

Intensity Modulated Radiation Therapy

Final Evidence Report

Appendix J. Peer Review Comments and Disposition

August 17, 2012

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Intensity Modulated Radiation Therapy

Appendix J. Peer Review Comments and Disposition

August 2012

Center for Evidence-based Policy

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Peer Review Comments and Disposition

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RESPONSE TO PEER REVIEW COMMENTS

The Center for Evidence-based Policy is an independent vendor contracted to produce evidence assessment reports for the WA HTA program. For transparency, all comments received during the comments process are included in this response document. Comments related to program decisions, process, or other matters not pertaining to the evidence report are acknowledged through inclusion only.

This document responds to comments from the following peer review from:

- Edward Kim, MD (University of Washington)
- Charlotte Dai Kubicky, MD (Oregon Health and Science University)

Specific responses pertaining to each comment are included in Table 1 below. The full version of each peer review received is available in the Peer Review Comments section, beginning on page 7.

Table 1. Response to Peer Review on Draft Report

Reviewer	Comment	Disposition
Edward Kim, MD (University of Washington)		
	<p>Is the target population explicitly defined and relevant?</p> <p>One exception - anal and rectal cancer patients are grouped together in this assessment– they should be considered separately as the treatment strategy (dose of radiation, areas of the pelvis that are treated, type of chemotherapy administered, and combination of radiation with surgery) differs between the two diseases.</p>	<i>Thank you for your comment. Anal and rectal cancers have been separated into separate section as suggested.</i>
	<p>Were any interventions, comparators or outcomes omitted that should be included?</p> <p>Studies that incorporated chemotherapy were omitted (with the exception of head and neck cancers). This is an appropriate choice for certain disease sites, such as breast cancer, prostate cancer, or sarcoma, in which radiotherapy is typically administered without chemotherapy. However, concurrent administration of chemotherapy and radiotherapy is standard of care in many disease sites (anal, rectal, pancreas, lung, female pelvis). Omission of trials that include chemotherapy for these disease sites does not reflect current medical practice and may reduce the external validity of the findings. The use of concurrent chemotherapy should not be used to exclude studies from this assessment for disease sites in which chemotherapy is routinely administered with radiation.</p>	<i>Thank you for your comment. Evidence including chemotherapy and radiation has been added to the report for other cancers (in addition to head and neck cancers).</i>
	<p>Were any interventions, comparators or outcomes omitted that should be included?</p> <p>The findings related to breast cancer do not address the reduction in cardiac dose that is possible with IMRT for patients with left sided breast cancers. This is a commonly cited rationale for the use of IMRT in breast cancer patients.</p>	<i>Thank you for your comment. Dose information was not included in the report even though it may affect the radiation therapy given. The evidence for the effects of dose on outcomes and harms was not reported.</i>
	<p>Does [the executive summary] accurately reflect the methods and results of the</p>	<i>Thank you for highlighting this. The costs described on page 1 and 31 of the report are</i>

