Evidence-Based Series 21-3-4-EDUCATION AND INFORMATION 2013

The Role of IMRT in Central Nervous System Cancer

N. Laperriere, R.B. Rumble, P. Warde, and members of the IMRT Indications Expert Panel

A Quality Initiative of the
Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)
and the Radiation Treatment Program, CCO

Report Date: October 29, 2010

An assessment conducted in November 2013 put Evidence-based Series (EBS) 21-3-4 in the Education and Information section. This means that the recommendations will no longer be maintained but may still be useful for academic or other information purposes. The PEBC has a formal and standardized process to ensure the currency of each document (PEBC Assessment & Review Protocol).

EBS 21-3-4 is comprised of 3 sections
and is available on the CCO website (http://www.cancercare.on.ca)
P Bancare Group page at:
http://www.cancercare.on.ca/toolbox/qualityguidelines/clin-program/radther/

Section 1: Guideline Recommendations
Section 2: Evidentiary Base
Section 3: EBS Development Methods and External Review Process

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Phone: 905-527-4322 ext.42822     Fax: 905-526-67756775     E-mail: ccopgi@mcmaster.ca

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Evidence-Based Series 21-3-4: Section 1

The Role of IMRT in Central Nervous System Cancer:
Guideline Recommendations

N. Laperriere, R.B. Rumble, P. Warde, and members of the IMRT Indications Expert Panel

A Quality Initiative of the
Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO), and the Radiation Treatment Program, CCO

Report Date: October 29, 2010

QUESTION
What is the role of intensity modulated radiation therapy (IMRT) compared with three-dimensional conformal radiation therapy (3DCRT) in the treatment of primary brain tumours? Outcomes of interest included clinical recurrence-free survival, disease-specific survival, and acute or late toxicities.

TARGET POPULATION
The target population is comprised of all patients with primary brain tumours for whom treatment with radiation is being considered.

INTENDED USERS
This guideline is targeted for radiation oncologists, physicists, dosimetrist, patients, and others involved in the treatment of primary brain tumours where treatment with IMRT is being considered. Administrators may find the report of value when considering the benefits of IMRT over 3DCRT for primary brain tumours.

BACKGROUND
IMRT is a newer method of delivering radiation to target structures that differs from traditional methods of radiation delivery. The basis of IMRT is the use of intensity-modulated beams that can provide two or more intensity levels for any single beam direction and any single source position (1). Through this mechanism, IMRT treatment plans are able to generate concave dose distributions and dose gradients with narrower margins than those allowed using traditional methods (1,2). This fact makes IMRT especially suitable for treating complex treatment volumes and avoiding close-proximity organs at risk (OAR) that would otherwise necessitate dose limitations (1). As a consequence of OAR sparing, IMRT theoretically may provide benefits in terms of increased tumour control through escalated dose and reduced normal tissue complications. It must be noted that as total radiation dose...
delivered via IMRT would be the same as the total radiation dose given via any other method of radiation therapy, no difference in disease-related outcomes would be expected. The main benefit expected with IMRT is a reduction in adverse event rates, especially those associated with radiation damage to nearby OARs.

Given the potential dosimetric advantages of IMRT and the commercial availability of IMRT-enabled treatment planning systems and linear accelerators, IMRT has been introduced clinically for a number of disease sites, including head and neck cancer and prostate cancer. This evidence-based series reviews the published experience with IMRT in the treatment of primary brain tumours to quantify the potential benefits of this new technology and make recommendations for radiation treatment programs considering adopting this technique.

**RECOMMENDATIONS AND KEY EVIDENCE**

<table>
<thead>
<tr>
<th>Qualifying Statement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Despite the lack of comparative evidence central nervous system (CNS) cancer, there remain compelling reasons why IMRT should be offered to patients as an alternative to the standard treatment of 3DCRT.</td>
</tr>
<tr>
<td>If disease-related outcomes are the primary outcomes of interest, then any treatment decision made should be informed by the knowledge that, due to IMRT's highly conformal fields, the maximum dose of radiation to the tumour could be increased, which may translate into increased local control.</td>
</tr>
<tr>
<td>If minimizing or avoiding treatment-related adverse effects is the primary outcome of interest, then any treatment decision made should be informed by the knowledge that IMRT has a demonstrated ability to create fields with very narrow margins, avoiding OARs and sparing patients significant short- and long-term morbidity. For this reason, IMRT may be considered a viable treatment option, as it is ethical to recommend a treatment with little known harm over one with greater expected harm prior to scientific proof of the difference in harm being established.</td>
</tr>
<tr>
<td>Based on these two important aspects of IMRT, the IMRT Indications Expert Panel recommends the use of IMRT for patients being treated for CNS cancers where radiation is the treatment modality of choice.</td>
</tr>
</tbody>
</table>

