Evidence-Based Series 21-3-6-EDUCATION AND INFORMATION 2013

The Role of IMRT in Soft-Tissue Sarcomas

C. Catton, 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) 21-3-6 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 21-3-6 is comprised of 3 sections and is available on the CCO website (http://www.cancercare.on.ca)

PEBC Cancer Screening 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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The Role of IMRT in Soft-Tissue Sarcomas: Guideline Recommendations

C. Catton, R.B. Rumble, P. Warde, and members of the IMRT Indications Expert Panel

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QUESTIONS
1. When external-beam radiotherapy is selected as the primary modality of choice, what is the role of IMRT (compared with three-dimensional conformal radiotherapy [3DCRT] or two-dimensional radiotherapy [2DRT]) in treating soft-tissue sarcomas (STS)?
2. When external beam is given as adjuvant post-operative treatment, what is the role of IMRT (compared with 3DCRT or 2DRT) in treating soft-tissue sarcoma?
3. When external beam is given as adjuvant pre-operative treatment, what is the role of IMRT (compared with 3DCRT or 2DRT) in treating soft-tissue sarcoma?

TARGET POPULATION
The target population is comprised of all adult patients with STS for whom treatment with radiation is being considered.

INTENDED USERS
This guideline is targeted for radiation oncologists, physicists, dosimetrists, patients, and others involved in the treatment of sarcomas where treatment with IMRT is being considered. Administrators may find the report of value when considering the benefits of IMRT over 3DCRT or 2DRT for sarcoma.

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 may theoretically provide benefits in terms of reduced normal tissue complications in the setting of combined modality therapy. It may also increase the proportion of patients who present with disease in challenging anatomic locations who can be safely treated with combined modality therapy, or primary radiotherapy. 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 sarcomas to quantify the potential benefits of this new technology and to make recommendations for radiation treatment programs considering adopting this technique.

RECOMMENDATIONS AND KEY EVIDENCE

<table>
<thead>
<tr>
<th>Insufficient evidence was obtained in this systematic review; therefore, it is not possible to propose recommendations on the use of IMRT for STS informed by evidence.</th>
</tr>
</thead>
</table>

**Qualifying Statement**

Despite the lack of evidence in this disease site, there remain compelling reasons why IMRT should be offered to patients as an alternative to the standard treatment for STS. In other settings, IMRT has a demonstrated ability to conform to the planning target volume (PTV), avoiding organs at risk and sparing patients significant short- and long-term morbidity. In non-extremity sites, IMRT may also provide enhanced therapeutic flexibility in dealing with challenging anatomical presentations and increase the proportion of patients who can be safely treated with combined modality therapy.

FUTURE RESEARCH

Due to the rarity of the disease, it is unlikely that the role of IMRT for treatment of STS will be investigated in phase III trials. Prospective phase II trials investigating the toxicity and risk of local relapse with adjunctive IMRT given with or without image-guided RT (I-G RT) are presently accruing internationally for patients with extremity tumours. These trials will provide valuable new data on the long-term risks and benefits of high-precision radiotherapy in the management of extremity STS and help to inform decisions on its use in clinical practice.

RELATED GUIDELINES

Funding
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Phone: 905-527-4322, ext. 42822   Fax: 905-526-6775   E-mail: ccopgi@mcmaster.ca
REFERENCES


Evidence-Based Series 21-3-6: Section 2

The Role of IMRT in Soft-Tissue Sarcomas: Evidentiary Base

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QUESTIONS
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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 near-by 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...
sarcomas to quantify the potential benefits of this new technology and to make recommendations for radiation treatment programs considering adopting this technique.

INTRODUCTION
Radiotherapy (RT) is an essential adjunct to surgery for adult soft-tissue sarcomas (STS) for optimizing both local control (3-7) and functional outcome (8,9). Soft-tissue sarcomas are rare, and limited level one data exist concerning local management with RT. These trials identified local control or treatment-related complications (7) as their primary endpoints rather than functional outcome. The local control rates for combined therapy are excellent in these trials, and any improvements in local management will be directed at reducing treatment-related complications such as delayed wound healing, bone fracture, fibrosis and edema.