Reviewer	Comment	Disposition
	<p>report?</p> <p>There is a discrepancy between the costs for IMRT described on page 2 and costs in the section describing WA state data (in particular, the costs for lung cancer).</p>	<p><i>abstracted from a study of 86 patients with inoperable non-small cell lung cancer. Additional national reimbursement rates for IMRT from the Medicare Physicians Fee Schedule have been added to the report. Washington state cost data is likely to vary from the results published in the small cohort study (Lanni 2010) and from national Medicare physician fee rates.</i></p>
	<p>Are the tables clear and easy to read?</p> <p>Overall the tables were very clear. Table 3.1 (page 36) may benefit from more explanation.</p>	<p><i>Thank you. The tables have been slightly revised.</i></p>
	<p>Clinical Overview: Is there an adequate and/or accurate clinical overview of the question?</p> <p>Several of the cancer sites discussed in the policy are not included in table 1 (page 1). Information about the incidence/prevalence of these tumors (i.e. sarcoma) may help place the wealth or lack of clinical data in perspective.</p>	<p><i>Thank you for your comment. We have updated the table to reflect the incidence and prevalence of all malignancies discussed in the report. We have removed the statistics for malignancies not included in the report.</i></p>
	<p>Policy Context: Is the policy context clear?</p> <p>Page 30, paragraph 2 makes reference to FDA oversight of devices that can be used to deliver IMRT. It's not clear how this relates to the purpose of the policy review (is this meant as a criticism of FDA policy/procedure?) Several of the trials describing the use of IMRT originate outside the US.</p> <p>It may be helpful to include a sentence that explicitly states, "The purpose of this technology assessment is to..."</p>	<p><i>Thank you for your comment. A sentence was added to this section as suggested.</i></p>
	<p>Are the methods for identifying relevant studies clearly described?</p> <p>Were references submitted during the public commentary period included or reviewed for relevance? I did not see anything in the methods section that describes review of the references submitted by the public. Appendix I (public comments) contains many references, but several of them were not included in</p>	<p><i>Thank you for highlighting this. We have included a section in the report that discusses how comments and references submitted through the public comment process and peer review process are taken into account in report development.</i></p>

Reviewer	Comment	Disposition
	the final report or in Appendix B (excluded studies).	
	<p>Are the methods for identifying relevant studies clearly described?</p> <p>It would be useful to explain the rationale for excluding dosimetric studies from the analysis. Dosimetric parameters can be used to predict the risk of treatment related toxicity and often guide decisions regarding dosage and radiation treatment modality.</p>	<p><i>Thank you for your comment. A footnote was added to the methods section detailing the rationale for not including dosimetric studies.</i></p>
	<p>Was something excluded that should have been included?</p> <p>Page 4, line 7 “Studies that... included patients who were concurrently receiving chemotherapy (with the exception of head and neck patients) were excluded.” It is standard of care for patients to receive concurrent chemotherapy and radiation for many disease sites (anal, rectal, prostate, CNS, lung, etc) and omission of these trials creates a data set that does not accurately represent the population of patients being treated. The use of concurrent chemotherapy should not be the basis for excluding a trial from the assessment.</p>	<p><i>Thank you for your comment. See above comment/disposition on chemoradiation.</i></p>
	<p>Was something excluded that should have been included?</p> <p>Anal cancer – there is a prospective multicenter phase II trial looking at the use of IMRT in anal cancer that is relevant to the section on anal cancer. It was a cooperative group trial, RTOG 0529 - (<i>Kachnic et al. Int J Radiat Oncol Biol Phys 2012, 82, 153-8</i>)</p>	<p><i>Thank you, this study has been incorporated into the report.</i></p>
	<p>Was something excluded that should have been included?</p> <p>For sarcomas, the reports from Memorial Sloan Kettering and Emory were described as “fair” and “good” quality but were not described in the findings section (the findings summary on page 87 lists only one study although there were 3 studies included in appendix F on pages 225-227)</p>	<p><i>Thank you for your comment. Emory has EBRT as the intervention and not IMRT. Some of the patients were treated with IMRT and some with EBRT but the results do not distinguish between the two groups. Emory was therefore excluded and has been removed from the evidence tables.</i></p> <p><i>Alektiar had brachytherapy as a comparator. Brachytherapy is not outlined as a comparator in the PICO or Key Questions. Alektiar was therefore</i></p>