**FUTURE RESEARCH**

There are many ongoing uncontrolled studies of IMRT in children with brain tumours (3) where longitudinal outcomes in terms of cognition, hormonal effects, and carcinogenesis are being documented with the newer high-precision radiotherapy. No randomized studies of IMRT versus 3DCRT are ever expected to be undertaken.

**RELATED GUIDELINES**

Funding
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REFERENCES


The Role of IMRT in Central Nervous System Cancer: Evidentiary Base

N. Laperriere, R.B. Rumble, P. Warde, and members of the IMRT Indications Expert Panel

A Quality Initiative of the Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO) and the Radiation Treatment Program, CCO

Report Date: October 29, 2010

QUESTION
What is the role of IMRT compared with three-dimensional conformal radiation therapy (3DCRT) in the treatment of primary brain tumours?

BACKGROUND
IMRT is a newer method of delivering radiation to target structures that differs from traditional methods of radiation delivery. The basis of IMRT is the use of intensity-modulated beams that can provide two or more intensity levels for any single beam direction and any single source position (1). Through this mechanism, IMRT treatment plans are able to generate concave dose distributions and dose gradients with narrower margins than those allowed using traditional methods (1,2). This fact makes IMRT especially suitable for treating complex treatment volumes and avoiding close-proximity organs at risk (OAR) that would otherwise necessitate dose limitations (1). As a consequence of OAR sparing, IMRT theoretically may provide benefits in terms of increased tumour control through escalated dose and reduced normal tissue complications. It must be noted that as total radiation dose delivered via IMRT would be the same as the total radiation dose given via any other method of radiation therapy, no difference in disease-related outcomes would be expected. The main benefit expected with IMRT is a reduction in adverse event rates, especially those associated with radiation damage to nearby OARs.

Given the potential dosimetric advantages of IMRT and the commercial availability of IMRT-enabled treatment planning systems and linear accelerators, IMRT has been introduced clinically for a number of disease sites, including head and neck cancer and prostate cancer. This evidence-based series reviews the published experience with IMRT in the treatment of primary brain tumours to quantify the potential benefits of this new technology and make recommendations for radiation treatment programs considering adopting this technique.
INTRODUCTION

Radiotherapy plays a significant role in the management of most tumours arising within or adjacent to the brain (3). It is most often used following a primary surgical procedure to deal with macroscopic/microscopic residual disease, although more recently it is increasingly being used as the primary modality where a tumour is well characterized by imaging studies and the tumour is either unresectable or the surgical risks are prohibitively high.

The best possible approach to treating primary brain tumours with radiotherapy would satisfy the following imperatives: a full dose sufficient for cure to the gross tumour volume, an appropriate dose to the infiltrative margins of microscopic disease that is infiltrating normal brain, the avoidance of any adjacent non-involved critical structures, and a minimal dose to adjacent, uninvolved normal brain tissue. The critical structures within the brain that would be associated with catastrophic outcomes if injured by radiotherapy would be the optic nerves and chiasm (blindness) and the brain stem, which would be associated with a range of effects, from significant long tract signs (hemiparesis, hemianesthesia) and possible cranial nerve deficits (double vision, facial palsy, swallowing difficulties) to the patient requiring management on a ventilator in an intensive care unit or even possible death.

