

# **Intensity Modulated Radiation Therapy**

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## **Appendix E. Summary of Findings Table by Malignancy**

September 6, 2012

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**August 2012**

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## About the Center for Evidence-based Policy

The Center for Evidence-based Policy (Center) is recognized as a national leader in evidence-based decision making and policy design. The Center understands the needs of policymakers and supports public organizations by providing reliable information to guide decisions, maximize existing resources, improve health outcomes, and reduce unnecessary costs. The Center specializes in ensuring diverse and relevant perspectives are considered, and appropriate resources are leveraged to strategically address complex policy issues with high-quality evidence and collaboration. The Center is based at Oregon Health & Science University in Portland, Oregon.

## Nature and Purpose of Technology Assessments

This technology assessment report is based on research conducted by a contracted technology assessment center, with updates as contracted by the Washington State Health Care Authority. This report is an independent assessment of the technology question(s) described based on accepted methodological principles. The findings and conclusions contained herein are those of the investigators and authors who are responsible for the content. These findings and conclusions may not necessarily represent the views of the HCA/Agency and thus, no statement in this report shall be construed as an official position or policy of the HCA/Agency.

The information in this assessment is intended to assist health care decision makers, clinicians, patients and policy makers in making sound evidence-based decisions that may improve the quality and cost-effectiveness of health care services. Information in this report is not a substitute for sound clinical judgment. Those making decisions regarding the provision of health care services should consider this report in a manner similar to any other medical reference, integrating the information with all other pertinent information to make decisions within the context of individual patient circumstances and resource availability.

This document was prepared by the Center for Evidence-based Policy at Oregon Health & Science University (the Center). This document is intended to support organizations and their constituent decision-making bodies to make informed decisions about the provision of health care services. The document is intended as a reference and is provided with the understanding that the Center is not engaged in rendering any clinical, legal, business or other professional advice.

The statements in this document do not represent official policy positions of the Center. Researchers and authors involved in preparing this document have no affiliations or financial involvement that conflict with material presented in this document.

## Appendix E. Summary of Findings Table by Malignancy

### Introduction

This summary of findings provides an overview of the strength of evidence for the use of IMRT compared to EBRT. This summary of findings is intended to *supplement* the Washington Health Technology Assessment Program's *Intensity Modulated Radiation Therapy* report. The findings presented in this document are in aggregate. For specific details and findings per malignancy, please refer to the full report on the WA HTA website.

#### Strength of Evidence

⊕⊕⊕⊕	High
⊕⊕⊕○	Moderate
⊕⊕○○	Low
⊕○○○	Very Low

#### Outcomes

↔	No Significant Difference
↕	Inconsistent Evidence
↑	Increased
↓	Decreased

### Overview

The summary table provides a detailed summary of the strength and direction of evidence per malignancy, comparator, and outcomes.

Procedure		Strength of Evidence <sup>1</sup>		
Malignancy Comparator	# of SRs (# included studies in SRs), # of subsequently published studies	⊕⊕⊕○ Moderate	⊕⊕○○ Low	⊕○○○ Very Low
<b>Abdomen – Anal Cancer</b>				
3 SRs (2 cohort, 1 case series), 2 case series				
<b>KQ # 1 Efficacy</b>				
2 SRs (1 cohort, 1 case series), 1 case series				
External beam radiation therapy (EBRT)				↑ 3-yr OS ↑ 3-yr locoregional survival ↑ 3-yr PFS
No comparator <sup>2</sup>				2-yr OS, 2-yr DFS, 2-yr colostomy-free survival
<b>KQ # 2 Harms</b>				
3 SRs (2 cohorts, 1 case series), 1 case series				
EBRT				↓ Diarrhea ↓ Skin/mucosal toxicity ↓ > Grade 2 skin and mucosal eruptions in the female genital area ↓ > Grade 2 nonhematologic toxicity
No comparator				≤ Grade 2 non-haematological, gastrointestinal toxicities, ≥ Grade 3 dermatologic toxicities, ≥ Grade 3 hematologic toxicities
<b>KQ # 3 Subpopulations – HIV Positive patients</b>				
No comparator	1 case series			3-yr RFS, 3-yr OS
<b>KQ # 4 Cost and Cost-Effectiveness</b>				
<i>No studies on costs or cost-effectiveness identified.</i>				

<sup>1</sup> No procedure had a high strength of evidence, thus this column is not displayed in this table.