O’Sullivan et al (4) considered functional outcome as a secondary endpoint for their randomized trial of pre-operative versus post-operative RT for extremity sarcomas. These patients were all treated with 2D planning, and radiation treatment volume and radiation dose were identified as independent factors predicting for grade 2 or higher fibrosis, edema and joint stiffness. The presence of these complications was associated with inferior functional outcomes (4,8) in those tested. Griffin et al (10) demonstrated that the improved conformality of pre-operative IMRT is technically capable of reducing the dose to subcutaneous tissues and bone in extremity sarcomas compared to 3DCRT treatment plans on the same patients.

The implication of these findings is that treatment-related complications and functional outcome will be positively influenced by limiting the size of the RT planning target volume (PTV) as much as possible and by applying RT treatment techniques that are best able to make the radiation treatment volume conform to the PTV. The former may be achieved with pre-operative RT and use of image-guided RT (I-G RT) techniques, and the latter with IMRT.

Level two and three evidence supports the use of adjunctive RT in non-extremity anatomical sites such as the retroperitoneum and head and neck (3,11,12). The specific anatomical constraints to attaining adequate surgical margins in these locations result in less effective local control than for extremity tumours. The radiotherapeutic considerations in these sites, therefore, include improvement in local control and maintaining a good functional outcome. However, the effective use of adjunctive RT faces anatomical constraints similar to that seen with surgery in these locations.

Despite the extreme rarity of STS presentations in these sites, there is substantial diversity in the therapeutic challenges presented, and treatment must frequently be individualized. Treatment policies and RT techniques that optimize the PTV and make the radiation dose conform to the PTV will enhance flexibility in therapeutic decision-making and increase the proportion that can be offered with safe and effective combined therapy. The former may be achieved with pre-operative RT and use of I-G RT techniques, and the latter with 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 (13). 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 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 sarcoma. The body of evidence in this review is primarily
comprised of published reports of comparative studies between IMRT and 3DCRT or 2DRT. That evidence forms the basis of the recommendations developed by the IMRT Indications Expert Panel and will be published when completed. 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 sarcomas and IMRT on June 3 and 4, 2009. In both databases, the keyword “sarcoma” was 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, 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 or 2DRT in sarcoma and report on at least one of the following outcomes of interest: freedom from local failure, clinical recurrence-free survival, disease-specific survival, wound healing complications, functional outcomes (for sarcomas in the extremities only), improved conformality, and acute or late adverse affects:
  - CPGs, SRs, HTAs
  - Randomized phase II or phase III trials
  - Dose escalation studies, toxicity reports, quality-of-life (QoL) reports, case series, and retrospective studies

They must also meet the following criteria:

- Report on 10 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
- Reports on fewer than 10 patients
- Published prior to the year 2000
Synthesizing the Evidence
No statistical analyses were planned in this systematic review; however, analysis would be considered if data allow.

RESULTS

Literature Search Results
The MEDLINE and EMBASE search returned 27 and 38 potential articles, respectively. After removing ineligible articles based on title and abstract review, one was ordered for full-text review. This single paper (14) comprises the body of evidence in this systematic review.

Study Design
The single paper (14) obtained was a retrospective cohort study. Table 1 details the years on study, the disease sites, the total number of patients, and funding source where reported.

Table 1. Study design of included evidence.

<table>
<thead>
<tr>
<th>Author, year published</th>
<th>Years on study</th>
<th>Disease site</th>
<th>Total included [N]</th>
<th>Sponsorship</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retrospective cohort study</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Koshy et al (14)</td>
<td>2000-2002</td>
<td>Retroperitoneal sarcomas (n=10) Inguinal sarcoma (n=1)</td>
<td>11</td>
<td>NR</td>
</tr>
</tbody>
</table>

Note: N, total number; n, sample size; NR, not reported.

Table 2 describes the study details, including the comparison that was made, the radiation dose administered in each group, the number of patients in each group, the disease stages included in the study population, the overall median follow-up, and what outcomes were reported.

Table 2. Details of the included studies.

<table>
<thead>
<tr>
<th>Author, year published</th>
<th>Comparison</th>
<th>Dose</th>
<th>Total n</th>
<th>Disease stage</th>
<th>Median follow-up in months</th>
<th>Outcomes reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retrospective cohort study</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Koshy et al (14)</td>
<td>Surgery+IMRT Surgery+3DCRT</td>
<td>50.4Gy/1.8f 50.4Gy/1.8f</td>
<td>8</td>
<td>T1b-T2b</td>
<td>14.5</td>
<td>TRO, AE</td>
</tr>
</tbody>
</table>

Note: IMRT, intensity-modulated radiotherapy; 3DCRT, three-dimensional radiotherapy; Gy, gray; f, fraction; n, sample size; T, tumour stage; TRO, treatment-related outcomes; AE, adverse effects.