Central nervous system (CNS) tumours can originate anywhere throughout the brain, but also can include tumours arising in adjacent tissues (meninges, bones of the skull base) whose main mode of invasion or morbidity is by way of pressure on brain tissue. These latter tumours include meningiomas and skull base chordomas and chondrosarcomas. While the majority of meningiomas are grade 1 and are successfully dealt with by complete surgical resections, there are grade 1 meningiomas that occur in the skull base and adjacent to the superior or inferior sagittal sinuses that are not resectable, and grade II and III tumours that invade brain. In these cases, radiotherapy has a major tumour-controlling role, or at least can improve the length of survival. In addition, pituitary adenomas (although most often benign) can be difficult to cure surgically and often require radiotherapy to achieve long-term control.

Historically, most radiotherapy for the management of brain tumours was based on two-dimensional (2D) treatment planning, where, in addition to the tumour volume, large areas of normal uninvolved brain were included in the high-dose volume. This has been well documented to be associated with unacceptable late effects, including significant blunting of higher cognitive functions (occasionally as severe as an encephalopathy/dementia); cerebrovascular events, resulting in significant loss of neurologic function; endocrine disturbances; radiation necrosis; vision loss; hearing loss; and increased risk of radiation-induced tumours (4). Moreover, these complications have been demonstrated to be related to radiation fraction sizes, total radiation dose, and increased volumes of normal brain (5-12).

Improvements in imaging arose with the introduction of computerized tomography (CT) scans in the late 1970s, and magnetic resonance imaging (MRI) in the late 1980s, and these new imaging modalities were gradually introduced into the treatment planning process, resulting in the gradual move from 2D treatment planning to 3DCRT planning. This change became widespread in the late 1990s when commercial versions of CT simulators for radiation treatment planning became commonplace. These improvements were then complimented by the ability to incorporate MRIs into the treatment planning process in the early 2000s, when good image-registration software was integrated into the radiation treatment planning software (3).

The advent of 3DCRT resulted in a significant reduction in the volume of normal brain structures outside the tumour volume receiving high-dose radiotherapy. Based on the known effects of normal tissue volume and dose established in earlier studies, it is inevitable that there will then be a significant reduction in late radiation toxicity (5,6,9).
IMRT represents a further evolution in the ability to shape the high-dose radiation volume to the complex three-dimensional shape of the tumour and microscopically involved adjacent normal tissues. IMRT results in the sparing of more normal tissue than is possible with 3DCRT and is associated with a significant reduction in the radiation dose received by critical structures adjacent to tumour volumes (13-16). As a result, an increased dose can be delivered to the tumour, which can possibly be associated with an improvement in local control and survival, as has been seen with the use of particle therapy in the management of skull base chordomas and chondrosarcomas (13,17,18).

The incidence of brain tumours in children is fortunately far less common than in adults, but that population is at increased risk for late radiation complications related to the relative immaturity of their developing brain and their possible increased sensitivity to the effects of ionizing radiotherapy (19). The long-term tumour control and survival rates seen in children with brain tumours are higher than those seen in adults, meaning that their increased sensitivity to the late effects of ionizing radiotherapy make them a particularly important subgroup of patients that would benefit more from the use of IMRT.

Because of the known and well-established relationship between the incidence and severity of late effects from ionizing radiotherapy and the volume of normal brain and critical structures receiving significant radiation doses, it is doubtful there will ever be randomized studies analyzing the use of 3DCRT versus the use of IMRT in the management of brain tumours. In addition, the fact that there often is a delay of two to 25 years before one is able to evaluate the full extent of late effects from radiation therapy for brain tumours further complicates the ability to fully document the differences between 3DCRT and IMRT.

METHODS
The evidence-based series (EBS) guidelines developed by Cancer Care Ontario’s Program in Evidence-Based Care (PEBC) use the methods of the Practice Guidelines Development Cycle (20). For this project, the core methodology used to develop the evidentiary base was the systematic review. Evidence was selected and reviewed by one member of the IMRT Indications Expert Panel (See Appendix 1 for Panel membership) and one methodologist.

The systematic review is a convenient and up-to-date source of the best available evidence on the role of IMRT in CNS cancers. The systematic review and companion recommendations are intended to promote evidence-based practice in Ontario, Canada. The PEBC and Radiation Treatment Program (RTP) are supported by the Ontario Ministry of Health and Long-Term Care through Cancer Care Ontario. All work produced by the PEBC is editorially independent from its funding source.