<sup>2</sup> Due to lack of comparative data, no directionality can be given for outcomes

**Outcomes:** ↔ No Significant Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased

**Abbreviations:** OS – overall survival; PSF – progression free survival; DSS – disease specific survival; DFS – disease free survival; QoL – quality of life; RFS – recurrence free survival; EBRT – external beam radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence <sup>1</sup>		
<b>Malignancy Comparator</b>	<b># of SRs (# included studies in SRs), # of subsequently published studies</b>	<b>⊕⊕⊕○ Moderate</b>	<b>⊕⊕○○ Low</b>	<b>⊕○○○ Very Low</b>
<b>Abdomen – Esophageal Cancer</b>	1 case series			
KQ # 1 Efficacy	1 case series			
No comparator				2-yr actuarial loco-regional control, 1- and 2-yr OS
KQ # 2 Harms	1 case series			
No comparator				≥ acute Grade 3 complications, late complications
KQ # 3 Subpopulations				
<i>No studies on subpopulations identified.</i>				
KQ # 4 Cost and Cost-Effectiveness				
<i>No studies on costs or cost-effectiveness identified.</i>				
<b>Abdomen – Liver Cancer</b>	3 case series			
KQ # 1 Efficacy	3 case series			
No comparator				1-yr survival, OS, PFS
KQ # 2 Harms	3 case series			
No comparator				Grade 0 to 2 hepatic toxicity, hematologic toxicity (anorexia, nausea and vomiting, hepatitis, pancreatitis, GI bleeding), esophagitis
KQ # 3 Subpopulations				
<i>No studies on subpopulations identified.</i>				
KQ # 4 Cost and Cost-Effectiveness				
<i>No studies on costs or cost-effectiveness identified.</i>				

**Outcomes:** ↔ No Significant Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased

**Abbreviations:** OS – overall survival; PSF – progression free survival; DSS – disease specific survival; DFS – disease free survival; QoL – quality of life; RFS – recurrence free survival; EBRT – external beam radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence <sup>1</sup>		
Malignancy Comparator	# of SRs (# included studies in SRs), # of subsequently published studies	⊕⊕⊕○ Moderate	⊕⊕○○ Low	⊕○○○ Very Low
<b>Abdomen – Pancreatic Cancer</b>	1 case series, 1 cost- effectiveness study			
KQ # 1 Efficacy	1 case series			
No comparator				1- and 2-yr OS
KQ # 2 Harms	1 case series			
No comparator				≤ Grade 2 anorexia, dehydration, nausea and vomiting; ≥ Grade 3 acute and late GI complications
KQ # 3 Subpopulations				
<i>No studies on subpopulations identified.</i>				
KQ # 4 Cost and Cost-Effectiveness 1 cost-effectiveness study				
EBRT			IMRT is less cost- effective than EBRT	
<b>Abdomen – Rectum</b>	1 case series			
KQ # 1 Efficacy	1 case series			
No comparator				2-yr PFS, 2-yr OS
KQ # 2 Harms				
No comparator				Grade 3 diarrhea, Grade 3 dermatitis, Grade 3 neutropenia
KQ # 3 Subpopulations				
<i>No studies on subpopulations identified.</i>				
KQ # 4 Cost and Cost-Effectiveness				
<i>No studies on costs or cost-effectiveness identified.</i>				

**Outcomes:** ↔ No Significant Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased

**Abbreviations:** OS – overall survival; PSF – progression free survival; DSS – disease specific survival; DFS – disease free survival; QoL – quality of life; RFS – recurrence free survival; EBRT – external beam radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence <sup>1</sup>		
Malignancy Comparator	# of SRs (# included studies in SRs), # of subsequently published studies	⊕⊕⊕○ Moderate	⊕⊕○○ Low	⊕○○○ Very Low
<b>Abdomen – Stomach</b>	2 cohorts			
KQ # 1 Efficacy	2 cohorts			
EBRT				↕ 2-yr actuarial DFS ↕ 2-yr survival ↔ 2-yr loco-regional control
<b>KQ # 2 Harms</b>	2 cohorts			
EBRT				↓ renal harms ↔ ≥ Grade 2 GI toxicities
<b>KQ # 3 Subpopulations</b>				
<i>No studies on subpopulations identified.</i>				
<b>KQ # 4 Cost and Cost-Effectiveness</b>				
<i>No studies on costs or cost-effectiveness identified.</i>				
<b>Abdomen – Whole Pelvis Radiation</b>	1 cohort			
KQ # 1 Efficacy				
<i>No studies on efficacy identified.</i>				
<b>KQ # 2 Harms</b>	1 cohort			
EBRT				↔ Acute GI toxicity ↔ Acute GU toxicity No ≥ Grade 3 toxicities in IMRT group.
<b>KQ # 3 Subpopulations</b>				
<i>No studies on subpopulations identified.</i>				
<b>KQ # 4 Cost and Cost-Effectiveness</b>				
<i>No studies on costs or cost-effectiveness identified.</i>				