Study Quality
The single paper obtained (14) was assessed for quality according to criteria such as balance between the treatment groups, identification of prognostic factors, and reporting of differences between baseline prognostic factors. Other variances in study design that could affect the reliability of the study findings were also reported.

In this retrospective cohort study, the groups were unbalanced (IMRT: 8 versus [vs.] 3DCRT: 3). Prognostic factors were identified and reported on, but differences between the groups were not reported on. No adjustments were reported.
Outcomes: Treatment-Related

The single paper (14) obtained did not report any significant differences between IMRT compared with 3DCRT for freedom from local failure, clinical recurrence-free survival, or disease-specific survival. As the setting was not sarcomas in an extremity, functional outcomes were not reported. Treatment-related outcomes appear in Table 3.

<table>
<thead>
<tr>
<th>Author, year published</th>
<th>Comparison</th>
<th>Freedom from local failure %</th>
<th>Clinical recurrence-free survival %</th>
<th>Disease-specific survival %</th>
<th>Functional outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retrospective cohort study</td>
<td>IMRT</td>
<td>100</td>
<td>87.5</td>
<td>100</td>
<td>N/A</td>
</tr>
<tr>
<td>Koshy et al (14)</td>
<td>3DCRT</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

Note: IMRT, intensity-modulated radiotherapy; 3DCRT, three-dimensional radiotherapy; N/A, not applicable.

Outcomes: Conformality and Sparing of Organs at Risk

In this study (14), IMRT was associated with improved coverage of the PTV along with a reduction in dose to the OAR (liver, small bowel, kidneys). This improvement was statistically significant (p<0.05) for the dose to small bowel (from 36Gy with 3DCRT to 27Gy with IMRT) and for the combined maximum (p=0.011) and minimum (p=0.055) dose to the PTV. The volume of small bowel receiving >30Gy was significantly decreased from 63.5±25.2% to 43.1±20.6% with IMRT compared with 3DCRT (p=0.043). No significant differences were detected for the dosages to the liver or kidneys.

Outcomes: Adverse Effects

The single paper (14) obtained reported on both acute and late adverse effects. No acute effects were observed, and the single late effect was reported in a patient from the 3DCRT group who experienced grade 3 liver toxicity six months post-RT and was hospitalized for ascites management. At 58 weeks of follow-up, this patient had the ascites and hepatitis resolved and was recurrence free. Acute and late adverse effects appear in Table 4.

<table>
<thead>
<tr>
<th>Author, year published</th>
<th>Comparison</th>
<th>Skin</th>
<th>Upper GI</th>
<th>Lower GI</th>
<th>Liver</th>
<th>GU</th>
<th>Wound</th>
</tr>
</thead>
<tbody>
<tr>
<td>Koshy et al (14)</td>
<td>IMRT</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3DCRT</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>33.3%*</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Note: IMRT, intensity-modulated radiotherapy; 3DCRT, three-dimensional radiotherapy; GI, gastrointestinal; GU, genitourinary.

* Late effect

ONGOING TRIALS

The U.S. National Institutes of Health online directory of clinical trials (located at http://www.clinicaltrial.gov) was searched on September 30, 2009, for listings of relevant trials. The details of the single relevant trial appear in Table 5.
Table 5. Ongoing trials.

<table>
<thead>
<tr>
<th>Image-Guided Radiation Therapy in Treating Patients With Primary Soft-Tissue Sarcoma of the Shoulder, Arm, Hip or Leg</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Phase:</strong> Phase II</td>
</tr>
<tr>
<td><strong>Type:</strong> Interventional</td>
</tr>
<tr>
<td><strong>Status:</strong> Open, recruiting</td>
</tr>
<tr>
<td><strong>Age:</strong> 18+</td>
</tr>
<tr>
<td><strong>Sponsor:</strong> Radiation Therapy Oncology Group, National Cancer Institute</td>
</tr>
<tr>
<td><strong>Protocol IDs:</strong> CDR0000582196, RTOG-0630</td>
</tr>
<tr>
<td><strong>Description:</strong> This phase II trial is meant to study the side effects and how well image-guided radiation therapy works in treating patients with primary soft-tissue sarcoma of the shoulder, arm, hip or leg.</td>
</tr>
</tbody>
</table>

**DISCUSSION**

The evidence to support the use of IMRT for the treatment of STS is indirect and derived from evidence showing that radiation-related toxicity in STS is related to total dose and to field size. IMRT is one readily available way to favourably influence the high-dose radiation treatment volume without compromising tumour coverage. The application of IMRT to the treatment of STS should reduce the risk of developing treatment-related toxicities for extremity STS and may also increase the proportion of those with non-extremity STS who become eligible for combined therapy. This assumption was supported in the one report (14) comparing toxicity of IMRT to 3D-CRT planning for retroperitoneal sarcoma, identified in the systematic review.

