Comparative Effectiveness Research on Emerging Radiation Therapies

Grace Smith, MD, PhD
University of Texas M D Anderson Cancer Center

Comparative Effectiveness Research

Objectives

- Examine recent studies of emerging radiation technologies.
- Identify persistent challenges in the current science.
- Propose approaches to address these challenges.

Definition

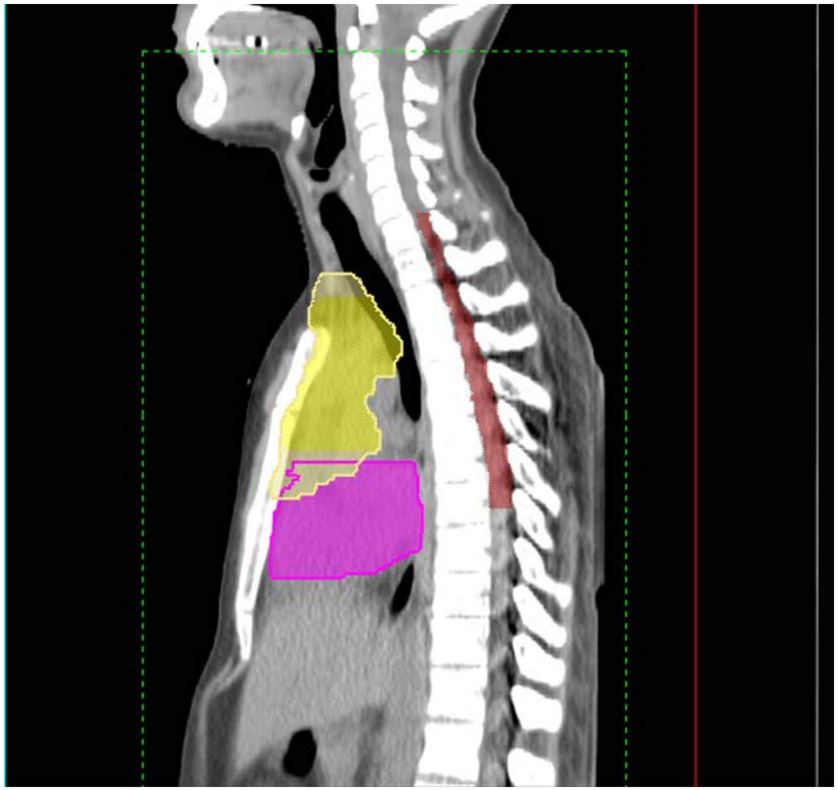
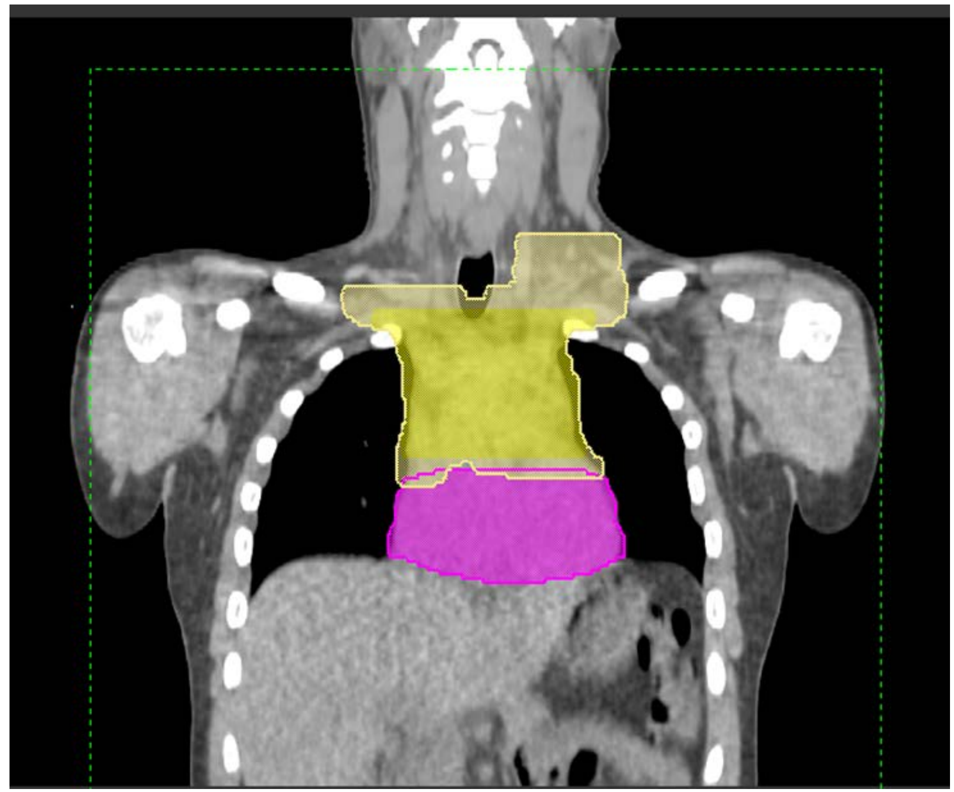
- Comparative effectiveness research
  - Compare treatments
  - Examine the relative benefits and harms
  - To make decisions about treatment alternatives