**Outcomes:** ↔ No Significant Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased

**Abbreviations:** OS – overall survival; PSF – progression free survival; DSS – disease specific survival; DFS – disease free survival; QoL – quality of life; RFS – recurrence free survival; EBRT – external beam radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence <sup>1</sup>		
<b>Malignancy Comparator</b>	<b># of SRs (# included studies in SRs), # of subsequently published studies</b>	<b>⊕⊕⊕○ Moderate</b>	<b>⊕⊕○○ Low</b>	<b>⊕○○○ Very Low</b>
<b>Brain - Astrocytoma</b>	2 SR (1 cohort)			
KQ # 1 Efficacy	1 SR (1 cohort)			
EBRT				↑ 1-yr, 2-yr OS ↑ 1-yr, 2-yr PFS
KQ #2 Harms	2 SRs (1 cohort)			
EBRT				↓ Acute Grade 1 toxicities ↑ Acute Grade 2 and 3 toxicities
KQ #3 Subgroups <i>No studies on subpopulations identified.</i>				
KQ #4 Cost and Cost-Effectiveness <i>No studies on costs or cost-effectiveness identified.</i>				
<b>Brain – Brain Metastases</b>	1 case series			
KQ # 1 Efficacy	1 case series			
No comparator				6-month OS, quality of life (QoL), global health functioning, physical functioning, role functioning
KQ #2 Harms	1 case series			
No comparator				Grade 1 and 2 alopecia
KQ #3 Subgroups <i>No studies on subpopulations identified.</i>				
KQ #4 Cost and Cost-Effectiveness <i>No studies on costs or cost-effectiveness identified.</i>				

**Outcomes:** ↔ No Significant Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased

**Abbreviations:** OS – overall survival; PSF – progression free survival; DSS – disease specific survival; DFS – disease free survival; QoL – quality of life; RFS – recurrence free survival; EBRT – external beam radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence <sup>1</sup>		
<b>Malignancy Comparator</b>	<b># of SRs (# included studies in SRs), # of subsequently published studies</b>	<b>⊕⊕⊕○ Moderate</b>	<b>⊕⊕○○ Low</b>	<b>⊕○○○ Very Low</b>
<b>Brain – Glioblastoma multiforme</b>	1 SR (8 case series), 3 case series			
KQ # 1 Efficacy	1 SR (8 case series), 3 case series			
No comparator				1-yr OS, 2-yr OS, OS, 1-yr PFS, 2-yr PFS, PFS
KQ #2 Harms	1 SR (8 case series), 3 case series			
No comparator				Acute Grade 3 neurotoxicity, late radiation necrosis, Grade 3 otitis with hearing loss, nausea, vomiting, fatigue, Grade 1 anemia, ≤ Grade 2 hepatotoxicity
KQ #3 Subgroups				
<i>No studies on subpopulations identified.</i>				
KQ #4 Cost and Cost-Effectiveness				
<i>No studies on costs or cost-effectiveness identified.</i>				
<b>Brain – High-Grade Glioma</b>	2 case series			
KQ # 1 Efficacy	2 case series			
No comparator				OS (Grade III and IV tumors), 1-yr OS, 2-yr OS, PFS (Grade III and IV tumors), 1-yr PFS, 2-yr PFS
KQ #2 Harms	1 case series			
No comparator				Grade 2 and 3 edema, Grade 1 worsening of neurological symptoms

