Practical Radiation Oncology (2014) 4, 349-355

practical radiation oncology
pro
www.practicalradonc.org

Special Article

Choosing Wisely: The American Society for Radiation Oncology's Top 5 list

Carol Hahn MD [a,*,1], Brian Kavanagh MD, MPH [b,1], Ajay Bhatnagar MD, MBA [c], Geraldine Jacobson MD, MBA [d], Stephen Lutz MD [e], Caroline Patton MA [f], Louis Potters MD [g], Michael Steinberg MD [h]

[a]*Department of Radiation Oncology, Duke University Medical Center, Durham, North Carolina*
[b]*Department of Radiation Oncology, University of Colorado, Denver, Colorado*
[c]*Cancer Treatment Services Arizona, Affiliate of 21st Century Oncology, Casa Grande, Arizona*
[d]*Department of Radiation Oncology, West Virginia University, Morgantown, West Virginia*
[e]*Blanchard Valley Regional Cancer Center, Findlay, Ohio*
[f]*American Society for Radiation Oncology, Fairfax, Virginia*
[g]*Department of Radiation Medicine, North Shore-LIJ Health System, New Hyde Park, New York*
[h]*Department of Radiation Oncology, David Geffen School of Medicine, University of California Health System, Los Angeles, California*

Received 31 May 2014; accepted 10 June 2014

Abstract

Purpose: To highlight 5 interventions that patients should question, as part of the Choosing Wisely campaign. This initiative, led by the American Board of Internal Medicine Foundation, fosters conversations between physicians and patients about treatments and tests that may be overused, unnecessary, or potentially harmful.

Methods and materials: Potential items were initially compiled using an online survey. They were then evaluated and refined by a work group representing the American Society for Radiation Oncology (ASTRO) Clinical Affairs and Quality, Health Policy, and Government Relations Councils. Literature reviews were carried out to support the recommendation and narrative, as well as to provide references for each item. A final list of 5 items was then selected by the ASTRO Board of Directors.

Results: ASTRO's 5 recommendations for the Choosing Wisely campaign are the following: (1) Don't initiate whole-breast radiation therapy as a part of breast conservation therapy in women age ≥ 50 with early-stage invasive breast cancer without considering shorter treatment schedules; (2) don't initiate management of low-risk prostate cancer without discussing active surveillance; (3) don't routinely use extended fractionation schemes (>10 fractions) for palliation of bone metastases; (4) don't routinely recommend proton beam therapy for prostate cancer outside of a prospective clinical trial or registry;

Note–Earn CME credit by taking a brief online assessment at http://www.astro.org/JournalCME.

Conflicts of interest: Brian Kavanagh, MD, MPH is a section editor for UpToDate and receives royalties for this activity. Ajay Bhatnagar, MD, MBA is a consultant for Varian and has received honoraria and travel expenses. He is also a consultant for DermEbx and has received research funding from Icad. Dr Bhatnagar owns stock options in Radion and stock in Cancer Treatment Services International. Stephen Lutz, MD owns stock in Tosk and Oculus.

* Corresponding author. Department of Radiation Oncology, Duke University Medical Center, PO Box 3085, Durham, NC 27710.
E-mail address: carol.hahn@duke.edu (C. Hahn).

[1] Co-first authors.

http://dx.doi.org/10.1016/j.prro.2014.06.003

and (5) don't routinely use intensity modulated radiation therapy to deliver whole-breast radiation therapy as part of breast conservation therapy.

Conclusions: The ASTRO list for the Choosing Wisely campaign highlights radiation oncology interventions that should be discussed between physicians and patients before treatment is initiated. These 5 items provide opportunities to offer higher quality and less costly care.

Introduction

Are cancer patients in the United States receiving appropriate, timely, and cost effective care of the highest possible quality? This question is part of the larger national discussion of how best to reform health care delivery. Mortality for many cancers has decreased in the US over the last several decades, but costs have risen steeply.[1] While it is widely recognized that fee-for-service reimbursement models incentivize high volume care, an ideal system would reward high value care. In the interim, physicians should consider it an essential part of their social responsibility to consider and utilize means in which efficiencies might be achieved without compromising the highest quality of patient care. The Choosing Wisely campaign offers physicians an opportunity to identify diagnostic tests or therapeutic interventions that should at least prompt thoughtful discussions about treatment options and resource utilization with their patients.