Literature Search Strategy
The MEDLINE and Embase databases were searched for evidence on CNS cancers and IMRT on March 20, 2009 (Appendix 2). In both databases, keywords for “central nervous system cancer” were combined with keywords for “intensity-modulated radiotherapy” and the following terms were excluded: “brachytherapy”, “proton therapy”, “biological markers”, “gene therapy”, “children”, “childhood cancer”, “pediatric cancer”, “quality assurance”, “treatment plan comparison”, “aperture optimization”, independent dose calculation”, “EPID dosimetry”, and “set up errors.” Results were limited to those published in English from the year 2000 to the current date in 2009.

A search for Clinical Practice Guidelines (CPG), Systematic Reviews (SR), and Health Technology Assessments (HTA) was also performed. A search of the National Guidelines Clearinghouse (located at: http://www.guideline.gov) was performed on March 9, 2009. Additionally, a search of the MEDLINE and Embase databases was performed on March 25,
2009 using keywords for IMRT in combination with terms for all disease sites and limited to review articles published after 2000. Finally, the Scottish Collegiate Guidelines Network (SIGN) (located at: http://www.sign.ac.uk), the National Institute for Health & Clinical Evidence (NICE) (located at: http://www.nice.org.uk), and the Agency for Healthcare Research & Quality (AHRQ) (located at: http://www.ahrq.gov) were searched on March 25, 2009 using keywords for “IMRT”, and “radiation” in combination with disease-site-specific terms.

Study Selection Criteria

Inclusion Criteria

All of the following publication types must include comparative data on IMRT versus 3DCRT in the treatment of primary brain tumours and must also report on at least one of the outcomes of interest, including clinical recurrence-free survival, disease-specific survival, and acute or late toxicities:

- CPGs, SRs, HTAs
- Randomized phase II or phase III trials
- Dose escalation studies, toxicity reports, quality of life (QoL) reports, case-series, and prospective studies

They must also meet the following criteria:

- Report on 50 or more patients
- Be published in English
- Be published in the year 2000 to current date

Exclusion Criteria

- Published in a language other than English
- Do not provide comparative data
- Report on fewer than 50 patients
- Published prior to 2000

Synthesizing the Evidence

No statistical analyses were planned in this systematic review; however, this would be considered if data allow.

RESULTS

Literature Search Results

The MEDLINED and Embase searches returned 16 and 57 potential articles, respectively. After removing ineligible articles based on title and abstract review, none of the remainder was ordered for full-text review. No evidence was found in this systematic review, and the recommendations drafted were based on expert opinion.

ONGOING TRIALS

The U.S. National Institutes of Health online directory of clinical trials (located at http://www.clinicaltrial.gov) was searched on September 29, 2009 for listings of relevant trials. The details of the single relevant trial appear in Table 1.

Table 1. Ongoing trials.

<table>
<thead>
<tr>
<th>Observation or Radiation Therapy in Treating Patients With Grade I, Grade II, or Grade III Meningioma</th>
<th>Phase: Phase II</th>
<th>Type: Interventional</th>
</tr>
</thead>
</table>
DISCUSSION

The expectation is that there will never be a randomized study of IMRT versus 3DCRT in the management of primary brain tumours. IMRT represents an evolution of conformal radiotherapy with the ability to better spare OARs and safely increase the dose to tumours, potentially improving local control.

The major concern with radiotherapy to brain tumours relates to the late effects of a decline in cognition, hormonal loss, and possible radiation-related carcinogenesis. These effects usually take many years to decades to be fully manifested, so the study of these effects is challenging. The population of patients most likely to develop these late effects are children managed with radiotherapy for brain tumours. For this reason, IMRT may be considered a viable treatment option, as it is ethical to recommend a treatment with little known harm over one with greater expected harm prior to scientific proof of the difference in harm being established.

Recent studies have documented that cognitive loss is significantly related to the volume of normal brain receiving doses in the range of 30-60 Gy, with less cognitive loss being associated with lesser amounts of brain receiving doses in that range (21). Recent dosimetric studies comparing 3DCRT with IMRT for various primary tumours in various locations of the brain all had the same result: better and more conformal treatment volume coverage with significant sparing of OAR (chiasm, brain stem, normal brain) (14,22). Accordingly, when one considers that there are data demonstrating better cognitive outcomes when less normal brain tissue receives between 30-60 Gy, and IMRT dosimetric comparisons show that IMRT better spares normal brain tissue from these intermediate doses, it is reasonable to expect that cognition will be less affected with the use of IMRT techniques. But it will take from years to decades to demonstrate this outcome.

