, 100 mg.	J9310	44,100	1,569	0.1	$742,549	#######	$589,941	$13,377
Ambulance service, BLS, emergency transport	A0429	1,591,600	2,307	0.1	729,621	458	575,184	361
Injection, epoetin alfa, (for non-ESRD use), 1000 units	J0885	199,300	3,512	0.2	679,740	3,411	538,676	2,703
Office consultation, new or established patient, level 3	99243	4,405,420	5,122	0.3	613,219	139	451,008	102
Subsequent hospital care, per day, evaluation and management, level 1	99231	3,220,380	17,962	1.0	608,505	189	481,784	150
Injection, infliximab, 10 mg	J1745	48,900	274	(3)	585,891	11,981	457,278	9,351
Initial inpatient consultation, new or established patient, level 5	99255	1,840,100	2,895	0.2	576,580	313	454,671	247
ESRD related services during the course of treatment, for patients age 20 years and over with 4 or more physician visits per month	G0317	259,300	1,300	0.1	337,944	2,177	448,178	1,717
Radiation treatment delivery, intensity modulated, single or multiple fields	77418	29,860	837	(3)	555,859	18,615	443,461	14,851
Injection, pegfilgrastim, 6mg	J2505	72,140	249	(3)	530,963	7,360	420,613	5,831
Emergency department visit for evaluation and management of patient, level 4	99284	3,911,860	5,422	0.3	519,414	133	396,370	101
Magnetic resonance (eg, Proton) imaging, brain (including brain stem); without contrast material, followed by contrast material(s) and further sequences	70553	1,043,060	1,278	0.1	519,387	498	408,712	392

See footnotes at end of table.

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Concern over Increasing Radiation Oncology Reimbursement

MEDICARE PART B PHYSICIAN/SUPPLIER NATIONAL DATA - CALENDAR YEAR 2005
EXPENDITURES AND SERVICES BY SPECIALTY

SPECIALTY	ALLOWED SERVICES	ALLOWED CHARGES	PAYMENT AMOUNT
RADIATION THERAPY CENTER (EFF. 2003)	336,583	$47,295,981	$37,633,249
SLIDE PREPARATION FAC (EFF. 2003)	201,155	$12,512,732	$9,751,536
PERIPHERAL VASCULAR DISEASE	277,083	$27,785,920	$21,731,548
VASCULAR SURGERY	4,357,879	$581,791,778	$456,040,296
CARDIAC SURGERY	1,357,292	$386,767,200	$305,623,406
ADDICTION MEDICINE	67,822	$4,832,167	$3,560,000
LIC CLINICAL SOCIAL WORKER	4,141,907	$280,852,905	$139,512,011
CRITICAL CARE (INTENSIVISTS)	2,088,960	$179,075,777	$141,008,866
HEMATOLOGY	12,006,746	$282,825,871	$224,546,488
HEMATOLOGY/ONCOLOGY	227,892,325	$5,032,234,311	$3,991,102,667
PREVENTIVE MEDICINE	268,949	$9,037,048	$7,191,498
MAXILLOFACIAL SURGERY	96,470	$12,225,381	$9,448,903
NEUROPSYCHIATRY	148,663	$8,661,740	$5,884,450
ALL OTHER SUPPLIERS (DRUG AND DEPARTME	733,640	$80,503,440	$64,235,368
UNKOWN SUPPLIER/PROVIDER	171,686	$6,543,940	$5,369,923
CERTIFIED CLINICAL NURSE SPECIALIST	946,488	$44,079,360	$26,977,216
MEDICAL ONCOLOGY	87,349,399	$1,988,484,671	$1,575,256,774
SURGICAL ONCOLOGY	495,857	$47,926,774	$37,486,870
RADIATION ONCOLOGY	12,318,150	$1,509,126,840	$1,195,991,906

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Implications for Rising Healthcare Expenditures in US

	Health system's main source of financing		
	Taxes	Social Security Funds	Private Insurance
Australia (1992)	✓		
Canada (1990)	✓		
Denmark (1993)	✓		
France (1990)		✓	
Germany (1989)		✓	
Italy (1988)	✓		
Japan (1991)		✓	
Netherlands (1983)		✓	
Norway	✓		
Sweden	✓		
Switzerland (1991)			✓
United Kingdom (1994)	✓		
United States (1990)			✓