Reviewer	Comment	Disposition
		<i>excluded and removed from the evidence tables.</i>
	<p>Was something excluded that should have been included?</p> <p>For pancreas cancer, Univ of Maryland published an analysis of toxicity with IMRT and compared to reported toxicities from a 3D CRT trial (Yovino, et al. IJROBP 2011). This reference was included in the appendix of excluded studies based on the fact that patients received concurrent chemotherapy. However, pancreas radiotherapy is almost always delivered with concurrent chemotherapy. This should not be a basis for exclusion.</p>	<i>Thank you for your comment. Yovino has a study size of 46 and does not report on clinical effectiveness outcomes. This study size falls below the n=50 cutoff for Key Question 2 “Harms” and was therefore excluded.</i>
	<p>Was something included that should have been excluded?</p> <p>Page 28 – the estimate of secondary malignancies described in the Hall (2003) reference is not widely accepted and is not based on observed/measured secondary malignancy rates. It should be omitted or additional references that address the risk of second malignancies based on clinical data (rather than projections) should be added to the report to place this estimate in context.</p>	<i>Thank you for your comment. This section has been removed at your suggestion.</i>
	<p>Is the presentation of the results well-structured and organized?</p> <p>Several of the findings under KQ2 (potential harms of IMRT) describe reductions in toxicity related to 3D conformal radiotherapy. I would consider this a potential benefit of IMRT, rather than potential harm (relative to 3D CRT). Unless, the intent is to classify any adverse side effect of treatment as a potential harm – in this case, it makes sense to keep this in KQ2 (even though this would be “harm reduction” relative to 3D CRT).</p>	<i>Thank you for your comment. The report authors made the decision to consider toxicity as a harm (Key Question 2) rather than “reduction of toxicity” as an outcome (Key Question 1) because they felt that it was clearer. The separation of toxicity from Outcomes is consistent for all cancers.</i>
	<p>Has the evidence been accurately synthesized?</p> <p>Page 65 describes a difference in grade 3-4 skin toxicity that did not reach statistical significance in the Pignol (2008) trial. The trial also demonstrated a statistically significant decrease in the risk of developing moist desquamation- this should be included in the findings.</p>	<i>Thank you for your comment. Additional data from Pignol has been included in the evidence tables and text.</i>
	<p>Does the report adequately address effectiveness?</p> <p>The report adequately addresses effectiveness, with the understanding that</p>	<i>Thank you for your comment. Please see disposition above.</i>

Reviewer	Comment	Disposition
	toxicity reduction is not addressed under KQ1, but is instead addressed in KQ2.	
	<p>Do they balance the effectiveness with the potential harms?</p> <p>Reductions in toxicity with IMRT are listed in the findings for KQ2, under a category of “potential harms of IMRT relative to conventional external beam radiation therapy,” rather than under KQ1 (“evidence of effectiveness for IMRT compared to conventional external beam radiation therapy”). The description of toxicity rates under KQ2 may suggest to the casual reader of the report that IMRT increases these toxicity rates (harm increase rather than harm reduction).</p>	<i>Thank you for your comment. Please see disposition above.</i>
	<p>General comments</p> <p>Methods were overall very well defined. However, the exclusion of trials that incorporate chemotherapy is a concern. For many disease sites, chemotherapy is routinely administered concurrently with radiation. Omission of these trials omits data applicable to a large number of patients. This affects the scientific accuracy of the overall report (an incomplete data set leads to inaccurate conclusions).</p> <p>Thank you for the opportunity to comment on this report.</p>	<i>Thank you for your comment. Please see disposition above on chemoradiation.</i>
Charlotte Dai Kubicky, MD		
	For brain tumors in certain locations, IMRT is superior than CRT in sparing normal tissues (optic nerves, chiasm, brainstem etc). Unfortunately, there is a lack of studies that specifically look at tumors close to critical structures in the brain.	<i>Thank you for your comments. No changes to report.</i>
	For spine metastases, there is a large body of literature reporting the efficacy and toxicity of spine radiosurgery or SBRT, both utilizing IMRT as the treatment planning technique. I don't see them included here.	<i>Thank you for your comment. This subject will be included in the upcoming WA HTA evidence report on SBRT.</i>
	<p>Page 101 “Thymoma”</p> <p>Page 103 For head and neck should be “fair” rather than “poor”</p>	<i>Thank you for your comments. We made the appropriate changes.</i>

PEER REVIEW COMMENTS – DRAFT REPORT**DUE DATE:** August 6, 2012**REVIEW:** WA State IMRT**REVIEWER INFORMATION:**

Name: Edward Kim

Title: MD, Assistant Professor of Radiation Oncology

Organization/University: University of Washington

Phone: 206-598-1168

E-mail: edykim@uw.edu

INSTRUCTIONS:

This form can be filled out electronically on your personal computer. In the shaded areas of the assessment, use the TAB key to move from field to field. The Peer Review Form is composed of check boxes to gauge your view of the quality of the report. Space has been provided to add comments. Additionally, any other comments including comments about the Peer Review form are welcome.