The use of IMRT has also now allowed the use of photon radiotherapy to compete with protons in terms of being able to treat skull base and/or intracranial tumours (chordomas, chondrosarcomas) with dose-escalated IMRT photons to 70-76 Gy and have results for tumour control and complication rates equivalent to those seen with proton therapy (23).

CONCLUSIONS

Good quality uncontrolled studies document significant improvement in the dose sparing of OAR and the ability to dose escalate with IMRT to doses previously not possible prior to its use in the radiotherapy management of brain tumours, with associated improved outcomes in terms of tumour control and less complications. Accordingly, the use of IMRT is recommended in the management of patients with primary tumours of the brain.

CONFLICT OF INTEREST

No conflicts of interest were declared.

ACKNOWLEDGEMENTS

The IMRT Indications Expert Panel would like to thank Dr. Normand Laperriere and Mr. R. Bryan Rumble for taking the lead in drafting this systematic review.
Funding
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REFERENCES


**Steering Panel**

<table>
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<th>Position and Affiliation</th>
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</tbody>
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**Expert Panel**

<table>
<thead>
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<th>Position and Affiliation</th>
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<tbody>
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<td>Radiation Treatment Program, Cancer Care Ontario</td>
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<td>Radiation Therapy Representative, Peel Regional Cancer Program</td>
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<td>Ms. Lisa Favell</td>
<td>Capital Project Representative, Cancer Care Ontario</td>
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<td>Radiation Therapy Representative, Grand River Regional Cancer Centre</td>
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<td>Ms. Esther Green</td>
<td>Chief Nursing Officer and Director of Health Human Resource Planning, Cancer Care Ontario</td>
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<td>Dr. Konrad Leszczynski</td>
<td>Physics Representative, Northeastern Ontario Regional Cancer Centre</td>
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<td>Dr. Michael Sharpe</td>
<td>Physics Representative, Princess Margaret Hospital</td>
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**Working Group**

<table>
<thead>
<tr>
<th>Name</th>
<th>Position and Affiliation</th>
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<tbody>
<tr>
<td>Dr. Normand Laperriere</td>
<td>Radiation Oncologist, Princess Margaret Hospital</td>
</tr>
<tr>
<td></td>
<td>Associate Professor, Department of Radiation Oncology, University of Toronto</td>
</tr>
</tbody>
</table>
Appendix 2. Literature search strategies.

Ovid MEDLINE(R) <1996 to March Week 2 2009> Search Strategy:

1. exp Central Nervous System Neoplasms/ or central nervous system cancer.mp. (47224)
2. imrt.mp. or exp Radiotherapy, Intensity-Modulated/ (2549)
3. brachytherapy.mp. or exp Brachytherapy/ (8490)
4. exp Protons/ or proton therapy.mp. (11375)
5. biological marker.mp. or exp Biological Markers/ (308241)
6. gene therapy.mp. or exp Gene Therapy/ (32926)
7. child.mp. or exp Child/ (515814)
8. pediatric cancer.mp. (657)
9. childhood cancer.mp. (1926)
10. exp Quality Assurance, Health Care/ or quality assurance.mp. (136493)
11. treatment plan comparison.mp. (5)
12. aperture optimization.mp. (27)
13. independent dose calculation.mp. (13)
14. EPID dosimetry.mp. (13)
15. set up errors.mp. (85)
16. planning.mp. (80527)
17. 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 (1046550)
18. 1 and 2 (146)
19. 1 and 17 (14190)
20. 18 not 19 (20)
21. limit 20 to (english language and humans and yr="2000 - 2009") (16)
22. from 21 keep 1-16 (16)