Source: Blanchette, Claude, "Public and Private Sector Involvement in Health Care Systems: An International Comparison," Bulletin 438E, Library of Parliament, 1997

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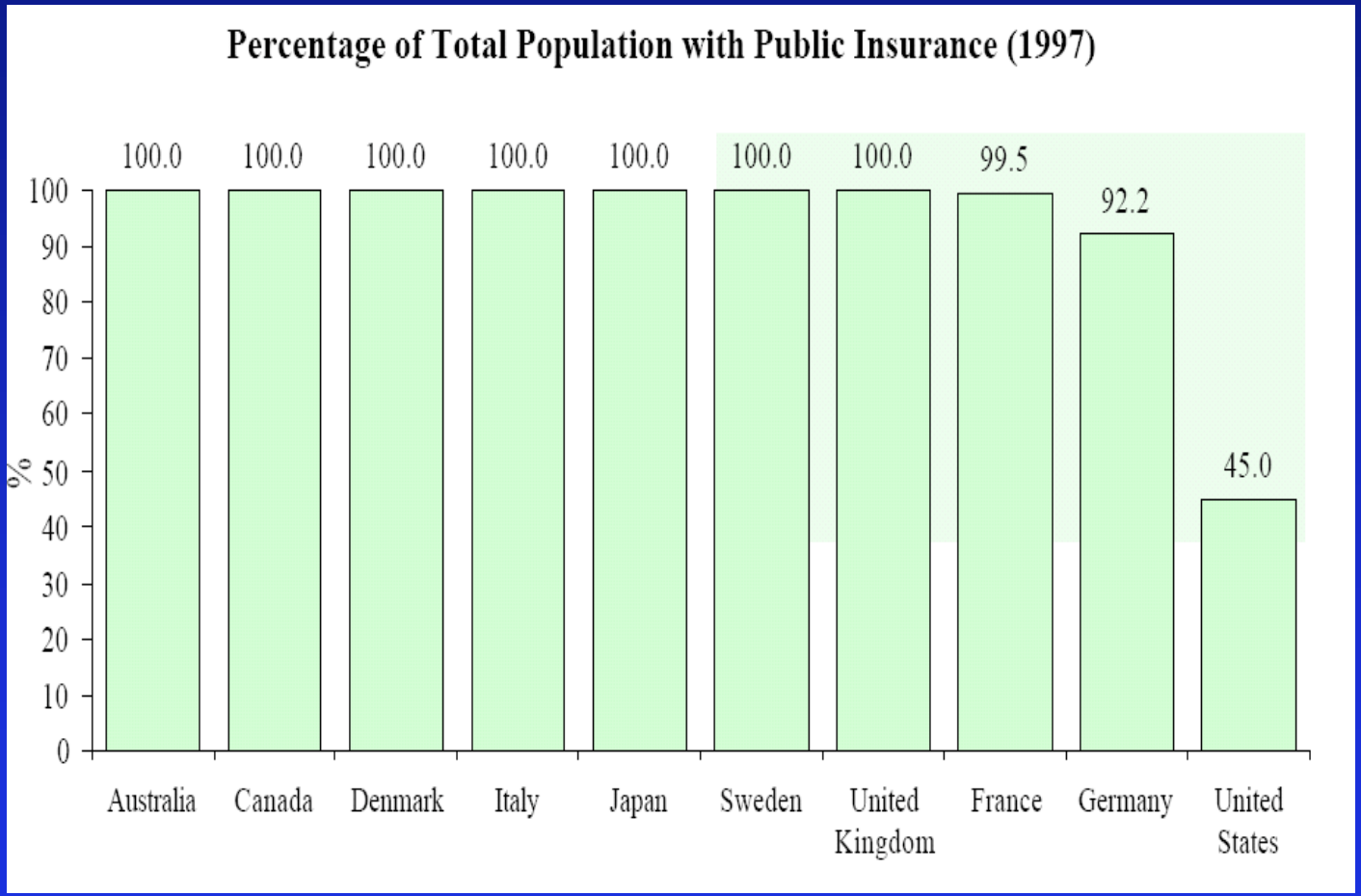
Implications for Rising Healthcare Expenditures in US