Data

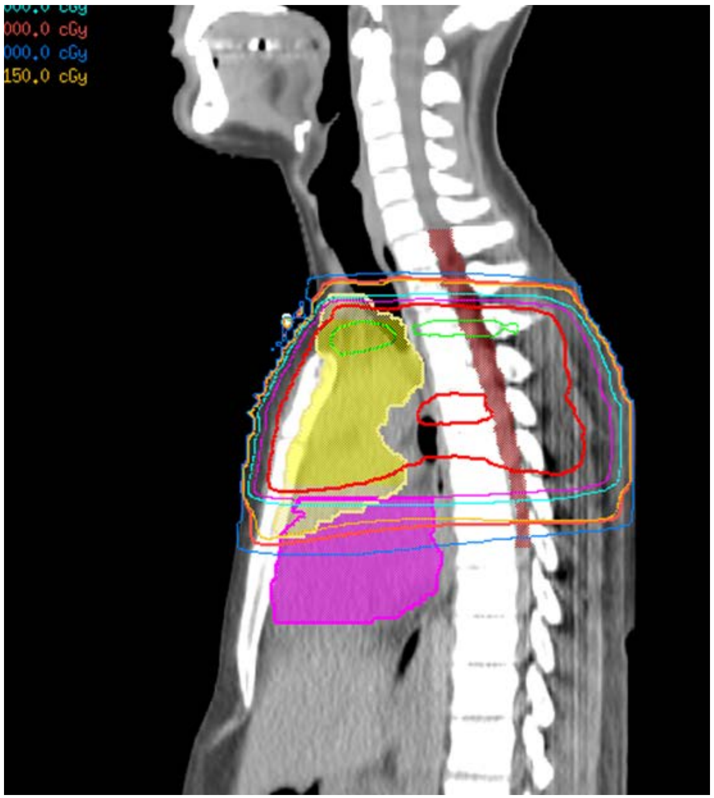
$\downarrow$

Decision

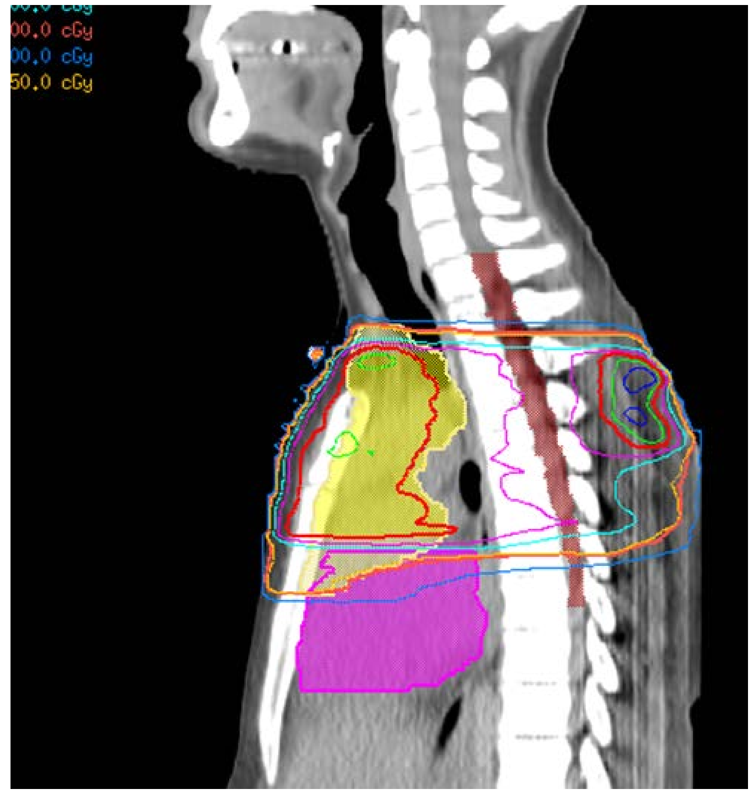
At the Bedside…

…From Bedside to Comparative Effectiveness

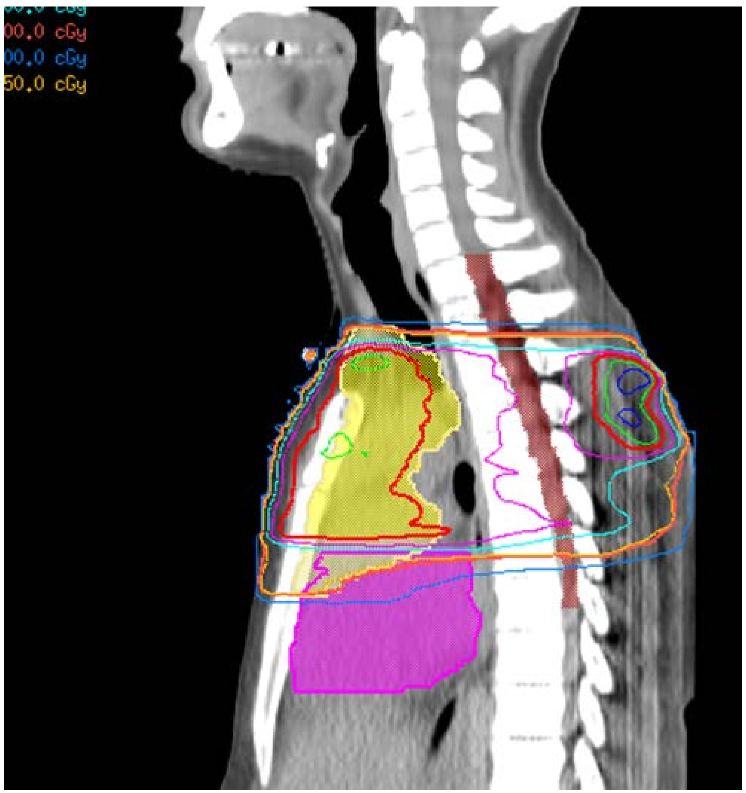


3D



IMRT

…From Bedside to Comparative Effectiveness



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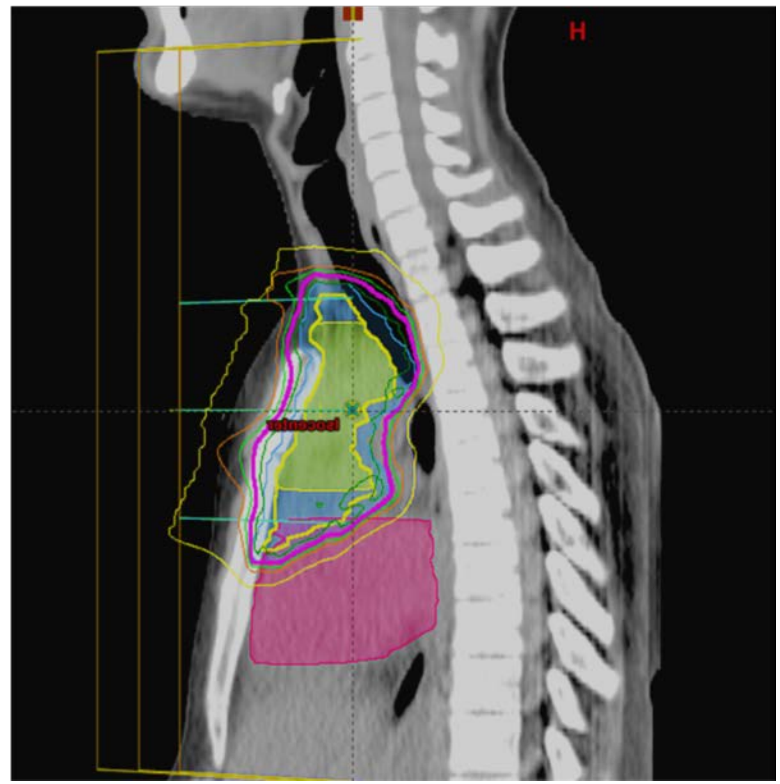
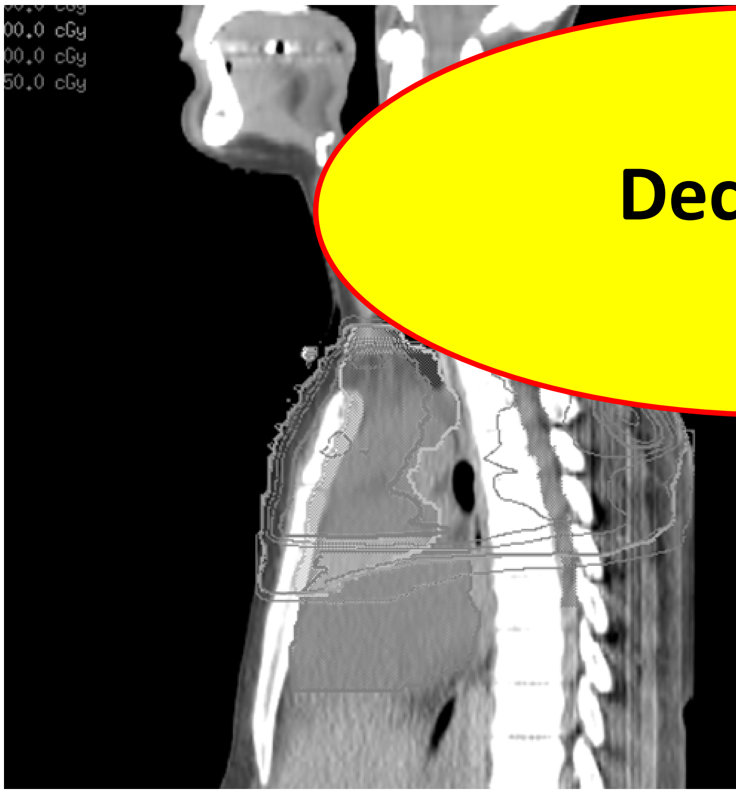


Protons

…From Bedside to Comparative Effectiveness

Decision??



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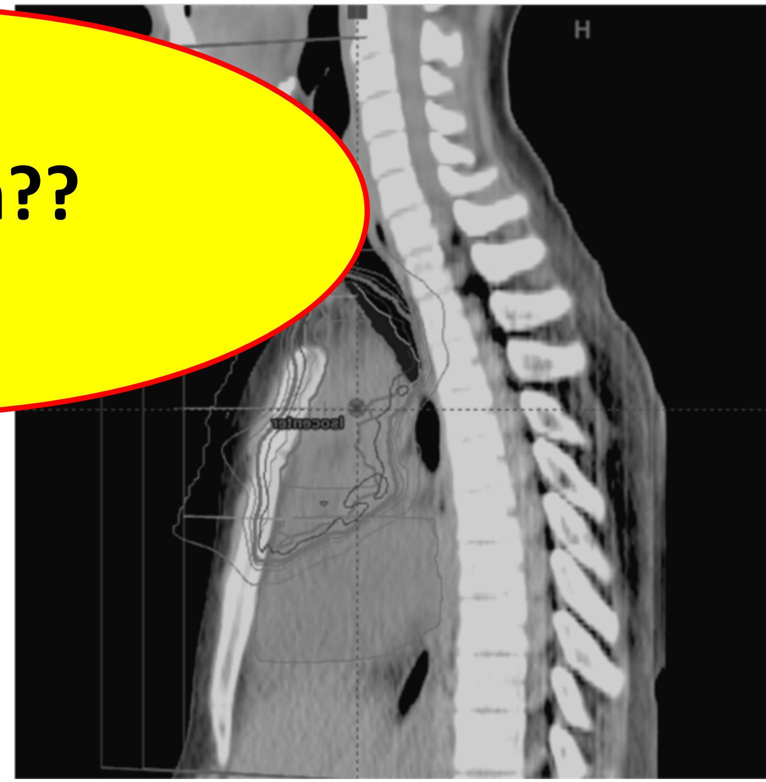


Protons

Goals of Advanced RT Technology

- Maximize tumor target coverage

Goals of Advanced RT Technology

- Maximize tumor target coverage

$\downarrow$

- Maximize tumor cure and patient survival

Goals of Advanced RT Technology

- Maximize tumor target coverage
- Minimize dose to surrounding organs

Goals of Advanced RT Technology

- Maximize tumor target coverage
- Minimize dose to surrounding organs

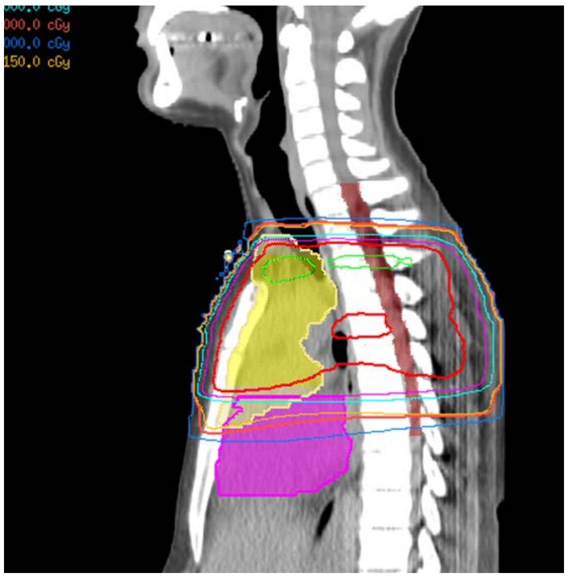
↓

- Minimize damage to actual organ function

Goals of Advanced RT Technology

- Maximize tumor target coverage
- Minimize dose to surrounding organs

- Deliver at an acceptable cost



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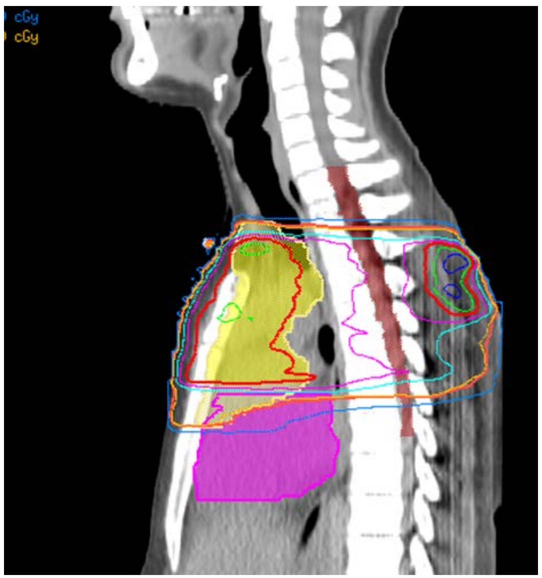

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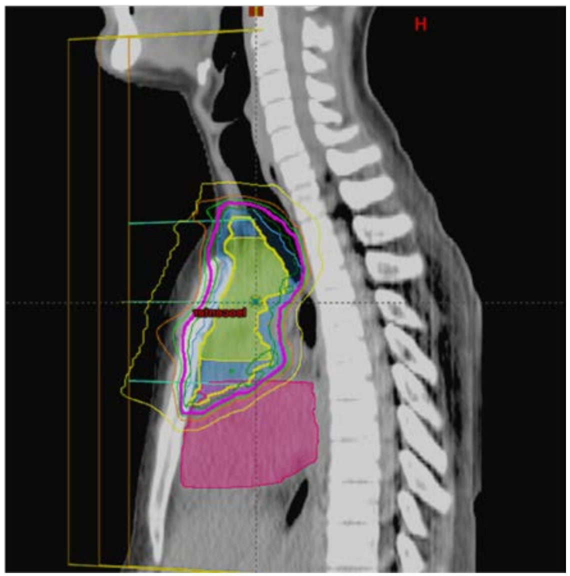

Protons

	3D	IMRT	Proton
Target Tumor	+ + -	+ + +	+ + +
Minimize Organ Dose	+	+ + +	+ + + +
Minimize Organ Damage	?	?	?
Payer Cost ($)	+ + +	+ +	+ -
*Medicare Reimbursement	1.0	1.4 - 2.6	2.9
Patient Cost ($)	?	?	?
Overall Cost	?	?	?
Comparative Effectiveness Metric	?	?	?