COI STATEMENT:

Do you have a conflict of interest or competing interest? Do you have, or believe that report users might reasonably perceive you to have something personal (e.g. grants, publications, money, reputation, significant relationship) to gain (or avoid losing) from the position you take in rating this report?

No, I do not have a conflict (Please proceed with review)

Yes, I have a potential conflict (Please notify Heidi Kriz at krizh@ohsu.edu or 503-494-2127)

PUBLIC ACKNOWLEDGEMENT:

The Washington State Health Care Authority Health Technology Assessment Program (HTA) is required to post the names of peer reviewers of public reports to public websites.

BACKGROUND:

The Washington State Health Care Authority Health Technology Assessment Program (HTA) is an innovative program that determines if health services used by state government are safe and effective. The primary purpose of the HTA program is to ensure medical treatments and services paid for with state health care dollars are safe and proven to work. The goals are to make health care safer by relying on scientific evidence and a committee of practicing clinicians, to make coverage decisions of state agencies more consistent and more cost effective by paying for medical tools and procedures that are proven to work, and the coverage decision process more open and inclusive by sharing information, holding public meetings, and publishing decision criteria and outcomes. The HTCC makes policy determinations based on the best available evidence, national guidelines, and public input (<http://www.hca.wa.gov/>).

WA HTA selected Intensity Modulated Radiation Therapy for review by the Health Technology Clinical Committee (HTCC) at the September 21st, 2012 public meeting. WA HTA requested an independent

vendor, the Center for Evidence-based Policy (CEbP) at Oregon Health and Science University, to systematically review the evidence and produce a report.

A ‘best evidence’ systematic review methodology was used to complete this report. Existing high quality systematic reviews and technology assessments were summarized for each key question. If there were two or more comparable reviews identified and one is more recent, of better quality, or more comprehensive, then the other review(s) will be excluded, and the rationale for selection was included in the report. Individual studies published after the search dates of the last high quality review were appraised and synthesized with the results of the high quality systematic reviews. If there were no high quality reviews identified for a key question or intervention, a search, appraisal, and summary of individual studies was completed for the last 10 years (January 2002 to March 2012).

The purpose of the Peer Review Form is for you to provide your expert opinion and comments on the quality of this WA HTA report. Specifically, we are asking for your suggestions for improvement in the report from your viewpoint, but within the scope of the review as outlined by the key questions, inclusion criteria, and methods. The key questions define the scope of the report and cannot be changed.

QUALITY OF THE REPORT

Please rate the quality of the report by selecting the appropriate boxes. Unlimited text can be inserted into the comments field.

I. Scope	Comments
Is the target population explicitly defined and relevant?	<input checked="" type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> NA One exception - anal and rectal cancer patients are grouped together in this assessment– they should be considered separately as the treatment strategy (dose of radiation, areas of the pelvis that are treated, type of chemotherapy administered, and combination of radiation with surgery) differs between the two diseases.
Were any interventions, comparators or outcomes omitted that should be included?	<input checked="" type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> NA Studies that incorporated chemotherapy were omitted (with the exception of head and neck cancers). This is an appropriate choice for certain disease sites, such as breast cancer, prostate cancer, or sarcoma, in which radiotherapy is typically administered without chemotherapy. However, concurrent administration of chemotherapy and radiotherapy is standard of care in many disease sites (anal, rectal, pancreas, lung, female pelvis). Omission of trials that include chemotherapy for these disease sites does not reflect current medical practice and may reduce the external validity of the findings. The use of

concurrent chemotherapy should not be used to exclude studies from this assessment for disease sites in which chemotherapy is routinely administered with radiation.