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- Factoring in costs borne by government, the private sector, and individuals, the United States spends over $1.9 trillion annually on healthcare expenses, more than any other industrialized country
- 2005 data from the U.S. Census Bureau showed employer-provided health benefits cover 175 million Americans, or about 60 percent of the population.
- Premiums have skyrocketed, rising 87 percent since 2000. In 2004, health coverage became the most expensive benefit paid by U.S. employers, according to a report by the Employment Policy Foundation.
- These ballooning dollar figures place a heavy burden on companies doing business in the United States putting them at a substantial competitive disadvantage in the international marketplace. For large multinational corporations like General Motors the company says it spent roughly $5.6 billion on healthcare expenses in 2006. GM says healthcare costs alone add $1,500 to the sticker price of every automobile it makes, and estimates that by 2008 that number could reach $2,000

Hazards to adoption of new techniques prior to full evaluation

- Radiation-induced malignancies after radiation for Tinea capitis
  - Shore RE et al. Health Phys 2003 85(4):404-8
- Radiation-induced thyroid cancer after radiation for enlarged thymus
  - Shore RE et al. Am J Epidemiol 1993 134(2): 217-23

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Hazards to adoption of new techniques prior to full evaluation

- Bone Marrow Transplant in the treatment of women with breast cancer
  - False Hope- Bone Marrow Transplantation for Breast Cancer
    - Richard A. Rettig
    - Peter D. Jacobson
    - Cynthia M. Farquhar
    - Wade M. Aubry

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Barriers to Evaluating New Technology

- Cost of placing new technology for testing
- Reluctance of companies to subject new technology to evaluation prior to return on investment (ROI) has been realized
- Reluctance of physicians involved in new technology development to have new technology undergo testing
- Reluctance of patients not to receive “the latest” treatment
- Insufficient sites for adequate number of patients to fully evaluate the technology

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Role of Randomized Trials in Medicine

- **Evidence in oncology**
  The Janeway Lecture
  American Radium Society 2000
  - RESULTS: Published reports suggest that res ipsa loquitur was the dominant mindset of researchers in the first half century and continuing into the second half century. **However, recognition of the scarcity of dramatic improvements in outcome and the possibility of incremental improvements led to the mounting of prospective randomized comparative trials that could identify such incremental improvements.** Findings from these trials have profoundly altered patient care in the past quarter century. Data suggest that there is a sequence of events-increased survival rates in patients at research institutions followed by significant increases in survival rates nationally-followed by a reduction in annual mortality rates that do reflect improvements in treatment.

Cancer J 2000; 6:351-7

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Role of Randomized Trials in Medicine

- **The Janeway Lecture**

  American Radium Society 2000

  - **Phase III comparative clinical trials yield the highest quality data in oncology. Meta-analysis of such data may be useful, but the most compelling data that alter medical practice come either from comparative clinical trials showing such significant differences in results as to necessitate their early termination on ethical grounds or from replicated phase III trials.**

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Hazard to Radiation Oncology in not taking lead in testing and evaluating new technology

CALIFORNIA TECHNOLOGY ASSESSMENT FORUM®

Summary of CTAF Roundtable on
Intensity Modulated Radiation Therapy (IMRT) for Prostate Cancer

for IMRT and suggested that clinical trials are warranted. However, there was a general consensus that randomized trials comparing the two technologies are probably not feasible, given the rapid diffusion of IMRT and its emergence as the standard of care. Other data and trial designs were discussed. Data on acute toxicities that is beginning to

In contrast to IMRT, proton beam therapy was identified as a distinct form of radiation therapy based on different radiobiologic principles of protons compared to photons. Proton beam therapy has not yet widely diffused into the general practice of radiation oncology. Given these two distinguishing factors, proton beam therapy may be a better focus for data collection, clinical trials and technology assessment.