**Outcomes:** ↔ No Significant Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased

**Abbreviations:** OS – overall survival; PSF – progression free survival; DSS – disease specific survival; DFS – disease free survival; QoL – quality of life; RFS – recurrence free survival; EBRT – external beam radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence <sup>1</sup>		
<b>Malignancy Comparator</b>	<b># of SRs (# included studies in SRs), # of subsequently published studies</b>	<b>⊕⊕⊕○ Moderate</b>	<b>⊕⊕○○ Low</b>	<b>⊕○○○ Very Low</b>
KQ #3 Subgroups <i>No studies on subpopulations identified.</i>				
KQ #4 Cost and Cost-Effectiveness <i>No studies on costs or cost-effectiveness identified.</i>				
<b>Brain – Medulloblastoma</b>	3 SRs (1 cohort, 1 case series), 2 case series			
KQ # 1 Efficacy	1 case series			
No comparator				5-yr PFS, 5-yr OS
KQ #2 Harms	3 SRs (1 cohort, 1 case series), 2 case series			
EBRT				↓ Grade 3 and 4 ototoxicity (children) ↑ Grade 1 and 2 toxicities ↔ neurocognitive functioning
No comparator				≥ Grade 3 ototoxicity, hearing loss
KQ #3 Subgroups <i>No studies on subpopulations identified.</i>				
KQ #4 Cost and Cost-Effectiveness <i>No studies on costs or cost-effectiveness identified.</i>				
<b>Brain – Meningioma</b>	3 case series			
KQ # 1 Efficacy	3 case series			
No comparator				survival, 3-yr actuarial survival, 3- and 5-yr recurrence free survival (RFS)

**Outcomes:** ↔ No Significant Difference; ⚡ Inconsistent Evidence; ↑ Increased; ↓ Decreased

**Abbreviations:** OS – overall survival; PSF – progression free survival; DSS – disease specific survival; DFS – disease free survival; QoL – quality of life; RFS – recurrence free survival; EBRT – external beam radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence <sup>1</sup>		
Malignancy Comparator	# of SRs (# included studies in SRs), # of subsequently published studies	⊕⊕⊕○ Moderate	⊕⊕○○ Low	⊕○○○ Very Low
KQ #2 Harms	1 case series			
No comparator				No severe toxicities reported.
KQ #3 Subgroups				
<i>No studies on subpopulations identified.</i>				
KQ #4 Cost and Cost-Effectiveness				
<i>No studies on costs or cost-effectiveness identified.</i>				
<b>Brain – Pituitary Adenoma</b>				
	1 case series			
KQ # 1 Efficacy	1 case series			
No comparator				Overall biochemical response
KQ #2 Harms	1 case series			
No comparator				Short-term (6 months) toxicities of fatigue, headache, nausea or vomiting, visual complaints, alopecia or ertherma, anxiety attack, epistaxis, dry eyes, excess tearing Long-term (≥ 12 months) toxicities of cognitive changes, visual decline, and cranial nerve deficit
KQ #3 Subgroups				
<i>No studies on subpopulations identified.</i>				
KQ #4 Cost and Cost-Effectiveness				
<i>No studies on costs or cost-effectiveness identified.</i>				

**Outcomes:** ↔ No Significant Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased

**Abbreviations:** OS – overall survival; PSF – progression free survival; DSS – disease specific survival; DFS – disease free survival; QoL – quality of life; RFS – recurrence free survival; EBRT – external beam radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence <sup>1</sup>		
Malignancy Comparator	# of SRs (# included studies in SRs), # of subsequently published studies	⊕⊕⊕○ Moderate	⊕⊕○○ Low	⊕○○○ Very Low
<b>Breast – Whole Breast Radiation</b>	1 SR (4 SRs, 3 RCTs, 9 cohorts, 3 case series, 1 cost, 1 cost-comparison)			
KQ # 1 Efficacy	1 SR (2 SRs, 2 RCTs, 3 cohorts, 2 case series)			
EBRT		↔ QoL	↕ OS ↕ DSS ↔ Ipsilateral breast tumor recurrence ↔ Contralateral breast tumor recurrence ↔ Distant metastases	
No comparator			Local regional recurrence	
KQ #2 Harms	1 SR (4 RCTs, 9 cohorts, 2 case series)			
EBRT		↓ Grade 1 to 3 telangiectasia ↔ Acute ≥ Grade 2 toxicities ↔ Grade 3 or 4 skin toxicities ↓ Moist desquamation	↔ Breast cosmesis ↔ Late ≥ Grade 2 toxicities	