In 2011, the American Board of Internal Medicine (ABIM) Foundation initiated the Choosing Wisely campaign to facilitate informed and collaborative discussions between physicians and patients about the necessity, efficacy, risks, and benefits of common tests and procedures. The Choosing Wisely initiative looks to physicians and the professional societies representing them to foster efforts to promote quality of care by identifying a list of 5 evidence-based recommendations that draw attention to potentially unnecessary tests or therapies. The items included are not interventions that should never be used, but rather ones physicians and patients should discuss to determine if the intervention is necessary or useful in a given clinical situation.

The inspiration for Choosing Wisely came from an article in 2010 by Howard Brody, which challenged specialty societies to create top 5 lists of tests or procedures that are often ordered by physicians but "have been shown by the currently available evidence not to provide any meaningful benefit to at least some major categories of patients for whom they are commonly ordered."[2(p284)] Nine specialty societies participated in the first round of the Choosing Wisely campaign in April 2012 and 18 additional lists were presented in February 2013. The American Society for Radiation Oncology (ASTRO) released its top 5 list (Table 1) at its annual meeting in September 2013 as 1 of more than 30 societies participating in late 2013 and early 2014 during the campaign's third round.

ASTRO participated in Choosing Wisely, demonstrating its commitment to responsible, high-quality patient care. The selection process identified cost-effective treatment strategies supported by evidence but possibly underutilized; a costly treatment implemented in a setting where less expensive options might be equally efficacious, and an indolent condition where treatment might be safely postponed or avoided altogether in many cases. The working group was cognizant of the multiple factors involved in treatment selection, regional variations in practice, and individual patient variability. The final selections were made on the basis of patient-centered, evidence-based, cost-effective care.

As the leading organization in radiation oncology with more than 10,000 members, ASTRO's highest priority continues to be providing its members with tools and professional guidance to ensure patients receive the safest, most effective treatments. One of the 5 goals in the ASTRO strategic plan is to shape the framework for delivery of safe, high-quality, high-value health care to all patients by the radiation oncology team. By committing to Choosing Wisely, ASTRO reinforced its dedication to improving patient care through education, clinical practice, and the advancement of the science underlying the specialty of radiation oncology.

Methods and materials

In September 2012, the ASTRO Board of Directors approved development of a top 5 list for the Choosing Wisely campaign. The ABIM Foundation allowed societies to use a self-defined methodology to develop their lists, as long as the process was fully and transparently documented, as well as publicly accessible. The recommendations were required to be evidence-based, address treatments that fall within the responsibility of the specialty, and are commonly used or involve substantial cost.

Potential items for the list were first solicited via an online survey of the ASTRO Clinical Affairs and Quality Committee; Health Policy Council and Committee; Government Relations Committee; Guidelines, Best Practices, Measures, Regulatory, and Health Services Research Subcommittees; state captains; and disease site resource panels in lung, prostate, breast, and head and neck cancer.

A workgroup with representation from the Clinical Affairs and Quality, Health Policy, and Government Relations Councils was then identified. The members selected their top 8 items from 34 proposed in the initial survey. The results were tabulated and a short list of 13 was created from the

highest scoring items. Three conference calls were held to further refine the list and finalize the wording of the items based on input from the ASTRO board. A literature review was conducted for each topic by ASTRO staff and each workgroup member took the lead on writing text and selecting references for 1 or more items. The final items submitted to the ABIM Foundation were chosen and endorsed by the ASTRO board.