	3D	IMRT	Proton
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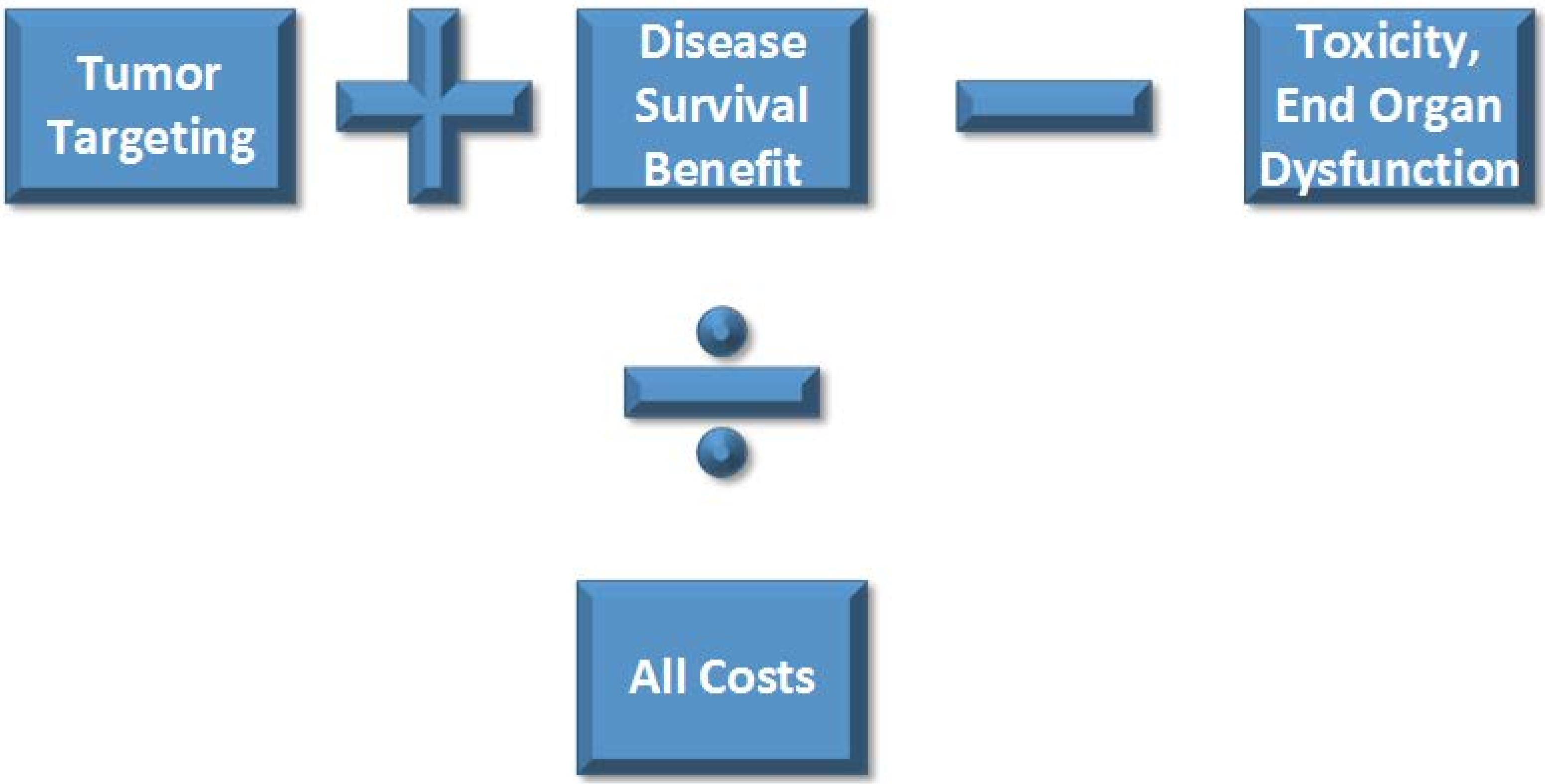
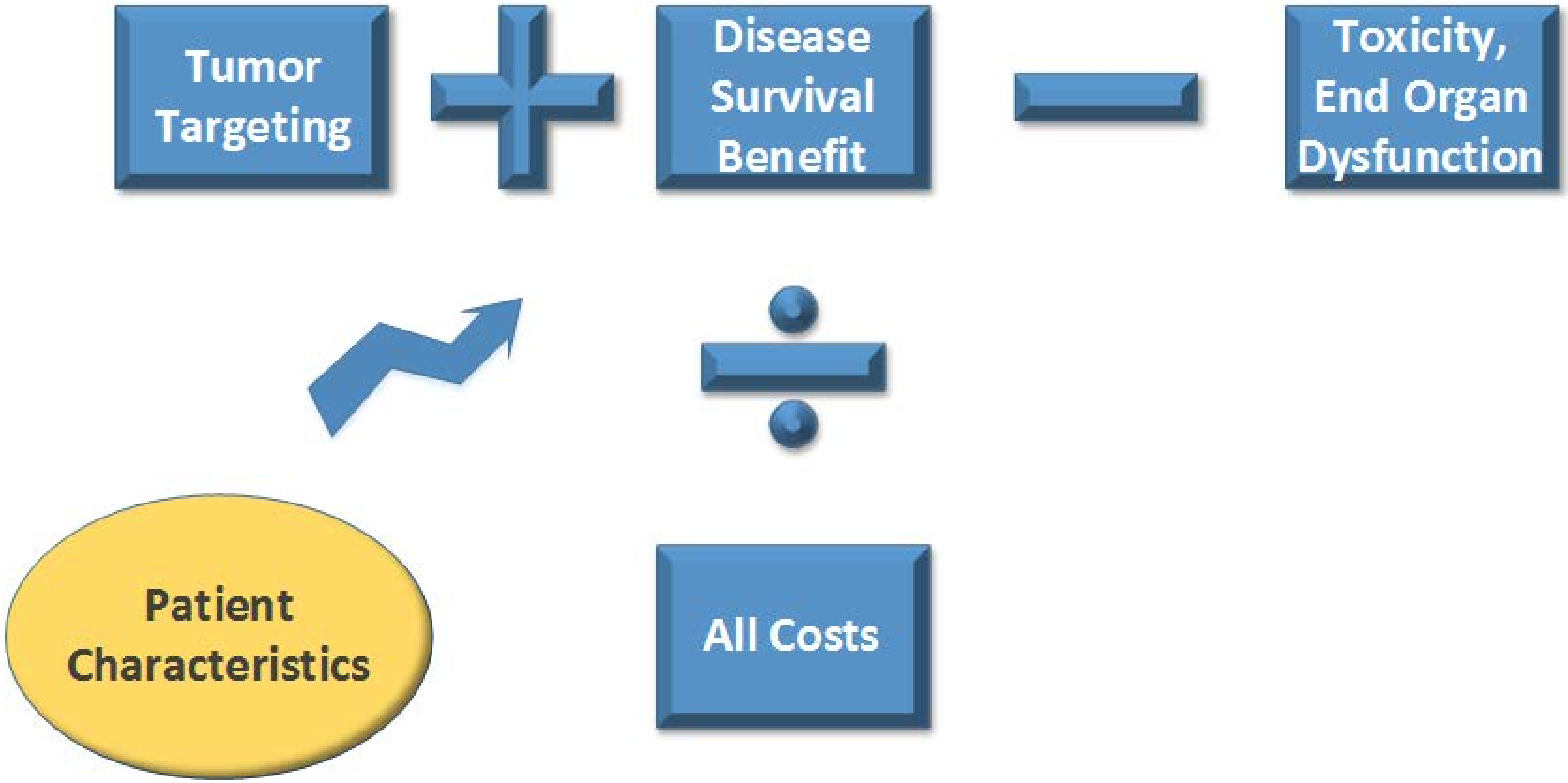
Payer Cost ($)	+ + +	+ +	+ -
*Medicare Reimbursement	1.0	1.4 - 2.6	2.8
Patient Cost ($)	?	?	?
Overall Cost	?	?	?
Comparative Effectiveness Metric	?	?	?

☑ CER Data?