**Outcomes:** ↔ No Significant Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased

**Abbreviations:** OS – overall survival; PSF – progression free survival; DSS – disease specific survival; DFS – disease free survival; QoL – quality of life; RFS – recurrence free survival; EBRT – external beam radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence <sup>1</sup>		
<b>Malignancy Comparator</b>	<b># of SRs (# included studies in SRs), # of subsequently published studies</b>	<b>⊕⊕⊕○ Moderate</b>	<b>⊕⊕○○ Low</b>	<b>⊕○○○ Very Low</b>
KQ #3 Subgroups <i>No studies on subpopulations identified.</i>				
KQ #4 Cost and Cost-Effectiveness				
EBRT			Costs: IMRT > EBRT	
<b>Breast – Partial Breast Radiation</b>	1 SR (1 RCT, 3 case series, 1 cost comparison)			
KQ # 1 Efficacy				
No comparator				Tumor recurrence
KQ #2 Harms				
No comparator	1 RCT, 3 case series			Grade 1 or 2: breast cosmesis, breast edema, breast pain, telangiectasia, erythema, hyperpigmentation, breast-chest wall tenderness, fibrosis Grade 3: telangiectasia
KQ #3 Subgroups <i>No studies on subpopulations identified.</i>				
KQ #4 Cost and Cost-Effectiveness				
EBRT			Costs: IMRT > EBRT	
<b>Female Pelvis – Cervical Cancer</b>	2 SR (2 cohort, 1 case series), 1 cohort, 3 case series			
KQ # 1 Efficacy				
	2 SR (2 cohort, 1 case series), 1 cohort, 3 case series			

**Outcomes:** ↔ No Significant Difference; ⚡ Inconsistent Evidence; ↑ Increased; ↓ Decreased

**Abbreviations:** OS – overall survival; PSF – progression free survival; DSS – disease specific survival; DFS – disease free survival; QoL – quality of life; RFS – recurrence free survival; EBRT – external beam radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence <sup>1</sup>		
Malignancy Comparator	# of SRs (# included studies in SRs), # of subsequently published studies	⊕⊕⊕○ Moderate	⊕⊕○○ Low	⊕○○○ Very Low
EBRT			↑ OS ↑ DSS ↔ 1-yr locoregional control ↔ Complete or partial response (stage IIB – IIIB)	
No comparator				3-yr OS, 3-yr DFS, 3-yr pelvic failure, 3-yr distant failure (stage I-IVA)
KQ #2 Harms	2 SRs (2 cohort, 1 case series), 1 cohort, 3 case series			
EBRT			↓ Late GI toxicity ↔ Late GU toxicity ↓ Grade 3 and 4 GI symptoms ↓ Grade 3 and 4 GU symptoms	
No comparator				Acute Grade 3 symptoms (stage I-IVA), chronic Grade 3 GI symptoms, chronic Grade 3 CU symptoms Acute ≥ Grade 3 toxicities in leukocytes, lymphopenia, platelets, constitutional fatigue, weight loss, GI, anorexia,

**Outcomes:** ↔ No Significant Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased

**Abbreviations:** OS – overall survival; PSF – progression free survival; DSS – disease specific survival; DFS – disease free survival; QoL – quality of life; RFS – recurrence free survival; EBRT – external beam radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence <sup>1</sup>		
<b>Malignancy Comparator</b>	<b># of SRs (# included studies in SRs), # of subsequently published studies</b>	<b>⊕⊕⊕○ Moderate</b>	<b>⊕⊕○○ Low</b>	<b>⊕○○○ Very Low</b>
				diarrhea, renal/GU fistula (female genital tract)
KQ #3 Subgroups				
<i>No studies on subpopulations identified.</i>				
KQ #4 Cost and Cost-Effectiveness				
<i>No studies on costs or cost-effectiveness identified.</i>				
<b>Female Pelvis – Endometrial Cancer</b>	<b>1 cohort</b>			
<b>KQ # 1 Efficacy</b>	<b>1 cohort</b>			
EBRT				2-yr OS (results were pooled) 2-yr DFS (results were pooled)
KQ #2 Harms				
EBRT				↓ Acute toxicities ↓ Small bowel obstruction ↑ Chronic proctitis
KQ #3 Subgroups				
<i>No studies on subpopulations identified.</i>				
KQ #4 Cost and Cost-Effectiveness				
<i>No studies on costs or cost-effectiveness identified.</i>				
<b>Female Pelvis – Paraaortic lymph node metastases</b>	<b>1 cohort, 2 case series</b>			
<b>KQ # 1 Efficacy</b>	<b>1 cohort, 1 case series</b>			
EBRT				↑ 2-yr survival ↑ 3-yr survival
No comparator				1-yr OS, 2-yr OS