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INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW

FINAL APPRAISAL DOCUMENT

INTENSITY MODULATED RADIATION THERAPY (IMRT)

FOR LOCALIZED PROSTATE CANCER

The discussion centering on the assignment of ICER evidence ratings revealed a strong majority of the ERG believed that there was only limited confidence in a small net health benefit for IMRT. One member of the ERG believed that IMRT's comparative clinical effectiveness should be rated as "Insufficient" due to the lack of high quality data. The ERG was unanimous in judging the comparative value of IMRT as "low" on the basis of the high incremental cost-effectiveness ratio and the high cost of preventing a single case of proctitis. Although the economic model showed that the cost/QALY was $117,000 for patients with a prior probability of proctitis of >75%, the clinical experts admitted that research had not been done to provide an evidence-based approach for identifying these patients.

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Number 13

Effective Health Care

Comparative Effectiveness of Therapies for Clinically Localized Prostate Cancer

Executive Summary

AHRQ Agency for Healthcare Research and Quality
Advancing Excellence in Health Care • www.ahrq.gov

Effective Health Care

Proton beam radiation therapy	Low	• No randomized trials compared clinical outcomes after proton beam radiation therapy vs. other treatments. 1 systematic review of nonrandomized studies found no direct evidence of comparative effectiveness of protons vs. photons in men with prostate cancer. 2 nonrandomized clinical trials, Phase II and several case series from 1 center, reported clinical outcomes in patients with localized prostate cancer after combined proton and photon radiation therapy. 86%-97% of subjects were disease free at the end of followup, and 73%-88% did not have biochemical failure. Distant metastases were diagnosed in 2.5%-7.5% of men. Less than 1% had GI and urinary toxicity. Absolute rates of outcomes after proton radiation appear similar to other treatments.
Intensity modulated radiation therapy	Low	• No randomized trials compared clinical outcomes after IMRT vs. other treatments. Case series report similar biochemical-free survival after IMRT compared with conformal radiation. There was no difference in survival without relapse between IMRT and conformal radiation at 25-66 months followup. The rate of distant metastases was 1%-3% after IMRT in case series.

Institute for Clinical and Economic Review
Scoping Committee and Evidence Review Group for:

Brachytherapy/Proton Beam Therapy for Clinically Localized, Low-Risk Prostate Cancer

Scoping Committee Call Summary
January 30, 2008

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- "In the Middle Ages, medicine was still in its infancy. The art of healing was conducted not by physicians, but by barbers. The medieval barbers were the forerunners of today's men of medicine, and many of the techniques they developed are still practiced today. This is the story of one such barber."

Saturday Night Live Transcripts
Season 3: Episode 18

http://www.jibjab.com/view/201643

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- You charlatan! You killed my daughter, just like you killed most of my other children! Why don't you admit it! You **don't** know what you're doing!

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- Wait a minute. Perhaps she's right. Perhaps I've been wrong to blindly follow the medical traditions and superstitions of past centuries.
- Maybe we barbers should test these assumptions analytically, through experimentation and a "scientific method". Maybe this scientific method could be extended to other fields of learning: the natural sciences, art, architecture, navigation. Perhaps I could lead the way to a new age, an age of rebirth, a Renaissance! [thinks for a minute]
- **Naaaaaahhh!**

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Comparison of Patient Reported Outcome of Proton Beam and Intensity Modulated Radiation Therapy (IMRT) in the treatment of Patients with Low and Intermediate Risk Prostate Cancer

2.0 OBJECTIVES

2.1 Primary

The primary objective of this trial will be to determine if changes in patient reported outcome (bowel function) as measured by the EPIC tool at 2 years following treatment is less in patients treated with proton beam therapy as compared to patients treated with IMRT.

2.2 Secondary

To determine if proton beam therapy will result in biochemical freedom from failure that is no worse than that observed following IMRT

To assess Quality-adjusted survival as measured by the EQ-5D and the Health Related Quality of Life (HRQOL) as measured by the Prostate Cancer Symptom Index and to determine if differences in patient reported quality of life exist as measured by Talcott and Epic instruments

To determine if patients treated with proton beam therapy will have fewer second malignancies at 10 years as compared to patients treated with IMRT

To investigate survival outcomes and time to progression responses between the two groups

To determine if changes in patient reported outcome (bowel function) as measured by the EPIC tool at 6 months following treatment is less in patients treated with proton beam therapy as compared to patients treated with IMRT.

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