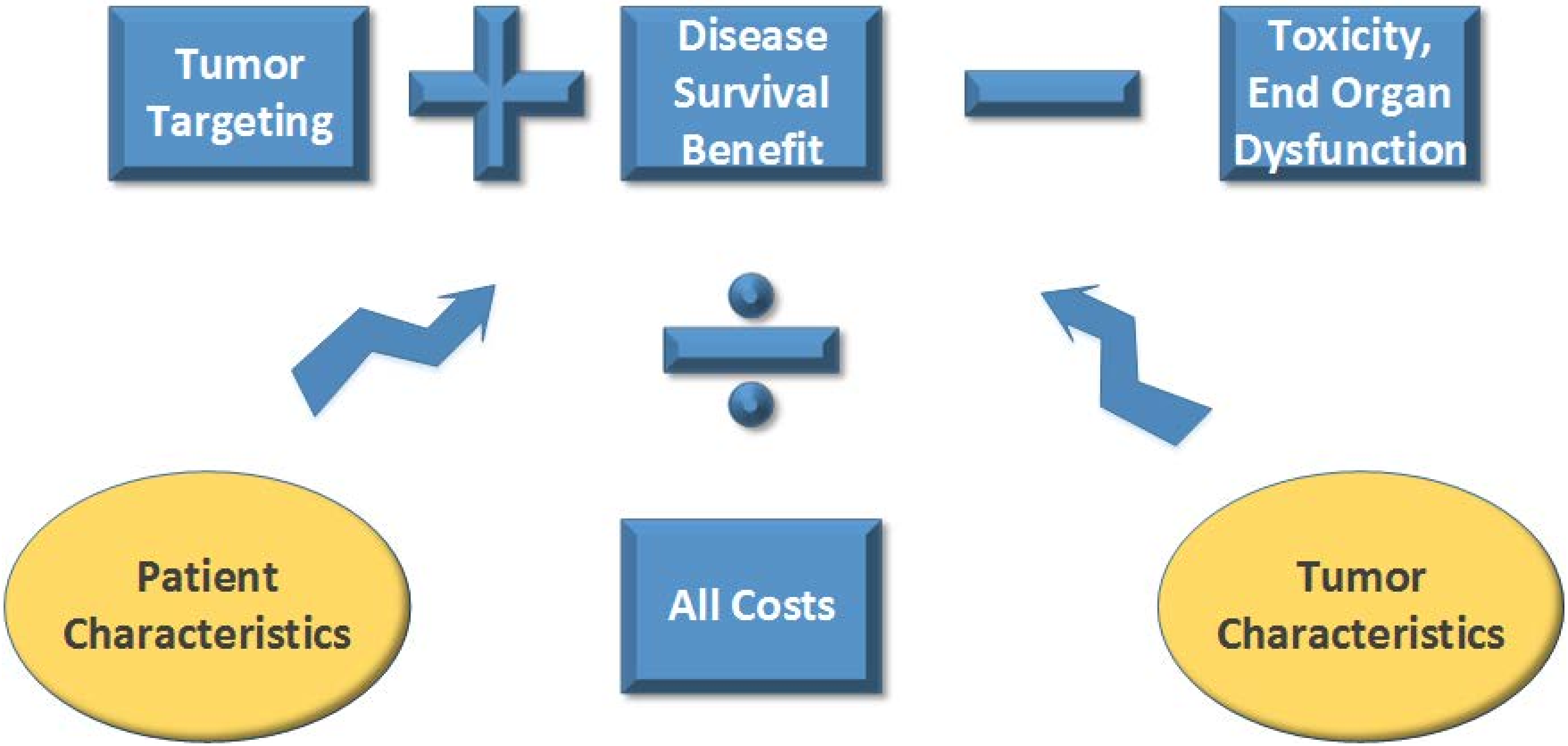
	3D	IMRT	Proton
Target Tumor	+ + -	+ + +	+ + +
Minimize Organ Dose	+	+ + +	+ + + +
Minimize Organ Damage	☑	☑	☑
Payer Cost ($)	+ + +	+ +	+ -
*Medicare Reimbursement	1.0	1.4 - 2.6	2.8
Patient Cost ($)	☑	☑	☑
Overall Cost	☑	☑	☑
Comparative Effectiveness Metric	?	?	?

Comparative Effectiveness Paradigm





Tumor Targeting
Disease Survival Benefit
Toxicity, End Organ Dysfunction
Patient Characteristics
All Costs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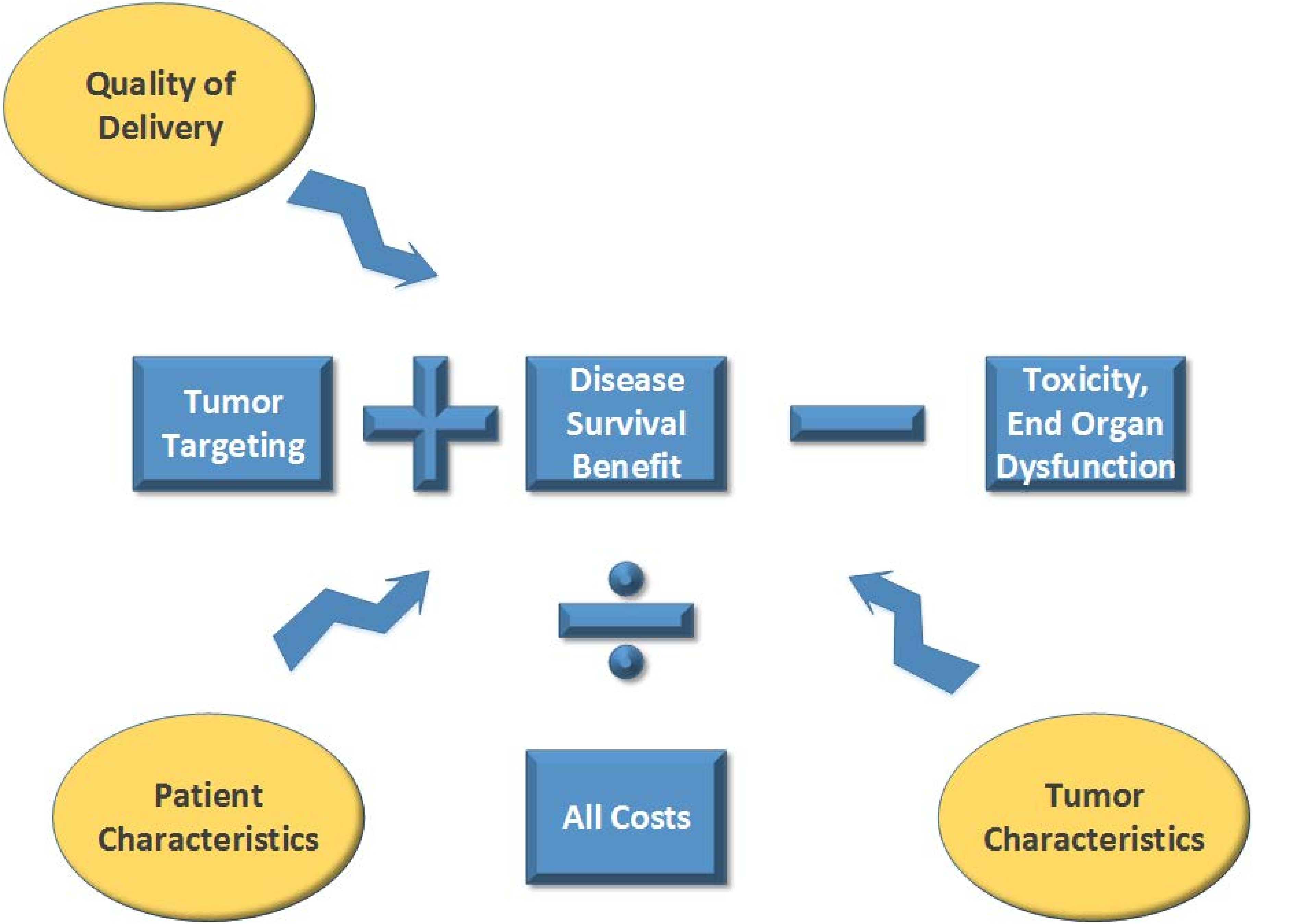
Quality of Delivery
Tumor Targeting
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All Costs
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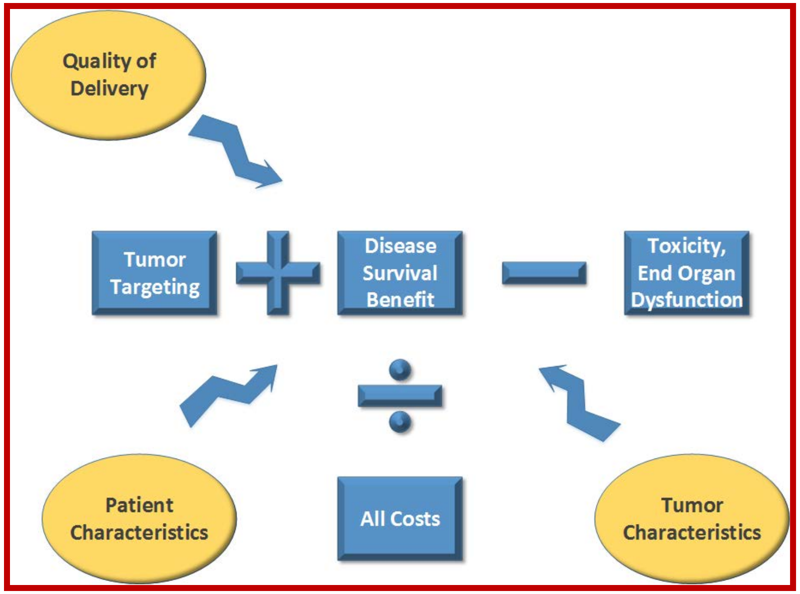
Tumor Characteristics

Data from CER



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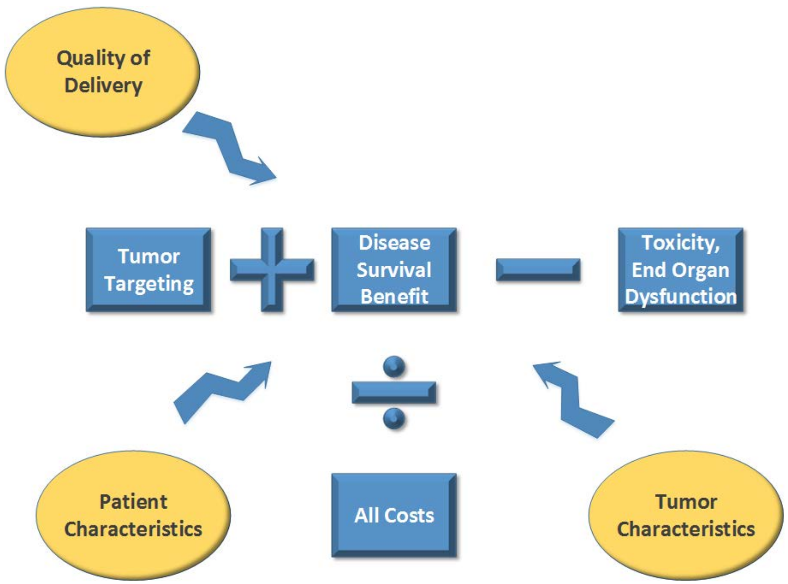
Data at the Bedside



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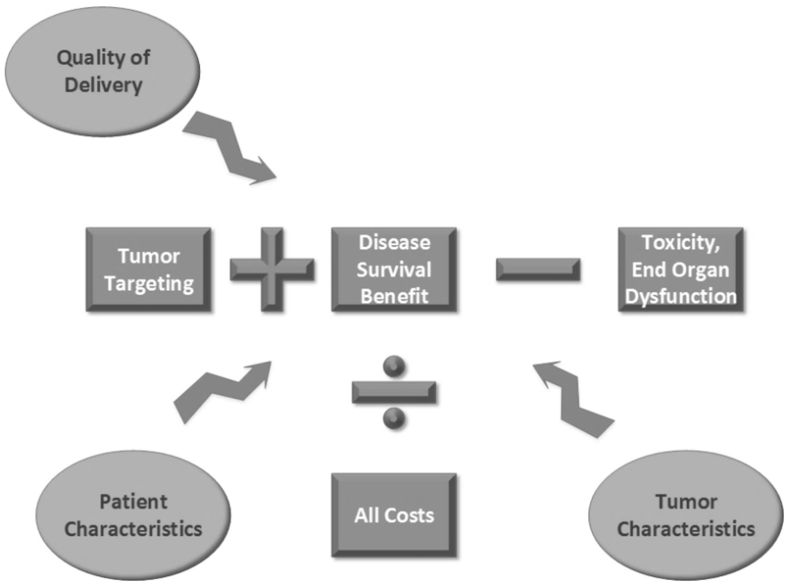
Decision-Making



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Overall Cost	?	?	?