These items are provided solely for informational purposes and are not intended as a substitute for consultation with a medical professional. Patients with any specific questions about items on this list or their individual situation

Table 1 American Society for Radiation Oncology (ASTRO) Top 5 list

1. Don't initiate whole-breast radiation therapy as a part of breast conservation therapy in women age ≥50 with early-stage invasive breast cancer without considering shorter treatment schedules.	• Whole-breast radiation therapy decreases local recurrence and improves survival of women with invasive breast cancer treated with breast conservation therapy. Most studies have utilized "conventionally fractionated" schedules that deliver therapy over 5-6 weeks, often followed by 1-2 weeks of boost therapy. • Recent studies, however, have demonstrated equivalent tumor control and cosmetic outcome in specific patient populations with shorter courses of therapy (approximately 4 weeks). Patients and their physicians should review these options to determine the most appropriate course of therapy.[5,6,12]
2. Don't initiate management of low-risk prostate cancer without discussing active surveillance.	• Patients with prostate cancer have a number of reasonable management options. These include surgery and radiation, as well as conservative monitoring without therapy in appropriate patients. • Shared decision making between the patient and the physician can lead to better alignment of patient goals with treatment and more efficient care delivery. • ASTRO has published patient-directed written decision aids concerning prostate cancer and numerous other types of cancer. These types of instruments can give patients confidence about their choices, improving compliance with therapy.[15,34-38]
3. Don't routinely use extended fractionation schemes (>10 fractions) for palliation of bone metastases.	• Studies suggest equivalent pain relief following 30 Gy in 10 fractions, 20 Gy in 5 fractions, or a single 8 Gy fraction. • A single treatment is more convenient but may be associated with a slightly higher rate of retreatment to the same site. • Strong consideration should be given to a single 8 Gy fraction for patients with a limited prognosis or with transportation difficulties.[16,39,40]
4. Don't routinely recommend proton beam therapy for prostate cancer outside of a prospective clinical trial or registry.	• There is no clear evidence that proton beam therapy for prostate cancer offers any clinical advantage over other forms of definitive radiation therapy. Clinical trials are necessary to establish a possible advantage of this expensive therapy.[24-26,41]
5. Don't routinely use intensity modulated radiation therapy (IMRT) to deliver whole-breast radiation therapy as part of breast conservation therapy.	• Clinical trials have suggested lower rates of skin toxicity after using modern 3D conformal techniques relative to older methods of 2D planning. • In these trials, the term "IMRT" has generally been applied to describe methods that are more accurately defined as field-in-field 3D conformal radiation therapy. • While IMRT may be of benefit in select cases where the anatomy is unusual, its routine use has not been demonstrated to provide significant clinical advantage.[28,31-33]

2D, 2-dimensional; 3D, 3-dimensional.

Note: These items are provided solely for informational purposes and are not intended as a substitute for consultation with a medical professional. Patients with any specific questions about the items on this list or their individual situation should consult their physician. ASTRO is not responsible for any injury or damage arising out of or related to any use of these items or to any errors or omissions.

are encouraged to consult their radiation oncologist. ASTRO is not responsible for any injury or damage arising out of or related to any use of these items or to any errors or omissions. The items are assessed annually for current validity and appropriateness and may be revised or updated in the future.

Results

Don't initiate whole-breast radiation therapy as a part of breast conservation therapy in women age ≥50 with early-stage invasive breast cancer without considering shorter treatment schedules

Breast cancer is the most commonly diagnosed malignancy in females in the US, with over 200,000 women diagnosed per year. A high proportion present with early-stage disease, and are candidates for breast-conserving therapy. Postoperative whole-breast radiation therapy (WBRT) is the standard of care in the US for these patients and numerous well-documented randomized studies have demonstrated significant decrease risk of local failure, as well as improved survival when the whole breast is treated with external beam radiation therapy after lumpectomy.[3-7]

Conventionally fractionated regimens traditionally deliver WBRT over approximately 5 weeks in 25-28 fractions to doses of 45-50 Gy, which is sufficient to sterilize microscopic disease. Additional "boost" radiation therapy, wherein additional dose is delivered to a limited area of the breast, has demonstrated further improvements in local control for many patients.[8] Typically delivered in 5 to 10 fractions to 10-16 Gy, it thus extends the treatment course by approximately 1 to 2 weeks for an overall treatment time of 6 to 7 weeks.