The findings related to breast cancer do not address the reduction in cardiac dose that is possible with IMRT for patients with left sided breast cancers. This is a commonly cited rationale for the use of IMRT in breast cancer patients.

II. Executive Summary		
Is it clear and concise?	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N <input type="checkbox"/> NA
Does it accurately reflect the methods and results of the report?	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N <input type="checkbox"/> NA
There is a discrepancy between the costs for IMRT described on page 2 and costs in the section describing WA state data (in particular, the costs for lung cancer).		
III. WA State Data		
Are the tables clear and easy to read?	<input type="checkbox"/> Y	<input checked="" type="checkbox"/> N <input type="checkbox"/> NA
Overall the tables were very clear. Table 3.1 (page 36) may benefit from more explanation.		
III. Introduction		
Background: Is the background adequately described?	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N <input type="checkbox"/> NA
Clinical Overview: Is there an adequate and/or accurate clinical overview of the question?	<input type="checkbox"/> Y	<input checked="" type="checkbox"/> N <input type="checkbox"/> NA
Several of the cancer sites discussed in the policy are not included in table 1 (page 1). Information about the incidence/prevalence of these tumors (i.e. sarcoma) may help place the wealth or lack of clinical data in perspective.		
Policy Context: Is the policy context clear?	<input type="checkbox"/> Y	<input checked="" type="checkbox"/> N <input type="checkbox"/> NA
Page 30, paragraph 2 makes reference to FDA oversight of devices that can be used to deliver IMRT. It's not clear how this relates to the purpose of the policy review (is this meant as a criticism of FDA policy/procedure?) Several of the trials describing the use of IMRT originate outside the US.		
It may be helpful to include a sentence that explicitly states, "The purpose of this technology assessment is to..."		

IV. Methods

Are the methods for identifying relevant studies clearly described? Y N NA

Were references submitted during the public commentary period included or reviewed for relevance? I did not see anything in the methods section that describes review of the references submitted by the public. Appendix I (public comments) contains many references, but several of them were not included in the final report or in Appendix B (excluded studies).

It would be useful to explain the rationale for excluding dosimetric studies from the analysis. Dosimetric parameters can be used to predict the risk of treatment related toxicity and often guide decisions regarding dosage and radiation treatment modality.

Are the criteria for the inclusion and exclusion of studies clearly described? Y N NA

See comment below re: exclusion of studies including concurrent chemotherapy

Are the methods for grading studies and guidelines clearly described? Y N NA

(insert comment)

Was something excluded that should have been included? Y N NA

Page 4, line 7 “Studies that... included patients who were concurrently receiving chemotherapy (with the exception of head and neck patients) were excluded.” It is standard of care for patients to receive concurrent chemotherapy and radiation for many disease sites (anal, rectal, prostate, CNS, lung, etc) and omission of these trials creates a data set that does not accurately represent the population of patients being treated. The use of concurrent chemotherapy should not be the basis for excluding a trial from the assessment.

Anal cancer – there is a prospective multicenter phase II trial looking at the use of IMRT in anal cancer that is relevant to the section on anal cancer. It was a cooperative group trial, RTOG 0529 - (Kachnic et al. *Int J Radiat Oncol Biol Phys* 2012, 82, 153-8)

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Memorial Sloan Kettering and Emory were described as “fair” and “good” quality but were not described in the findings section (the findings summary on page 87 lists only one study although there were 3 studies included in appendix F on pages 225-227)

For pancreas cancer, Univ of Maryland published an analysis of toxicity with IMRT and compared to reported toxicities from a 3D CRT trial (Yovino, et al. IJROBP 2011). This reference was included in the appendix of excluded studies based on the fact that patients received concurrent chemotherapy. However, pancreas radiotherapy is almost always delivered with concurrent chemotherapy. This should not be a basis for exclusion.