**Outcomes:** ↔ No Significant Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased

**Abbreviations:** OS – overall survival; PSF – progression free survival; DSS – disease specific survival; DFS – disease free survival; QoL – quality of life; RFS – recurrence free survival; EBRT – external beam radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence <sup>1</sup>		
Malignancy Comparator	# of SRs (# included studies in SRs), # of subsequently published studies	⊕⊕⊕○ Moderate	⊕⊕○○ Low	⊕○○○ Very Low
KQ #2 Harms				
1 cohort, 2 case series				
EBRT				↓ Acute and chronic GI and GU symptoms (i.e., leucopenia, enteritis, enterocolitis)
No comparator				Acute Grade 1 GI disorders, acute Grade 2 GI disorder, liver dysfunction, late Grade 1 and 2 disorders
KQ #3 Subgroups				
<i>No studies on subpopulations identified.</i>				
KQ #4 Cost and Cost-Effectiveness				
<i>No studies on cost or cost-effectiveness identified.</i>				
Head and Neck Cancer		5 SRs <sup>3</sup> , 1 RCT, 2 cohort, 45 case series, 1 cost study		
KQ # 1 Efficacy				
8 SRs, 1 RCT, 1 cohort				
EBRT		↑ QoL (xerostomia-related)	↔ OS ↔ tumor control ↔ local PFS (oropharyngeal cancer) ↑ 5-yr local RFS (nasopharyngeal cancer) ↔ 5-yr nodal relapse free survival	

<sup>3</sup> With multiple overlapping primary studies included

**Outcomes:** ↔ No Significant Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased

**Abbreviations:** OS – overall survival; PSF – progression free survival; DSS – disease specific survival; DFS – disease free survival; QoL – quality of life; RFS – recurrence free survival; EBRT – external beam radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence <sup>1</sup>		
<b>Malignancy Comparator</b>	<b># of SRs (# included studies in SRs), # of subsequently published studies</b>	<b>⊕⊕⊕○ Moderate</b>	<b>⊕⊕○○ Low</b>	<b>⊕○○○ Very Low</b>
			↔ 5-yr distant metastasis free survival ↔ 5-yr DFS ↕ QoL (for other outcomes)	
KQ #2 Harms		6 SRs, 1 RCT, 1 cohort, 45 case series		
EBRT		↓ ≥ Grade 2 xerostomia		↔ Trimus ↔ Sensorineural hearing loss ↔ Osteonecrosis
No comparator				Nausea, vomiting and fatigue, local symptoms including dermatitis and mucositis, xerostomia, dysphagia, laryngeal symptoms
KQ #3 Subgroups		No studies on subpopulations identified.		
KQ #4 Cost and Cost Effectiveness		1 cost study		
EBRT			Costs: IMRT > EBRT ↓ Direct costs for experienced treatment centers compared to centers initiating IMRT	

**Outcomes:** ↔ No Significant Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased

**Abbreviations:** OS – overall survival; PSF – progression free survival; DSS – disease specific survival; DFS – disease free survival; QoL – quality of life; RFS – recurrence free survival; EBRT – external beam radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence <sup>1</sup>		
Malignancy Comparator	# of SRs (# included studies in SRs), # of subsequently published studies	⊕⊕⊕○ Moderate	⊕⊕○○ Low	⊕○○○ Very Low
<b>Lung Cancer - NSCLC</b>				
3 SR (2 cohorts), 6 case series				
<b>KQ # 1 Efficacy</b>				
1 SR (1 cohort), 5 case series				
EBRT			↑ OS ↔ Locoregional PFS ↔ Distant metastasis-free survival	
No comparator				OS, 2-yr and 3-yr survival, distant metastasis free survival, 2-yr DFS, local PFS
<b>KQ #2 Harms</b>				
3 SRs (2 cohort), 6 case series				
EBRT			↓ ≥ Grade 3 pneumonitis	
No comparator				≥ Acute and late Grade 3 pneumonitis, Grade 3 pulmonary fibrosis, Grade 3 pulmonary fibrosis, ≥ acute Grade 3 esophagitis, Grade 2 and 3 esophageal strictures, Grade 2 esophageal toxicity, ≥ Grade 2 lung toxicity, Grade 3 dysphagia, Grade 3 skin toxicity, Grade 1-3 radiation pneumonitis, death from radiation pneumonitis