While conventionally fractionated regimens have demonstrated, in multiple randomized prospective trials with over 20 years of follow-up, effectiveness in optimizing disease control and preserving cosmesis, multiple studies have evaluated alternate techniques and dose scheduling to improve efficiency and cost of care delivery. Well-documented randomized studies in Canada and the UK have demonstrated that in selected low-risk patients, shorter treatment regimens (3 to 4 weeks) may be safe and effective with comparable medical outcome and cosmesis. These shorter regimens are less costly in monetary and social terms, and should be considered when medically appropriate. Given the development of significant evidence supporting equivalent effectiveness and safety of shorter schedules, ASTRO convened an expert panel in 2009 and developed an Evidence Based Clinical Practice Guideline on treatment schedules for breast cancer patients.[9-12]

As this is a highly prevalent area in radiation oncology practice and shorter treatment schedules can significantly benefit patients in terms of convenience, acceptance of therapy, and cost, this was selected by the ASTRO board as a salient item for the Choosing Wisely effort. It is the hope of the workgroup that reminding patients and physicians to consider shorter treatment courses will facilitate improved quality of care for women with breast cancer. Physicians ought to discuss with patients that hypofractionation is appropriate for selected women. Providers should also explain the shorter follow-up data for patient cohorts receiving this treatment; a decade, compared with several decades for conventional WBRT. Finally, physicians should address the patient's concerns about the treatment, factors that are important to the patient, and include the patient in the decision process.

Don't initiate management of low-risk prostate cancer without discussing active surveillance

The advent of prostate-specific antigen screening for prostate cancer, the most frequently diagnosed solid malignant tumor in men, has led to a considerable increase in the discovery of organ confined tumors. It has also decreased the relative incidence of high-risk aggressive tumors, with a stage shift to lower volume, lower grade tumors. Data from prostate-specific antigen screening trials remains controversial, which suggests the impact on overall mortality by early intervention remains questionable. In addition, because established autopsy data suggest that many of the low-risk tumors diagnosed under current screening regimens tend to resemble those found in men who died of other causes, there is limited need to offer immediate treatment for men with low-risk disease.[13]

Many patients with low-risk prostate cancer are unlikely to have disease progression and have a low risk of death if the disease is left untreated.[14] Findings from the Klotz et al study[15] of 452 men suggest that the 10-year survival rate of low grade prostate cancer on an active surveillance protocol was 97.2%. Treatment decision-making, even in men with low-risk prostate cancer, is difficult and associated with anxiety and concern. Active surveillance, a method of delayed curative treatment, offers men with low-risk disease the ability to avoid treatment-related harm until there is documentation of certain indications for intervention. The ability to maintain quality of life associated with excellent cancer-specific survival makes active surveillance a viable option and should be discussed by treating physicians. Raising the topic of active surveillance can be difficult for physicians. ASTRO has identified and highlighted this approach not only because it is supported by existing evidence, but also to support physicians in beginning these discussions.

Don't routinely use extended fractionation schemes (>10 fractions) for palliation of bone metastases

This item was chosen to acknowledge the large body of literature confirming success with shorter treatment

courses, as well as improved value of care by decreasing the time and effort required for the near end-of-life oncology patient. External beam radiation therapy palliates painful bone metastases in a manner that is effective and associated with minimal toxicity.[16] Multiple prospective, randomized trials have shown equivalent pain relief among a variety of fractionation schemes including 30 Gy in 10 fractions, 24 Gy in 6 fractions, 20 Gy in 5 fractions, and 8 Gy in a single fraction.[17] Despite this, 1 practice pattern survey showed over 100 fractionation schemes in use for the treatment of bone metastases worldwide.[18] While retreatment rates are about 20% following single fraction treatment versus 8% after multifraction treatment, a second single fraction can succeed in providing palliation.[19] Additionally, single fraction therapy is safe for patients with spine bone metastases and exhibits the same pain relief durability as multifraction courses.[20,21]

Patients with painful bone metastases are commonly fatigued. The tenets of humane and compassionate care argue for interventions that require the least possible time and resources. As such, prolonged treatment courses which do not add to symptom relief or survival are contrary to meaningful palliative care.

Patients sometimes believe that "more is better," so at first they may show reluctance to short-course radiation therapy. With a careful explanation of the data and the potential benefits of this approach, most will choose hypofractionated courses. Given the importance and impact of this topic, the limitation of bone metastases treatment to between 1 and 10 fractions has become the first quality measure submitted by ASTRO and endorsed by the National Quality Forum.