Was something included that should have been excluded?

Y N NA

Page 28 – the estimate of secondary malignancies described in the Hall (2003) reference is not widely accepted and is not based on observed/measured secondary malignancy rates. It should be omitted or additional references that address the risk of second malignancies based on clinical data (rather than projections) should be added to the report to place this estimate in context.

V. Results

Is the presentation of the results well-structured and organized?

Y N NA

Several of the findings under KQ2 (potential harms of IMRT) describe reductions in toxicity related to 3D conformal radiotherapy. I would consider this a potential benefit of IMRT, rather than potential harm (relative to 3D CRT). Unless, the intent is to classify any adverse side effect of treatment as a potential harm – in this case, it makes sense to keep this in KQ2 (even though this would be “harm reduction” relative to 3D CRT).

Has the evidence been accurately synthesized?

Y N NA

Page 65 describes a difference in grade 3-4 skin toxicity that did not reach statistical significance in the Pignol (2008) trial. The trial also

demonstrated a statistically significant decrease in the risk of developing moist desquamation- this should be included in the findings.

Does the report adequately address effectiveness? Y N NA The report adequately addresses effectiveness, with the understanding that toxicity reduction is not addressed under KQ1, but is instead addressed in KQ2.

Does the report adequately address harms? Y N NA (insert comment)

VI. Guidelines

Are the guidelines adequately summarized? Y N NA

Is the quality of the guidelines clearly described? Y N NA (insert comment)

Is there an adequate comparison of the guidelines to the evidence in the report? Y N NA (insert comment)

VII. General Conclusions

Do they summarize the effectiveness of the intervention? Y N NA (insert comment)

Do they balance the effectiveness with the potential harms? Y N NA Reductions in toxicity with IMRT are listed in the findings for KQ2, under a category of “potential harms of IMRT relative to conventional external beam radiation therapy,” rather than under KQ1 (“evidence of effectiveness for IMRT compared to conventional external beam radiation therapy”). The description of toxicity rates under KQ2 may suggest to the casual reader of the report that IMRT increases these toxicity rates (harm increase rather than harm reduction).

Do they address the strengths and limitations of the evidence adequately? Y N NA (insert comment)

VIII. Figures, tables and appendices

Are the figures clear and easy to read? Y N NA (insert comment)

Are the tables clear and easy to read? Y N NA (insert comment)

Are the appendices clear and easy to read? Y N NA (insert comment)

X. OVERALL REPORT RATING [1 = Very Poor, 2=Poor, 3=Average, 4=Good, 5 = Excellent]

Overall quality of the report:	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input checked="" type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
Clarity of the report:	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input checked="" type="checkbox"/> 4	<input type="checkbox"/> 5
Presentation (design/formatting):	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input checked="" type="checkbox"/> 5
Methods:	<input type="checkbox"/> 1	<input checked="" type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
Grading of the body of evidence:	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input checked="" type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
Scientific accuracy:	<input type="checkbox"/> 1	<input checked="" type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
Clinical relevance:	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input checked="" type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

XI. Other Comments

Methods were overall very well defined. However, the exclusion of trials that incorporate chemotherapy is a concern. For many disease sites, chemotherapy is routinely administered concurrently with radiation. Omission of these trials omits data applicable to a large number of patients. This affects the scientific accuracy of the overall report (an incomplete data set leads to inaccurate conclusions).

Thank you for the opportunity to comment on this report.

DUE DATE: 8/10/2012

REVIEW: Charlotte Dai Kubicky

REVIEWER INFORMATION:

Name: Charlotte Dai Kubicky

Title: MD, PhD

Organization/University: Oregon Health Science University

Phone: 503-681-4200

E-mail: kubickyc@ohsu.edu

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QUALITY OF THE REPORT

Please rate the quality of the report by selecting the appropriate boxes. Unlimited text can be inserted into the comments field.