Current State of the Research

- Some examples
- Strengths of current approaches
- Persistent challenges

Ex. 1: Radiation vs. Surgery

Research

Original Investigation

Lobectomy, Sublobar Resection, and Stereotactic Ablative Radiotherapy for Early-Stage Non–Small Cell Lung Cancers in the Elderly

Shervin M. Shirvani, MD, MPH; Jing Jiang, MS; Joe Y. Chang, MD, PhD; James Welsh, MD;
Anna Likhacheva, MD, MPH; Thomas A. Buchholz, MD; Stephen G. Swisher, MD; Benjamin D. Smith, MD

Disease Survival Benefit

JAMA Surg. 2014;149(12):1244-1253. doi:10.1001/jamasurg.2014.556
Published online October 15, 2014.

Ex. 1: Radiation vs. Surgery

- QUESTION: In eligible pts, stereotactic ablative radiosurgery vs. surgery?
- CHALLENGE: Prospective trials have not accrued.

Ex. 1: Radiation vs. Surgery

- DESIGN: Retrospective analysis of SEER-Medicare cohort.
- RATIONALE: Use statistical modeling to account for patient differences.
- ANALYSIS: Proportional hazards analysis and propensity score matching.

Ex. 1: Radiation vs. Surgery

	Stereotactic Radiation			Sublobar Surgery		
	HR	**95% CI**	**P-value**	**HR**	**95% CI**	**P-value**
Overall Survival	**1.01**	**0.74 – 1.38**	**0.94**	**1.36**	**1.17 – 1.58**	**<.001**
Lung Cancer Survival	**1.00**	**0.52 – 1.92**	**0.99**	**1.46**	**1.13 – 1.90**	**.004**
Cost						

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Cost						

Cost-effectiveness of stereotactic radiation, sublobar resection, and lobectomy for early non-small cell lung cancers in older adults

Benjamin D. Smith[a,*], *Jing Jiang*[a], *Joe Y. Chang*[a], *James Welsh*[a], *Anna Likhacheva*[b], *Thomas A. Buchholz*[a], *Stephen G. Swisher*[a], *Shervin M. Shirvani*[b]

[a]*The University of Texas MD Anderson Cancer Center, Houston, TX, United States*
[b]*Banner MD Anderson Cancer Center, Gilbert, AZ, United States*

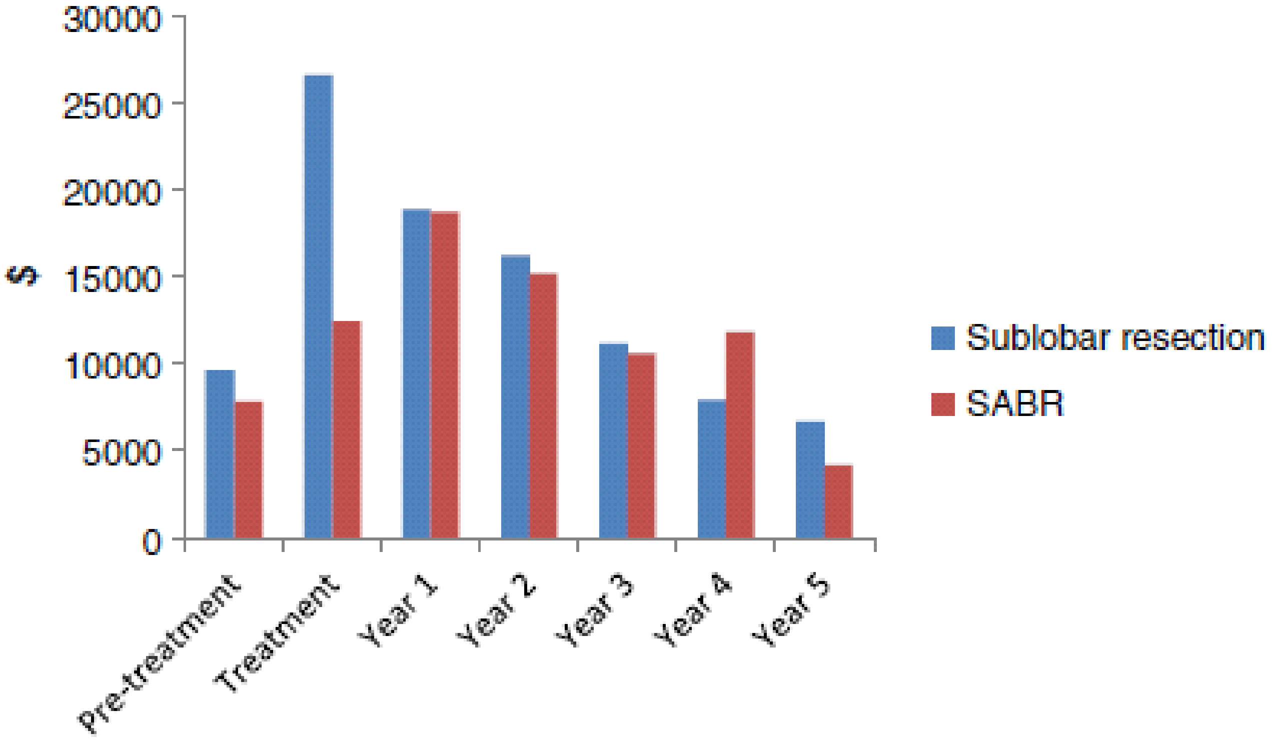
JOURNAL OF GERIATRIC ONCOLOGY

http://dx.doi.org/10.1016/j.jgo.2015.05.002

All Costs

Ex. 1: Radiation vs. Surgery

	Stereotactic Radiation	Surgery
Cost	**$55,000**	**$78,000**



Ex. 1: Radiation vs. Surgery

	Stereotactic Radiation	Surgery
Cost	**$55,000**	**$78,000**
Cost Model*	**$40,000**	**$51,000**

*Shah et al., *Cancer* 2013; 119: 3123

Ex. 1: Lessons Learned

- When randomized data difficult, large population and claims data provide insights into comparative effectiveness.

- Advanced technology <u>can</u> be less costly than prevailing practice

Ex. 1: Challenges

- True cost data difficult to obtain
- No consensus on how to reconcile divergent cost data from different sources.
- No consensus on how to translate divergent data into a quantitative metric for decisions.

Ex. 2: Radiation vs. Radiation

ARTICLE

Proton Versus Intensity-Modulated Radiotherapy for Prostate Cancer: Patterns of Care and Early Toxicity

James B. Yu, Pamela R. Soulos, Jeph Herrin, Laura D. Cramer, Arnold L. Potosky, Kenneth B. Roberts, Cary P. Gross

Toxicity, End Organ Dysfunction

J Natl Cancer Inst 2013;105:25–32

Ex. 2: Radiation vs. Radiation

- QUESTION: Does proton therapy have better toxicity profile than IMRT?
- CHALLENGE: Prospective randomized trials face similar difficulties.

Ex. 2: Radiation vs. Radiation

- DESIGN: Retrospective analysis of Medicare.
- RATIONALE: Use diagnosis claims codes as surrogate for toxicity outcomes.
- ANALYSIS: Logistic regression with matching to account for systematic differences.

Ex. 2: Radiation vs. Radiation

	6-month toxicity					12-mo
Complications	**IMRT (%)**	**Proton (%)**	**OR**	**95% CI**	**P**	**P**
Genitourinary	**9.5**	**5.9**	0.60	0.38 – 0.96	**0.03**	0.66
Gastrointestinal	3.6	2.9	0.84	0.42 – 1.66	0.61	0.89
Other	2.5	<2.6	0.69	0.29 – 1.66	0.41	0.46

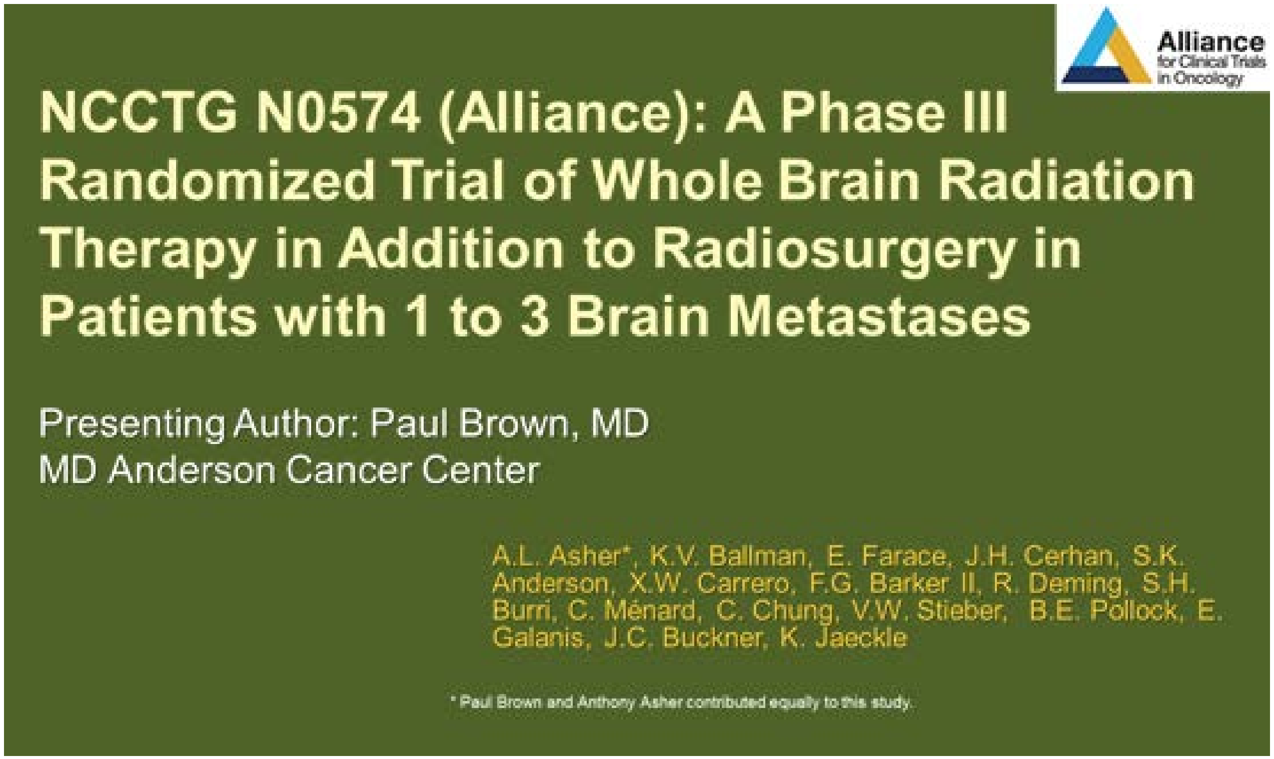
Ex. 2: Radiation vs. Radiation

- Lessons: Feasible to detect clinical differences in toxicity between proton radiation vs IMRT.