Don't routinely recommend proton beam therapy for prostate cancer outside of a prospective clinical trial or registry

Proton therapy is a form of radiation therapy involving acceleration of a positively charged particle toward a tumor. This therapy has both potential advantages and technical challenges. The potential advantage lies in the pattern of radiation dose deposition; after an entry path during which a portion of the dose is deposited, there is a rapid surge in dose deposition called the Bragg peak. By modulating the energy of the proton beam, this peak may be spread out to treat the tumor with a full therapeutic dose while causing minimal exit dose. The technical challenges arise from the difficulty in determining precisely the tissue beam absorption characteristics based on pretreatment computed tomography or magnetic resonance imaging scans.[22] As a result, a small correction must be applied.[23]

While proton therapy has been used successfully for many years for a wide variety of malignancies, several recent reports have raised the question of whether the range uncertainty or other hurdles might abrogate the potential dosimetric advantages for prostate cancer. One analysis of Surveillance, Epidemiology, and End Results–Medicare (SEER-Medicare)-linked data for 2000-2009 found patients treated with proton therapy, intensity modulated radiation therapy (IMRT), or non-IMRT conformal external beam radiation therapy all experienced excellent clinical outcomes and low rates of serious toxicity. A propensity score–matched comparison revealed IMRT patients had a lower rate of gastrointestinal morbidity than proton therapy patients and there were no significant differences in rates of other morbidities or additional therapies.[24]

A more narrowly confined SEER-Medicare analysis of men treated in 2008-2009 revealed slightly lower genitourinary toxicity at 6 months after proton therapy but no difference at 12 months and no other differences in gastrointestinal or other toxicity regardless of modality. Notably, the latter analysis also tallied the Medicare reimbursements and illustrated the substantially higher expense associated with proton therapy compared with IMRT.[25]

Further, patients treated on the high dose (79.2 Gy equivalent using photons and protons) arm of the recent Proton Radiation Oncology Group 95-09 randomized trial were matched with patients treated with brachytherapy at Massachusetts General Hospital. Both groups enjoyed excellent clinical outcomes; the 8-year actuarial rates of biochemical failure were 7.7% and 16.1% for proton therapy and brachytherapy, respectively (P = .42). The results were similar after stratification for risk group (low and intermediate).[26]

The conundrum of proton therapy is just one of many situations where the process of evaluating expensive new radiation oncology technology is fraught with difficulty.[27] Physicians should communicate to patients that there are already successfully established means of treating prostate cancer with radiation therapy via external beam or brachytherapy that provide very high cure rates with low rates of serious toxicity. Proton therapy has appealing features that might ultimately be demonstrated to provide clinical advantage in this setting; however, at present it is also more expensive than other forms of radiation therapy. As a result, the field of radiation oncology should exercise discipline and study this indication carefully by means of structured clinical trials and properly executed registry enrollment.

Don't routinely use intensity modulated radiation therapy (IMRT) to deliver whole-breast radiation therapy as part of breast conservation therapy

Intensity modulated radiation therapy is a modern form of radiation therapy using sophisticated treatment planning techniques to achieve highly conformal dose distribution in order to spare surrounding critical structures and organs at risk, while delivering the prescribed dose to the target. IMRT comprises a range of techniques from simple to complex and can vary based on factors such as disease site.

The application of IMRT for whole-breast radiation therapy as part of breast conservation has been evaluated with the main goal of providing homogeneous dose distribution within the breast in attempts to reduce acute skin toxicity and preserve or improve cosmesis while also sparing organs at risk, mainly the heart for patients with left-sided breast cancer.

There are several randomized studies which have shown lower rates of skin toxicities with IMRT compared with conventional radiation therapy planning techniques.[28] A recently published study showed superior overall cosmesis with IMRT.[29] The controversy lies in the classification of these modern planning techniques for breast cancer, given the ambiguous definition of IMRT. The British study by Mukesh et al[29] has referred to the technique as simple IMRT but this technique is more accurately defined as "field in field" 3D conformal radiation therapy (3D-CRT) in the United States.[30] The 2 different descriptors, in this case, refer essentially to the same technique. True IMRT is significantly costlier than the field in a field 3D-CRT. Breast cancer patients can be misled by the perception that the use of IMRT is superior to the more conventional and less expensive 3D-CRT. This is not supported by the medical literature. Therefore, the patient should be educated that while IMRT can provide superior results or outcomes for a variety of cancer sites, IMRT for whole-breast radiation therapy is not typically advantageous compared with less costly modalities such as field in field 3D-CRT.