**CONCLUSIONS**

Insufficient evidence was obtained in this systematic review; therefore, it is not possible to propose evidence-based recommendations on the use of IMRT for STS. Despite the lack of evidence for this disease site, compelling reasons remain why IMRT should be offered to patients as an alternative to the standard treatment of STSs.

**CONFLICT OF INTEREST**

None declared.

**ACKNOWLEDGEMENTS**

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

**Funding**

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REFERENCES


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<th>Role and Affiliation</th>
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**Expert Panel**

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<th>Name</th>
<th>Role and Affiliation</th>
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<tbody>
<tr>
<td>Dr. Anthony Whitton</td>
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<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>Chief Nursing Officer and Director of Health Human Resource Planning, Cancer Care Ontario</td>
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<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>
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<tr>
<th>Name</th>
<th>Role and Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr. Charles Catton</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.

Database: Ovid MEDLINE(R) <1996 to May Week 5 2009>
Search Strategy:

1 sarcoma.mp. or exp Sarcoma/ (40715)
2 exp Radiotherapy, Intensity-Modulated/ or imrt.mp. (2675)
3 brachytherapy.mp. or exp Brachytherapy/ (8640)
4 exp Protons/ or proton therapy.mp. (11593)
5 biological marker.mp. or exp Biological Markers/ (315504)
6 gene therapy.mp. or exp Gene Therapy/ (33469)
7 children.mp. or exp Child/ (541171)
8 pediatric cancer.mp. (675)
9 childhood cancer.mp. (1985)
10 exp Quality Assurance, Health Care/ or quality assurance.mp. (139310)
11 treatment plan comparison.mp. (5)
12 aperture optimization.mp. (29)
13 independent dose calculation.mp. (13)
14 EPID dosimetry.mp. (14)
15 set up errors.mp. (87)
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 (1017703)
17 1 and 2 (50)
18 1 and 16 (10380)
19 17 not 18 (31)
20 limit 19 to (English language and humans and yr="2000 - 2009") (27)
21 from 20 keep 1-27 (27)
22 from 21 keep 1-27 (27)

Database: EMBASE <1996 to 2009 Week 22>
Search Strategy:

1 exp Sarcoma/ or sarcoma.mp. (43176)
2 imrt.mp. or exp Intensity Modulated Radiation Therapy/ (3457)
3 brachytherapy.mp. or exp Brachytherapy/ (10986)
4 proton therapy.mp. or exp Proton Therapy/ (713)
5 biological marker.mp. or exp Biological Marker/ (32990)
6 gene therapy.mp. or exp Gene Therapy/ (35072)
7 Child/ or child.mp. or children.mp. (466670)
8 exp Childhood Cancer/ or pediatric cancer.mp. (10072)
9 quality assurance.mp. or exp Quality Control/ (112351)
10 treatment plan comparison.mp. (0)
11 aperture optimization.mp. (31)
12 independent dose calculation.mp. (12)
13 EPID dosimetry.mp. (15)
14 set up errors.mp. (89)
15 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 (650234)
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19 limit 18 to (human and English language and yr="2000 - 2009") (38)
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The Role of IMRT in Soft-Tissue Sarcomas:
EBS Development Methods and External Review Process

C. Catton, 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

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 and other health care providers, as well as 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 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 soft-tissue sarcomas guideline was presented to members of the IMRT Expert Panel (n=23) and feedback was obtained on the quality and comprehensiveness of the evidence and the recommendations. The results are as follows:

Are you responsible for the care of patients for whom this draft report is relevant?

<table>
<thead>
<tr>
<th>Response</th>
<th>Yes</th>
<th>No</th>
<th>Unsure</th>
<th>TOTALS</th>
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<tbody>
<tr>
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<td>16</td>
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<td>69.6</td>
<td>0</td>
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</table>

Rate the overall quality of the guideline report.