- Challenges:
  - Claims-based surrogate treatment adequate?
  - Claims-based surrogate outcome adequate?
  - Retrospective matching adequate?

- Retrospective biases due to:
  - Disparate characteristics: adopt vs. non-adopt
  - Surrogate variables
  - Temporal factors
  - Variation from patient, tumor, and quality of care

Ex. 3: Less Radiation vs. Less Radiation



J Clin Oncol 33, 2015 (suppl; abstr LBA4)

Ex. 3: Less Radiation vs. More Radiation

- QUESTION:
  - In brain mets, stereotactic radiosurgery (SRS) delivers highly targeted radiation.
  - Effectiveness of targeted SRS vs added whole brain radiation (WBRT)?

Less Radiation vs. More Radiation

SRS

- Survival equivalent

SRS+WBRT

- Better tumor control

Less Radiation vs. More Radiation

SRS

- Survival equivalent
- Toxicity?

SRS+WBRT

- Better tumor control
- Toxicity?

Toxicity, End Organ Dysfunction

Less Radiation vs. More Radiation

SRS

SRS+WBRT

- Tumor progression causes more toxicity?

Toxicity, End Organ Dysfunction

Less Radiation vs. More Radiation

SRS

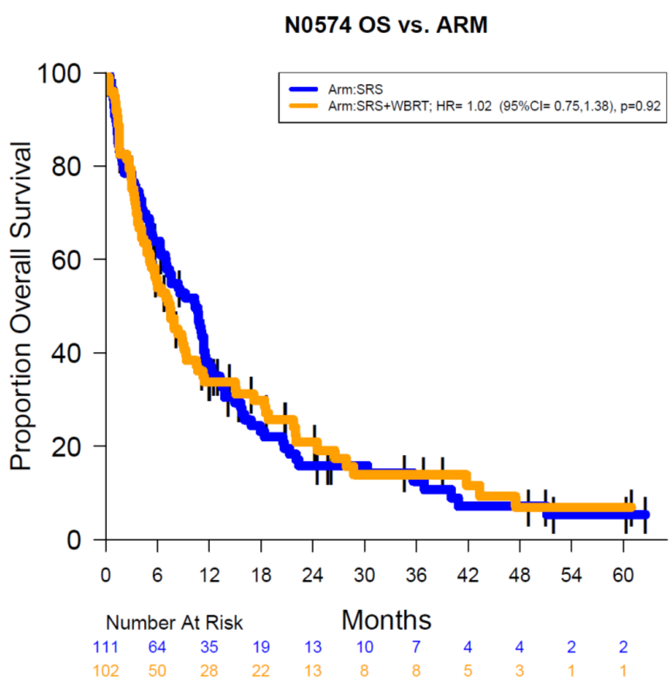
SRS+WBRT

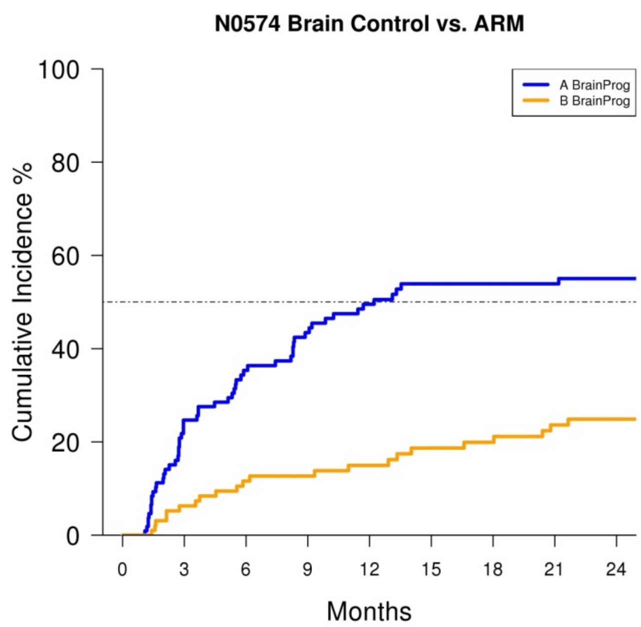
- Radiation treatment causes more toxicity?

Toxicity, End Organ Dysfunction

Ex. 3: Less Radiation vs. More Radiation

- No difference in overall survival (P=0.92)
- SRS had worse intracranial tumor control (P<0.0001)



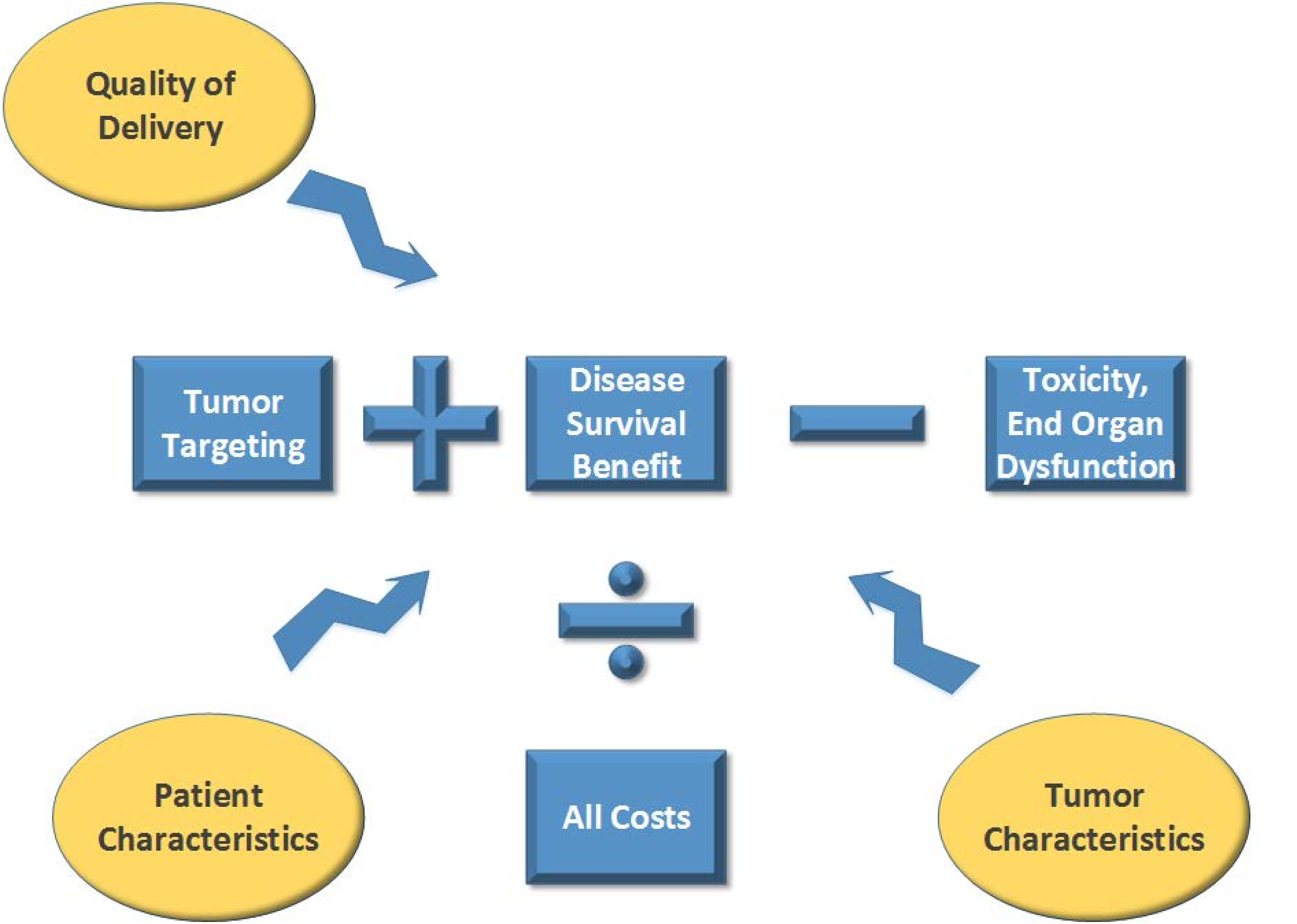


Ex. 3: Less Radiation vs. More Radiation

	Stereotactic Radiation (SRS)		SRS + WBRT		
		95% CI		95% CI	P-value
Cognitive Decline	**63.5%**	50.5 – 75.3	**91.7%**	80.0 – 97.7	**<.001**
Functional Well Being	**3**		**-22**		**.006**
Total QOL	**-1**		**-11**		**.002**

Cognitive Test	SRS	SRS+WBRT	P-value
HVLT Total Recall	8.2%	30.4%	0.0043
HVLT Delayed Recall	19.7%	51.1%	0.0009
HVLT Recognition	22.6%	40.4%	0.0585
TMT Part A	16.7%	30.4%	0.1063
TMT Part B	19.0%	37.2%	0.0677
COWA	1.9%	18.6%	0.0098
Pegboard-Dominant	29.3%	47.7%	0.0656

QOL Test/Subtest	SRS	SRS+WBRT	P-value
Physical Well Being	-4	-18	0.053
Social/FamilyWB	1	-3	0.369
Emotional Well Being	13	5	0.129
Functional Well Being	3	-22	0.006
FACT General	0	-12	0.001
FACT Brain Specific	-1	-9	0.029
FACT-BR Total	-1	-11	0.002