Intensity modulated radiation therapy (true IMRT techniques) may be useful for select patients, such as women with atypical anatomy, but the routine use of such IMRT to deliver whole-breast radiation therapy does not usually improve dose distributions or patient outcomes and therefore is not routinely recommended in the ASTRO Choosing Wisely list.[28,31-33]

Conclusions

The Choosing Wisely campaign was developed in order to promote use of high-value interventions, encourage discussions about treatments between patients and their physicians, and reduce overuse of tests and therapies that may be unnecessary and even potentially harmful. More than 50 specialty societies have now joined the initiative and have generated "top 5" lists of interventions within their specialty that are commonly used or represent substantial costs but which evidence suggests are often unneeded. ASTRO's participation in Choosing Wisely represents a continuation of the society's efforts to advance safe and high-quality radiation therapy. ASTRO will annually review this list to address changes in medical evidence and practice.

In our present health care environment with its emphasis on shared decision making, allowing patients to be partners in their health care decisions is imperative. The ASTRO list represents important considerations in delivery of cancer therapy for radiation oncologists to discuss with their patients. These items will serve as a tool for initiating evidence-based discussions with patients about their radiation treatment options so that they will be able to choose well and wisely.

References

1. Elkin EB, Bach PB. Cancer's next frontier: Addressing high and increasing costs. *JAMA.* 2010;303:1086-1087.
2. Brody H. Medicine's ethical responsibility for health care reform—the Top Five list. *N Engl J Med.* 2010;362:283-285.
3. Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med.* 2002;347:1233-1241.
4. Veronesi U, Luini A, Del Vecchio M, et al. Radiotherapy after breast-preserving surgery in women with localized cancer of the breast. *N Engl J Med.* 1993;328:1587-1591.
5. Clarke M, Collins R, Darby S, et al. Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: An overview of the randomised trials. *Lancet.* 2005;366:2087-2106.
6. Darby S, McGale P, Correa C, et al. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: Meta-analysis of individual patient data for 10,801 women in 17 randomised trials. *Lancet.* 2011;378:1707-1716.
7. Bartelink H, Horiot JC, Poortmans P, et al. Recurrence rates after treatment of breast cancer with standard radiotherapy with or without additional radiation. *N Engl J Med.* 2001;345:1378-1387.
8. Bartelink H, Horiot JC, Poortmans PM, et al. Impact of a higher radiation dose on local control and survival in breast-conserving therapy of early breast cancer: 10-year results of the randomized boost versus no boost EORTC 22881-10882 trial. *J Clin Oncol.* 2007;25:3259-3265.
9. Bentzen SM, Agrawal RK, Aird EG, et al. The UK Standardisation of Breast Radiotherapy (START) Trial A of radiotherapy hypofractionation for treatment of early breast cancer: A randomised trial. *Lancet Oncol.* 2008;9:331-341.
10. Bentzen SM, Agrawal RK, Aird EG, et al. The UK Standardisation of Breast Radiotherapy (START) Trial B of radiotherapy hypofractionation for treatment of early breast cancer: A randomised trial. *Lancet.* 2008;371:1098-1107.
11. Whelan TJ, Pignol JP, Levine MN, et al. Long-term results of hypofractionated radiation therapy for breast cancer. *N Engl J Med.* 2010;362:513-520.
12. Smith BD, Bentzen SM, Correa CR, et al. Fractionation for whole breast irradiation: An American Society for Radiation Oncology (ASTRO) evidence-based guideline. *Int J Radiat Oncol Biol Phys.* 2011;81:59-68.
13. Thompson IM, Klotz L. Active surveillance for prostate cancer. *JAMA.* 2010;304:2411-2412.
14. Bastian PJ, Carter BH, Bjartell A, et al. Insignificant prostate cancer and active surveillance: From definition to clinical implications. *Eur Urol.* 2009;55:1321-1330.
15. Klotz L, Zhang L, Lam A, Nam R, Mamedov A, Loblaw A. Clinical results of long-term follow-up of a large, active surveillance cohort with localized prostate cancer. *J Clin Oncol.* 2010;28:126-131.
16. Lutz S, Berk L, Chang E, et al. Palliative radiotherapy for bone metastases: An ASTRO evidence-based guideline. *Int J Radiat Oncol Biol Phys.* 2011;79:965-976.