<table>
<thead>
<tr>
<th>Response</th>
<th>1. Lowest</th>
<th>2.</th>
<th>3.</th>
<th>4.</th>
<th>5. Highest</th>
<th>TOTALS</th>
<th>Missing</th>
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<td>n</td>
<td>0</td>
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<td>43.5</td>
<td>47.8</td>
<td>8.7</td>
<td>23</td>
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<td>%</td>
<td>0</td>
<td>0</td>
<td>43.5</td>
<td>47.8</td>
<td>8.7</td>
<td>100</td>
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</tr>
</tbody>
</table>

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>%</td>
<td>0</td>
<td>14.3</td>
<td>28.6</td>
<td>42.9</td>
<td>14.3</td>
<td>100</td>
<td>8.7</td>
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</tbody>
</table>

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>
<th>TOTALS</th>
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<td>4.3</td>
<td>4.3</td>
<td>39.1</td>
<td>43.5</td>
<td>8.7</td>
<td>100</td>
<td>0</td>
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</tbody>
</table>

RECOMMENDATIONS
1. Insufficient evidence was obtained in this systematic review; therefore, it is not possible to propose recommendations on the use of IMRT for STS informed by evidence.

<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>6</td>
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<td>5</td>
<td>23</td>
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<tr>
<td>%</td>
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<td>0</td>
<td>26.1</td>
<td>52.2</td>
<td>21.7</td>
<td>100</td>
<td>0</td>
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</table>

Do you agree with this Recommendation?

<table>
<thead>
<tr>
<th>Response</th>
<th>Yes</th>
<th>No</th>
<th>Unsure</th>
<th>TOTALS</th>
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<td>73.9</td>
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<td>13</td>
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</table>
Additionally, the following feedback was also obtained (summarized to only include main points that were addressed in subsequent drafts):

<table>
<thead>
<tr>
<th>What are the barriers to the implementation of this guideline report?</th>
</tr>
</thead>
<tbody>
<tr>
<td>• There is limited relevance for guidelines that have little supporting evidence.</td>
</tr>
</tbody>
</table>

**Comments Recommendation One:**

- We need more statements about the ability of IMRT to avoid OARs (esp. bone and liver).
- STS needs to be defined following the first instance of soft-tissue sarcoma.

**Other Comments:**

- None that were responded to.

**Report Approval Panel**

Following presentation of this EBS draft report for Expert Panel review, the report was submitted to the PEBC Report Approval Panel (RAP) for review on May 25, 2010. The RAP is comprised of two members, including an oncologist, with expertise in clinical and methodological issues.

No key issues were raised by the RAP and the guideline was approved on June 25, 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 8 submitted responses (6% response rate). Results are as follows:

| 1. Rate the overall quality of the guideline report | Response | 1. Lowest | 2. | 3. | 4. | 5. Highest | TOTALS | Missing |
|---------------------------------------------------|-----------|-----------|----------------|----------------|----------------|----------|----------|
| N                                                  | 0         | 0         | 3              | 4              | 1              | 8        | 0        |
| %                                                  | 0         | 0         | 38             | 50             | 12             | 100      | 0        |

| 2. 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         | 0                   | 4              | 2              | 2              | 8        | 0        |
| %                                                                 | 0         | 0                   | 50             | 25             | 25             | 100      | 0        |

| 3. I would recommend this guideline for use in practice | Response | 1.Strongly disagree | 2. | 3. | 4. | 5.Strongly agree | TOTALS | Missing |
|-------------------------------------------------------|-----------|---------------------|----------------|----------------|----------------|----------|----------|
| N                                                     | 0         | 0                   | 4              | 2              | 2              | 8        | 0        |
| %                                                     | 0         | 0                   | 50             | 25             | 25             | 100      | 0        |

4. What are the barriers or enablers to the implementation of this guideline report?

**Barriers:**

- Resources required to use IMRT compared with 3DCRT, especially in the neoadjuvant setting.
- Lack of comparative evidence.

**Enablers:**

None submitted.

5. Additional comments.

None submitted.
**Funding**
The PEBC is a provincial initiative of Cancer Care Ontario 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.

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For information about the PEBC and the most current version of all reports, please visit the CCO Web site at http://www.cancercare.on.ca/ or contact the PEBC office at:
Phone: 905-527-4322, ext. 42822   Fax: 905-526-6775   E-mail: ccopgi@mcmaster.ca
REFERENCES