I. Scope			Comments
Is the target population explicitly defined and relevant?	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N <input type="checkbox"/> NA	(insert comment)
Were any interventions, comparators or outcomes omitted that should be included?	<input type="checkbox"/> Y	<input checked="" type="checkbox"/> N <input type="checkbox"/> NA	(insert comment)
II. Executive Summary			
Is it clear and concise?	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N <input type="checkbox"/> NA	(insert comment)
Does it accurately reflect the methods and results of the report?	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N <input type="checkbox"/> NA	(insert comment)
III. WA State Data			
Are the tables clear and easy to read?	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N <input type="checkbox"/> NA	(insert comment)
III. Introduction			
Background: Is the background adequately described?	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N <input type="checkbox"/> NA	(insert comment)
Clinical Overview: Is there an adequate and/or accurate clinical overview of the question?	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N <input type="checkbox"/> NA	(insert comment)
Policy Context: Is the policy context clear?	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N <input type="checkbox"/> NA	(insert comment)
IV. Methods			
Are the methods for identifying relevant studies clearly described?	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N <input type="checkbox"/> NA	(insert comment)
Are the criteria for the inclusion and exclusion of studies clearly described?	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N <input type="checkbox"/> NA	(insert comment)

Are the methods for grading studies and guidelines clearly described?	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> NA	(insert comment)	
Was something excluded that should have been included?	<input type="checkbox"/> Y	<input checked="" type="checkbox"/> N	<input type="checkbox"/> NA	(insert comment)	
Was something included that should have been excluded?	<input type="checkbox"/> Y	<input checked="" type="checkbox"/> N	<input type="checkbox"/> NA	(insert comment)	
V. Results					
Is the presentation of the results well-structured and organized?	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> NA	(insert comment)	
Has the evidence been accurately synthesized?	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> NA	(insert comment)	
Does the report adequately address effectiveness?	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> NA	(insert comment)	
Does the report adequately address harms?	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> NA	(insert comment)	
VI. Guidelines					
Are the guidelines adequately summarized?	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> NA	(insert comment)	
Is the quality of the guidelines clearly described?	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> NA	(insert comment)	
Is there an adequate comparison of the guidelines to the evidence in the report?	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> NA	(insert comment)	
VII. General Conclusions					
Do they summarize the effectiveness of the intervention?	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> NA	(insert comment)	
Do they balance the effectiveness with the potential harms?	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> NA	(insert comment)	
Do they address the strengths and limitations of the evidence adequately?	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> NA	(insert comment)	
VIII. Figures, tables and appendices					
Are the figures clear and easy to read?	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> NA	(insert comment)	
Are the tables clear and easy to read?	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> NA	(insert comment)	
Are the appendices clear and easy to read?	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> NA	(insert comment)	
X. OVERALL REPORT RATING [1 = Very Poor, 2=Poor, 3=Average, 4=Good, 5 = Excellent]					
Overall quality of the report:	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input checked="" type="checkbox"/> 5
Clarity of the report:	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input checked="" type="checkbox"/> 5
Presentation (design/formatting):	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input checked="" type="checkbox"/> 5
Methods:	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input checked="" type="checkbox"/> 4	<input type="checkbox"/> 5
Grading of the body of evidence:	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input checked="" type="checkbox"/> 4	<input type="checkbox"/> 5
Scientific accuracy:	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input checked="" type="checkbox"/> 5
Clinical relevance:	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input checked="" type="checkbox"/> 5

XI. Other Comments

For brain tumors in certain locations, IMRT is superior than CRT in sparing normal tissues (optic nerves, chiasm, brainstem etc). Unfortunately, there is a lack of studies that specifically look at tumors close to critical structures in the brain.

For spine metastases, there is a large body of literature reporting the efficacy and toxicity of spine radiosurgery or SBRT, both utilizing IMRT as the treatment planning technique. I don't see them included here.

Page 101 "Thymoma"

Page 103 For head and neck should be "fair" rather than "poor"