**Outcomes:** ↔ No Significant Difference; ⚡ Inconsistent Evidence; ↑ Increased; ↓ Decreased

**Abbreviations:** OS – overall survival; PSF – progression free survival; DSS – disease specific survival; DFS – disease free survival; QoL – quality of life; RFS – recurrence free survival; EBRT – external beam radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence <sup>1</sup>		
<b>Malignancy Comparator</b>	<b># of SRs (# included studies in SRs), # of subsequently published studies</b>	<b>⊕⊕⊕○ Moderate</b>	<b>⊕⊕○○ Low</b>	<b>⊕○○○ Very Low</b>
KQ #3 Subgroups <i>No studies on subpopulations identified.</i>				
KQ #4 Cost and Cost Effectiveness <i>No studies on costs or cost-effectiveness identified.</i>				
<b>Lung Cancer – Pleural Mesothelioma</b>		1 SR (2 case series), 2 case series		
KQ # 1 Efficacy		1 SR (1 case series), 2 case series		
No comparator				1yr to 5yr DFS, 1yr to 5yr DSS, local recurrence
KQ #2 Harms		1 SR (2 case series)		
No comparator				Fatal radiation pneumonitis, acute Grade 3 radiation-induced esophagitis, acute toxicities of nausea, vomiting, and fatigue, late death from liver toxicity and pericarditis
KQ #3 Subgroups <i>No studies on subpopulations identified.</i>				
KQ #4 Cost and Cost Effectiveness <i>No studies on costs or cost-effectiveness identified.</i>				
<b>Lung Cancer – SCLC</b>		1 case series		
KQ # 1 Efficacy		1 case series		
No comparator				Actuarial OS, RFS
KQ #2 Harms		1 case series		
No comparator				Acute pneumonitis, esophagitis

**Outcomes:** ↔ No Significant Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased

**Abbreviations:** OS – overall survival; PSF – progression free survival; DSS – disease specific survival; DFS – disease free survival; QoL – quality of life; RFS – recurrence free survival; EBRT – external beam radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence <sup>1</sup>		
<b>Malignancy Comparator</b>	<b># of SRs (# included studies in SRs), # of subsequently published studies</b>	<b>⊕⊕⊕○ Moderate</b>	<b>⊕⊕○○ Low</b>	<b>⊕○○○ Very Low</b>
KQ #3 Subgroups <i>No studies on subpopulations identified.</i>				
KQ #4 Cost and Cost Effectiveness <i>No studies on costs or cost-effectiveness identified.</i>				
<b>Prostate Cancer</b>	<b>4 SRs, 7 cohorts, 19 case series</b>			
<b>KQ # 1 Efficacy</b>	<b>3 SRs, 7 cohorts</b>			
EBRT			↔ bDFS (30 months) ↑ bDFS (60 months) ↔ Tumor control ↓ Recurrence ↔ QoL	
<b>KQ #2 Harms</b>	<b>3 SR, 6 cohorts, 19 case series</b>			
EBRT		↓ GI toxicities	↓ GU toxicity ↓ Hip fracture ↔ Erectile dysfunction	
KQ #3 Subgroups <i>No studies on subpopulations identified.</i>				
<b>KQ #4 Cost and Cost Effectiveness</b>	<b>1 SR</b>			
				↓ Cost-effectiveness
<b>Sarcoma</b>	<b>1 case series</b>			
<b>KQ # 1 Efficacy</b>	<b>1 case series</b>			
No comparator				Local recurrence
<b>KQ #2 Harms</b>	<b>1 case series</b>			
No comparator				Nausea, fatigue, dry mouth,