17. Chow E, Harris K, Fan G, Tsao M, Sze WM. Palliative radiotherapy trials for bone metastases: A systematic review. *J Clin Oncol.* 2007;25:1423-1436.
18. Fairchild A, Barnes E, Ghosh S, et al. International patterns of practice in palliative radiotherapy for painful bone metastases: Evidence-based practice? *Int J Radiat Oncol Biol Phys.* 2009;75:1501-1510.
19. Chow E, van der Linden YM, Roos D, et al. Single versus multiple fractions of repeat radiation for painful bone metastases: A randomised, controlled, non-inferiority trial. *Lancet Oncol.* 2013;15:164-171.
20. Howell DD, James JL, Hartsell WF, et al. Single-fraction radiotherapy versus multifraction radiotherapy for palliation of painful vertebral bone metastases-equivalent efficacy, less toxicity, more convenient: A subset analysis of Radiation Therapy Oncology Group trial 97-14. *Cancer.* 2013;119:888-896.
21. van der Linden YM, Steenland E, van Houwelingen HC, et al. Patients with a favourable prognosis are equally palliated with single and multiple fraction radiotherapy: Results on survival in the Dutch Bone Metastasis Study. *Radiother Oncol.* 2006;78:245-253.
22. Andreo P. On the clinical spatial resolution achievable with protons and heavier charged particle radiotherapy beams. *Phys Med Biol.* 2009;54:N205-N215.
23. Paganetti H. Range uncertainties in proton therapy and the role of Monte Carlo simulations. *Phys Med Biol.* 2012;57:R99-R117.
24. Sheets NC, Goldin GH, Meyer AM, et al. Intensity-modulated radiation therapy, proton therapy, or conformal radiation therapy and morbidity and disease control in localized prostate cancer. *JAMA.* 2012;307:1611-1620.
25. Yu JB, Soulos PR, Herrin J, et al. Proton versus intensity-modulated radiotherapy for prostate cancer: Patterns of care and early toxicity. *J Natl Cancer Inst.* 2013;105:25-32.
26. Coen JJ, Zietman AL, Rossi CJ, et al. Comparison of high-dose proton radiotherapy and brachytherapy in localized prostate cancer: A case-matched analysis. *Int J Radiat Oncol Biol Phys.* 2012;82:e25-e31.
27. Steinberg ML, Konski A. Proton beam therapy and the convoluted pathway to incorporating emerging technology into routine medical care in the United States. *Cancer J.* 2009;15:333-338.
28. Barnett GC, Wilkinson JS, Moody AM, et al. Randomized controlled trial of forward-planned intensity modulated radiotherapy for early breast cancer: interim results at 2 years. *Int J Radiat Oncol Biol Phys.* 2012;82:715-723.
29. Mukesh MB, Barnett GC, Wilkinson JS, et al. Randomized controlled trial of intensity-modulated radiotherapy for early breast cancer: 5-year results confirm superior overall cosmesis. *J Clin Oncol.* 2013;31:4488-4495.
30. Kavanagh BD, Rabinovitch R, Mohideen N. Improved cosmesis in early breast cancer using conformal radiotherapy. *J Clin Oncol.* 2013;31:4483-4484.
31. Donovan E, Bleakley N, Denholm E, et al. Randomised trial of standard 2D radiotherapy (RT) versus intensity modulated radiotherapy (IMRT) in patients prescribed breast radiotherapy. *Radiother Oncol.* 2007;82:254-264.
32. Pignol JP, Olivotto I, Rakovitch E, et al. A multicenter randomized trial of breast intensity-modulated radiation therapy to reduce acute radiation dermatitis. *J Clin Oncol.* 2008;26:2085-2092.
33. Smith BD, Pan IW, Shih YC, et al. Adoption of intensity-modulated radiation therapy for breast cancer in the United States. *J Natl Cancer Inst.* 2011;103:798-809.