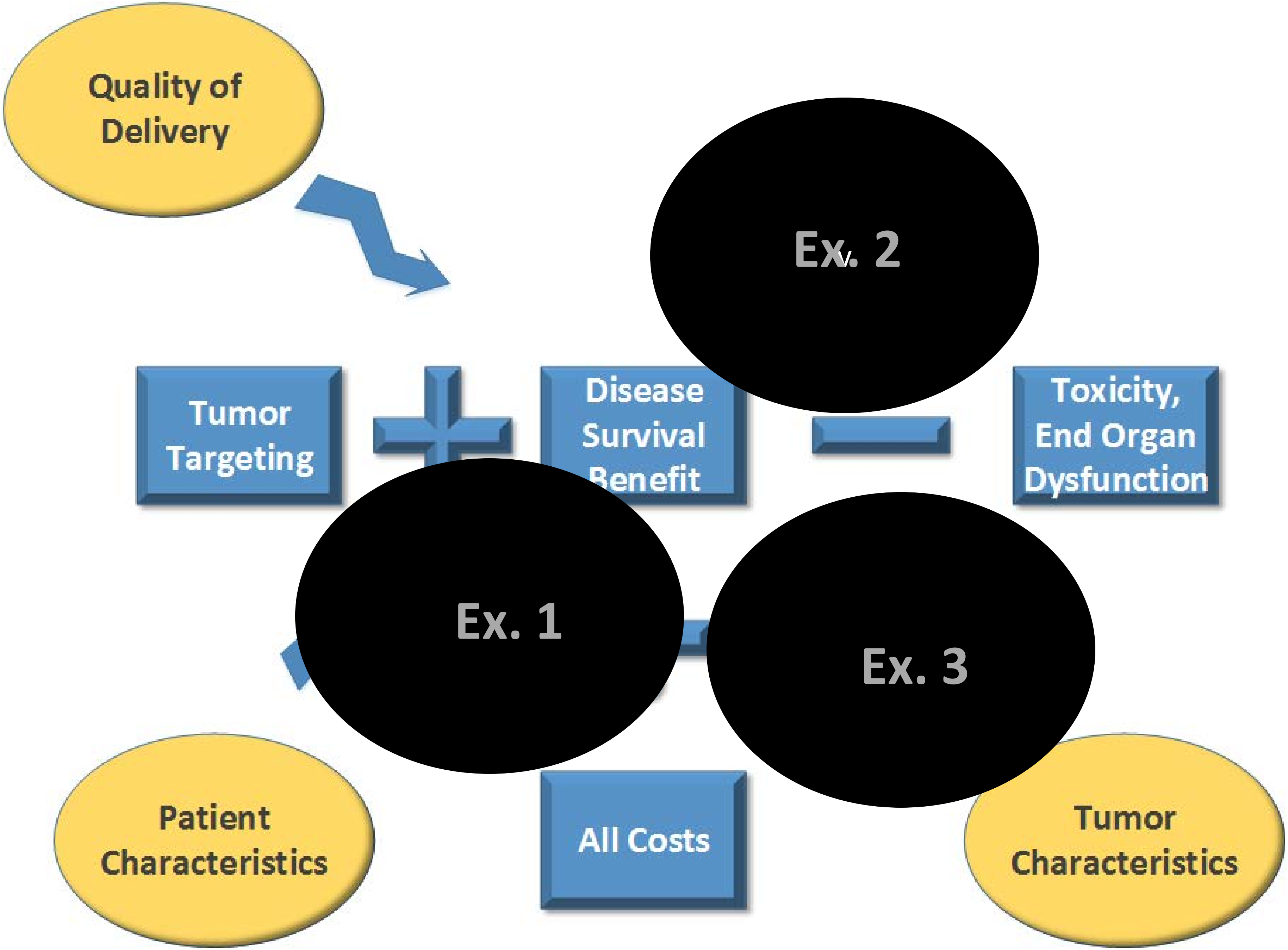
Quality of Delivery
Tumor Targeting
Disease Survival Benefit
Toxicity, End Organ Dysfunction
Patient Characteristics
All Costs
Tumor Characteristics

Ex. 3: Less Radiation vs. More Radiation

- Lessons: Prospective data can provide detailed comparisons.

- Challenges:
  – 10 year effort to collect data
  – No patient-level cost data collected
  – Single inst*: **SRS $119,000 vs SRS+WBRT $74,000**

Lal et al. Am J Clin Oncol 2012 35(1):45


Quality of Delivery
Ex. 2
Tumor Targeting
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Ex. 1
Ex. 3
Patient Characteristics
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Comparative Effectiveness Research

Current Challenges

- Retrospective biases
- Prospective trials barriers
  - Long period for accrual
  - Shifts in indications, target populations

Current Challenges

- Is the barrier a lack of data?

Current State of CER

Treatment Planning

Treatment Delivery

Medical Record

Population Databases

Current State of CER

Treatment Planning

Treatment Delivery

Medical Record

Population Databases

Toxicity

Quality

Outcomes

Comparative Costs

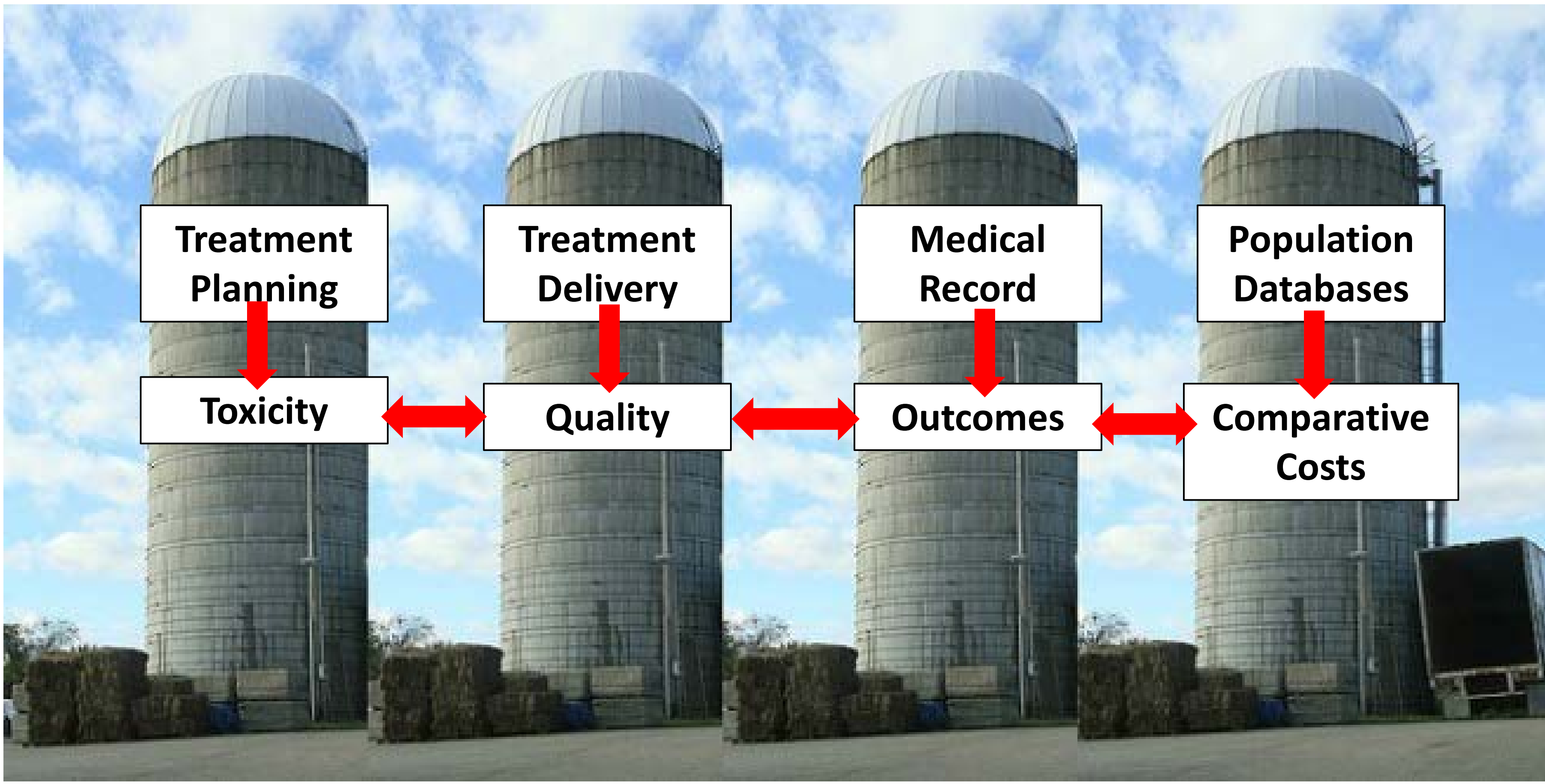
- Is the barrier a lack of data?
- Lacking design to optimally connect data.