EMBASE <1996 to 2009 Week 11>

1. exp Central Nervous System Tumor/ or central nervous system cancer.mp. (63905)
2. imrt.mp. or exp Intensity Modulated Radiation Therapy/ (3312)
3. brachytherapy.mp. or exp Brachytherapy/ (10760)
4. proton therapy.mp. or exp Proton Therapy/ (680)
5. biological marker.mp. or exp Biological Marker/ (31873)
6. gene therapy.mp. or exp Gene Therapy/ (34502)
7. child/ or child.mp. or children.mp. (457760)
8. exp Childhood Cancer/ or pediatric cancer.mp. (9951)
9. quality assurance.mp. or exp Quality Control/ (110835)
10. treatment plan comparison.mp. (5)
11. aperture optimization.mp. (28)
12. independent dose calculation.mp. (12)
13. EPID dosimetry.mp. (14)
14. set up errors.mp. (88)
15. exp Planning/ or planning.mp. (125942)
16. 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 (743645)
17. 1 and 2 (264)
18. 1 and 16 (14891)
19. 17 not 18 (69)
20. limit 19 to (human and english language and yr="2000 - 2009") (57)
21. from 20 keep 1-57 (57)
Evidence-Based Series 21-3-4: Section 3

The Role of IMRT in Central Nervous System Cancer: EBS Development Methods and External Review Process

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THE PROGRAM IN EVIDENCE-BASED CARE

The Program in Evidence-based Care (PEBC) is an initiative of the Ontario provincial cancer system, Cancer Care Ontario (CCO) (1). The PEBC mandate is to improve the lives of Ontarians affected by cancer, through the development, dissemination, implementation, and evaluation of evidence-based products designed to facilitate clinical, planning, and policy decisions about cancer care.

The PEBC supports a network of disease-specific panels, termed Disease Site Groups (DSGs) as well as other groups or panels called together for a specific topic, all mandated to develop the PEBC products. These panels are comprised of clinicians, other health care providers and decision makers, methodologists, and community representatives from across the province.

The PEBC is well known for producing evidence-based guidelines, known as Evidence-based Series (EBS) reports, using the methods of the Practice Guidelines Development Cycle (1,2). The EBS report consists of an evidentiary base (typically a systematic review), an interpretation of and consensus agreement on that evidence by our Groups or Panels, the resulting recommendations, and an external review by Ontario clinicians and other stakeholders in the province for whom the topic is relevant. The PEBC has a formal standardized process to ensure the currency of each document, through the periodic review and evaluation of the scientific literature and, where appropriate, the integration of that literature with the original guideline information.
The Evidence-Based Series
Each EBS is comprised of three sections:

- **Section 1: Guideline Recommendations.** Contains the clinical recommendations derived from a systematic review of the clinical and scientific literature and its interpretation by the Group or Panel involved and a formalized external review in Ontario by review participants.
- **Section 2: Evidentiary Base.** Presents the comprehensive evidentiary/systematic review of the clinical and scientific research on the topic and the conclusions reached by the Group or Panel.
- **Section 3: EBS Development Methods and External Review Process.** Summarizes the evidence-based series development process and the results of the formal external review of the draft version of Section 1: Guideline Recommendations and Section 2: Evidentiary Base.

**DEVELOPMENT OF THIS EVIDENCE-BASED SERIES**
**Development and Internal Review**
This EBS was developed by the IMRT Indications Expert Panel (Appendix 1) of the CCO PEBC and RTP. The series is a convenient and up-to-date source of the best available evidence on the role of IMRT in central nervous system cancer, developed through review of the evidentiary base, evidence synthesis, and input from external review participants in Ontario.

**IMRT Expert Panel Conference**
On December 3, 2009, the IMRT - CNS guideline was presented to members of the IMRT Expert Panel (N=25) and feedback was obtained on the quality and comprehensiveness of the evidence and the recommendations. Results are as follows:

| Are you responsible for the care of patients for whom this draft report is relevant? |
|-----------------------------------|----------------|-------------|---|---|---|
| Response | Yes | No | Unsure | TOTALS | Missing |
| N | 7 | 17 | 0 | 24 | 1 |
| % | 29.2 | 70.8 | 0 | 100 | 4 |

| Rate the overall quality of the guideline report. |
|-----------------------------------|----------------|-------------|---|---|---|---|
| Response | 1. Lowest | 2. | 3. | 4. | 5. Highest | TOTALS | Missing |
| N | 0 | 0 | 8 | 13 | 3 | 24 | 1 |
| % | 0 | 0 | 33.3 | 54.2 | 12.5 | 100 | 4 |