**Outcomes:** ↔ No Significant Difference; ⚡ Inconsistent Evidence; ↑ Increased; ↓ Decreased

**Abbreviations:** OS – overall survival; PSF – progression free survival; DSS – disease specific survival; DFS – disease free survival; QoL – quality of life; RFS – recurrence free survival; EBRT – external beam radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence <sup>1</sup>		
<b>Malignancy Comparator</b>	<b># of SRs (# included studies in SRs), # of subsequently published studies</b>	<b>⊕⊕⊕○ Moderate</b>	<b>⊕⊕○○ Low</b>	<b>⊕○○○ Very Low</b>
				pharyngitis or esophagitis, pain, Grade 4 skin toxicity
<b>KQ #3 Subgroups</b>				
<i>No studies on subpopulations identified.</i>				
<b>KQ #4 Cost and Cost Effectiveness</b>				
<i>No studies on costs or cost-effectiveness identified.</i>				
<b>Other Cancers – Sacral Chordoma</b>	1 case series			
<b>KQ # 1 Efficacy</b>	1 case series			
No comparator				Actuarial 1-, 2-, and 5-yr OS; 1-, 2-, and 5-yr DSS; actuarial 1-, 2-, and 5-yr DSS
<b>KQ #2 Harms</b>	1 case series			
No comparator				Diarrhea, bladder irritation, erythema, hyperpigmentation. No harms > Grade 3 reported.
<b>KQ #3 Subgroups</b>				
<i>No studies on subpopulations identified.</i>				
<b>KQ #4 Cost and Cost Effectiveness</b>				
<i>No studies on costs or cost-effectiveness identified.</i>				
<b>Other Cancers - Skin</b>	1 case series			
<b>KQ # 1 Efficacy</b>	1 case series			
No comparator				Disease recurrence
<b>KQ #2 Harms</b>	1 case series			
No comparator				Grade 1 or 2 erythema

**Outcomes:** ↔ No Significant Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased

**Abbreviations:** OS – overall survival; PSF – progression free survival; DSS – disease specific survival; DFS – disease free survival; QoL – quality of life; RFS – recurrence free survival; EBRT – external beam radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence <sup>1</sup>		
<b>Malignancy Comparator</b>	<b># of SRs (# included studies in SRs), # of subsequently published studies</b>	<b>⊕⊕⊕○ Moderate</b>	<b>⊕⊕○○ Low</b>	<b>⊕○○○ Very Low</b>
KQ #3 Subgroups <i>No studies on subpopulations identified.</i>				
KQ #4 Cost and Cost Effectiveness <i>No studies on costs or cost-effectiveness identified.</i>				
<b>Other Cancers - Thyroid</b>	<b>2 cohort, 1 case series</b>			
KQ # 1 Efficacy 1 cohort, 1 case series				
EBRT			↔ All survival measures	
No comparator				2-yr local PFS, 2-yr OS
KQ #2 Harms 2 cohort, 1 case series				
EBRT				↓ Late morbidity (e.g., esophageal structure, laryngeal stenosis, laryngeal edema, chronic dysphagia)
No comparator				Acute mucositis, pharyngitis, dysphagia, xerostomia, skin toxicity, laryngeal toxicity
KQ #3 Subgroups <i>No studies on subpopulations identified.</i>				
KQ #4 Cost and Cost Effectiveness <i>No studies on costs or cost-effectiveness identified.</i>				
<b>Other Cancers – Spinal Metastases</b>	<b>5 case series</b>			
KQ # 1 Efficacy 3 case series				
No comparator				OS, tumor recurrence, QoL

**Outcomes:** ↔ No Significant Difference; ⚡ Inconsistent Evidence; ↑ Increased; ↓ Decreased

**Abbreviations:** OS – overall survival; PSF – progression free survival; DSS – disease specific survival; DFS – disease free survival; QoL – quality of life; RFS – recurrence free survival; EBRT – external beam radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence <sup>1</sup>		
<b>Malignancy Comparator</b>	<b># of SRs (# included studies in SRs), # of subsequently published studies</b>	<b>⊕⊕⊕○ Moderate</b>	<b>⊕⊕○○ Low</b>	<b>⊕○○○ Very Low</b>
KQ #2 Harms	5 case series			
No comparator				Spinal fractures, Grade 1 to 2 skin reactions, Grade 2 esophagitis, myelitis, acute symptoms (pharyngitis, fatigue, diarrhea)
KQ #3 Subgroups				
<i>No studies on subpopulations identified.</i>				
KQ #4 Cost and Cost Effectiveness				
<i>No studies on costs or cost-effectiveness identified.</i>				

**Outcomes:** ↔ No Significant Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased

**Abbreviations:** OS – overall survival; PSF – progression free survival; DSS – disease specific survival; DFS – disease free survival; QoL – quality of life; RFS – recurrence free survival; EBRT – external beam radiation therapy; GI – gastrointestinal; GU – gastrourinary