Current State of CER

Current Challenges

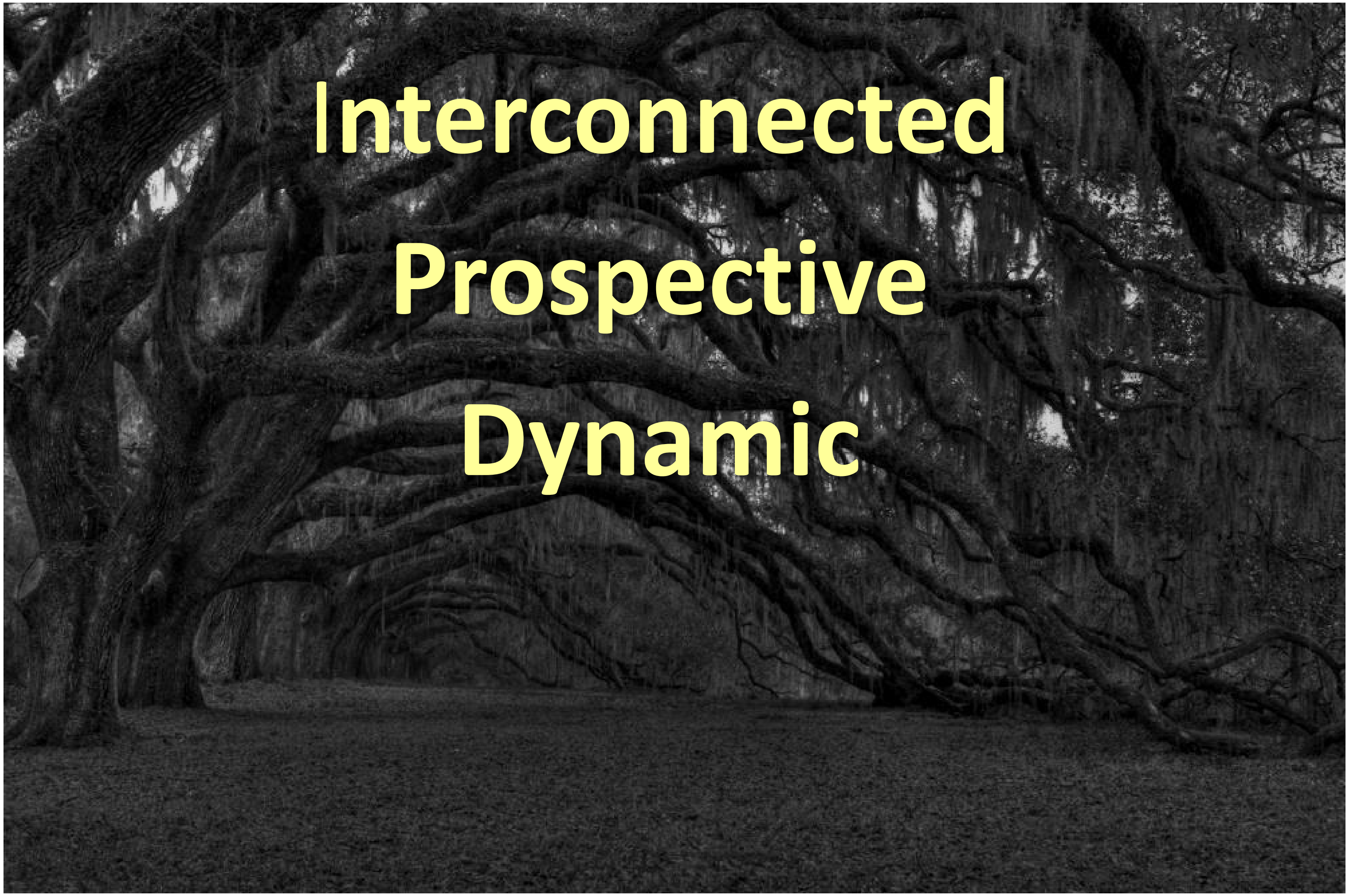
- Designs uni-dimensional, lacking plasticity

Future: A Cultural Shift

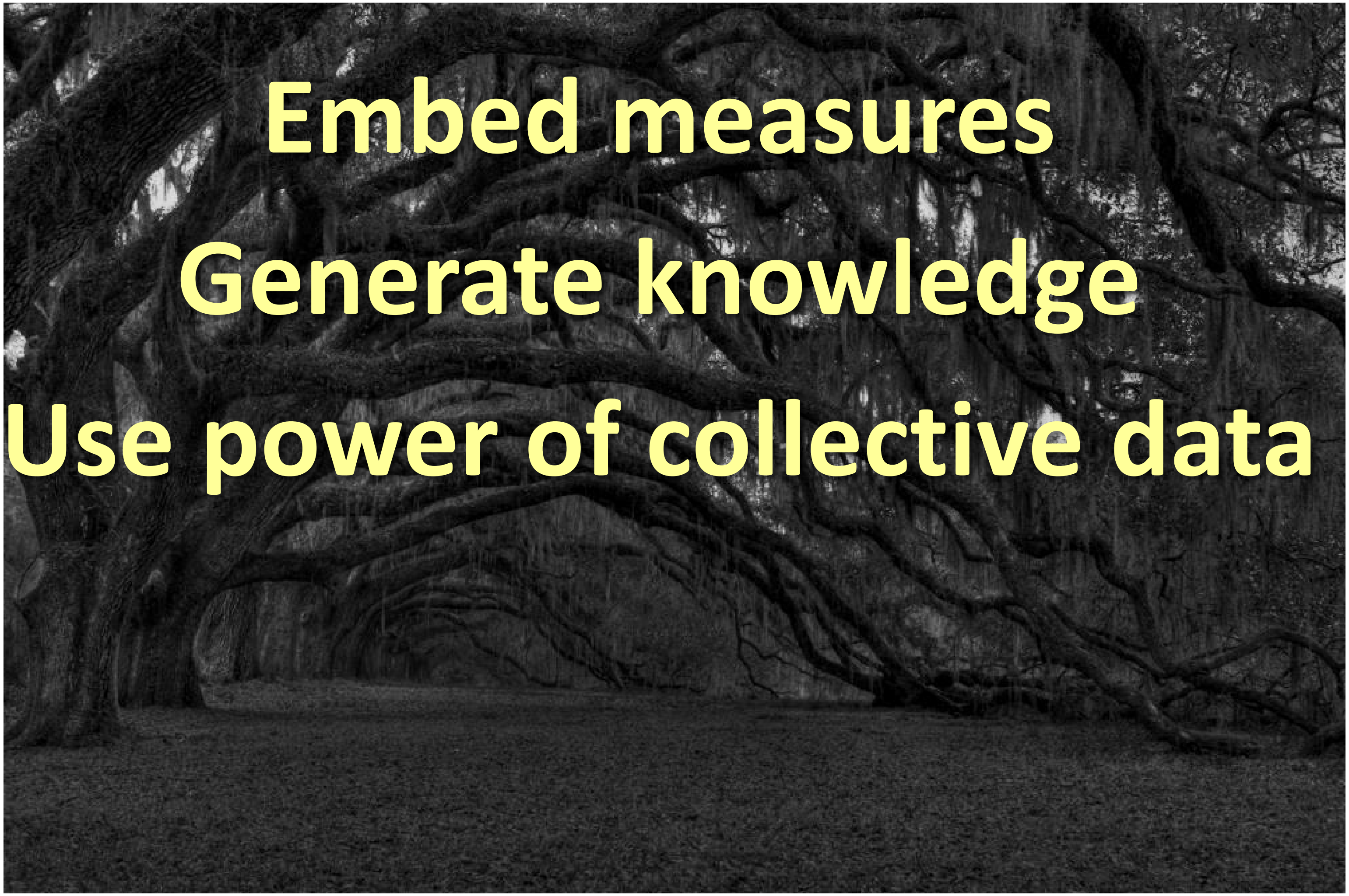


Future: A Cultural Shift

Future: A Cultural Shift



Future: A Cultural Shift



- The National Radiation Oncology Registry
  - Pilot effort
  - Multi-center
  - Prospective

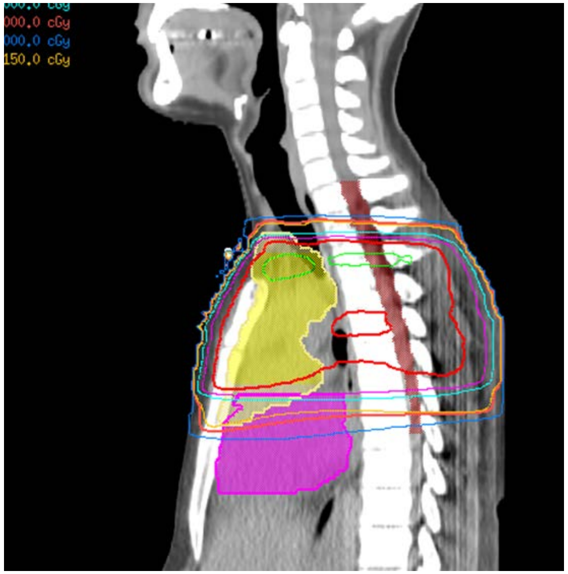
Practical Radiation Oncology (2012) **2**, 10–17

practical radiation oncology
pro
www.practicalradonc.org

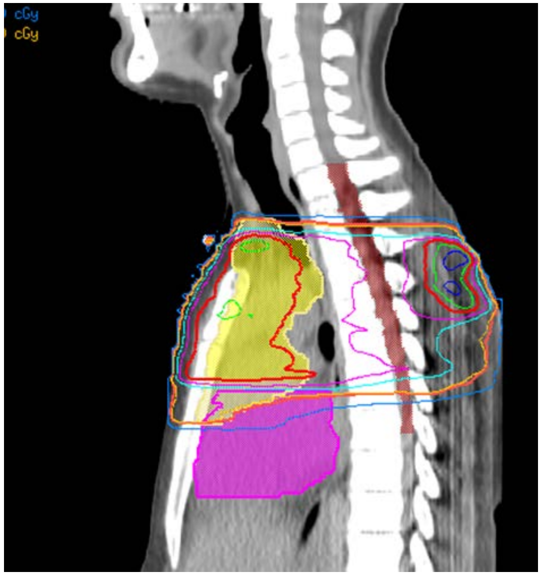
Special Article

Developing a national radiation oncology registry: From acorns to oaks

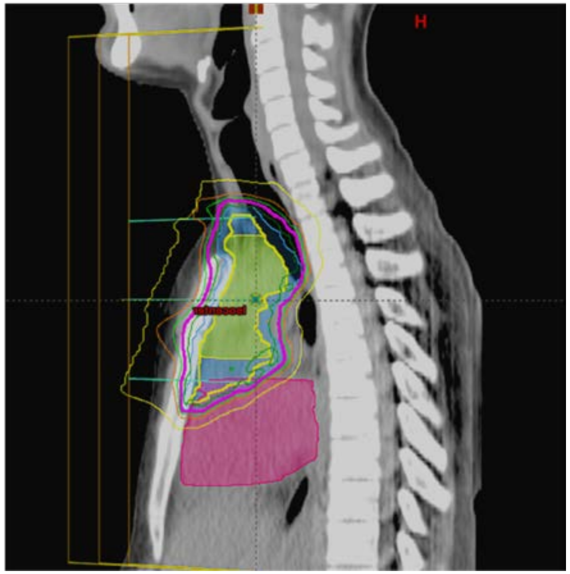
Jatinder R. Palta PhD[a,*], Jason A. Efstathiou MD, PhD[b], Justin E. Bekelman MD[c], Sasa Mutic PhD[d], Carl R. Bogardus MD[e], Todd R. McNutt PhD[f], Peter E. Gabriel MD[c], Colleen A. Lawton MD[g], Anthony L. Zietman MD[b], Christopher M. Rose MD[h]



3D



IMRT



Protons

Summary

- Technology continues to advance.
- More data is being generated.
- Need to contain costs remains.

Summary

- To balance competing demands, develop:
  - Culture
  - Sustainable method
- To move from data to decisions.
- To optimize radiation treatment strategies.