| I would make use of this guideline in my professional decisions. |
|-----------------------------------|----------------|-------------|---|---|---|
| Response | 1.Strongly disagree | 2. | 3. | 4. | 5.Strongly agree | TOTALS | Missing |
| N | 0 | 1 | 6 | 13 | 3 | 23 | 2 |
| % | 0 | 4.3 | 26.1 | 56.5 | 13 | 99.9 | 8 |

| I would recommend this guideline for use in practice. |
|-----------------------------------|----------------|-------------|---|---|---|
| Response | 1.Strongly disagree | 2. | 3. | 4. | 5.Strongly agree | TOTALS | Missing |
| N | 0 | 0 | 7 | 14 | 3 | 24 | 1 |
| % | 0 | 0 | 29.2 | 58.3 | 12.5 | 100 | 4 |
RECOMMENDATION
1. No evidence meeting the inclusion criteria was obtained in this systematic review; therefore, it is not possible to propose evidence-based recommendations.

<table>
<thead>
<tr>
<th>Response</th>
<th>1. Strongly disagree</th>
<th>2.</th>
<th>3.</th>
<th>4.</th>
<th>5. Strongly agree</th>
<th>TOTALS</th>
<th>Missing</th>
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<td>4</td>
<td>15</td>
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<td>17.4</td>
<td>65.2</td>
<td>13</td>
<td>99.9</td>
<td>8</td>
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Do you agree with this Recommendation?

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<th>Unsure</th>
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<td>14.3</td>
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What are the barriers to the implementation of this guideline report?
- Lack of equipment and other resources including HR.

Comments Recommendation One:
- There are compelling reasons to protect normal tissues from high dose radiotherapy in the disease area. The consequences that are known are so significant that protection should be accomplished at all costs and needs to be achieved using IMRT.

Other Comments:
- IMRT considered for patients where dose objectives (target, OAR) cannot be met with 3DCRT.

Report Approval Panel
Following the presentation of this EBS draft report for Expert Panel review, the draft was submitted to the PEBC Report Approval Panel (RAP) for review on March 8, 2010. The RAP is comprised of two members, including an oncologist, with expertise in clinical and methodological issues.

The key issue raised by the Report Approval Panel was:
- Add a description of the outcomes of interest to the clinical research question in both Sections One and Two.

In response to the RAP review feedback, the following was added to the guideline:
- A description of the outcomes of interest was added to the clinical research question in both Sections One and Two.

No RAP re-submission was requested, and the guideline was approved on April 5, 2010.

External Review: Professional Consultation
On September 20, 2010, the RAP-approved document was distributed to clinicians practicing within the Province of Ontario as part of a Profession Consultation review process. A total of 126 clinicians were invited to participate, and a total of 7 submitted responses (5.5% response rate) were obtained. Results are as follows:

1. Rate the overall quality of the guideline report

<table>
<thead>
<tr>
<th>Response</th>
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</table>

2. I would make use of this guideline in my professional decisions

<table>
<thead>
<tr>
<th>Response</th>
<th>1. Strongly disagree</th>
<th>2.</th>
<th>3.</th>
<th>4.</th>
<th>5. Strongly agree</th>
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<td>58</td>
<td>14</td>
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</tr>
</tbody>
</table>
3. I would recommend this guideline for use in practice

<table>
<thead>
<tr>
<th>Response</th>
<th>1. Strongly disagree</th>
<th>2.</th>
<th>3.</th>
<th>4.</th>
<th>5. Strongly agree</th>
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<tr>
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<td>29</td>
<td>42</td>
<td>14</td>
<td>100</td>
<td>0</td>
</tr>
</tbody>
</table>

4. What are the barriers or enablers to the implementation of this guideline report?
   Barriers:
   - Access to limited equipment and human resources.

   Enablers:
   - None were identified.

5. Additional comments.
   - There is still a lack of randomized data but the document states that this is not a possibility given the difficulties with this type of study in this population so we infer the benefits based on theory.
   - The methodology for this review, while following the methods used for all other disease sites, should have been modified for this topic to be more inclusive considering the lack of comparative evidence.

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REFERENCES
