Original Article

Advancements in Radiation Techniques for Gastric Cancer

Matthew D. Callister, MD, and Leonard L. Gunderson, MD, *Scottsdale, Arizona*

Key Words

Gastric cancer, image guidance, IMRT

Abstract

All but the earliest cases of nonmetastatic gastric cancer represent a therapeutic challenge given the high propensity of these patients to develop locoregional and distant relapse. Neoadjuvant or adjuvant strategies that include chemoradiotherapy or chemotherapy have been associated with significant toxicity, but also improvement in patient survival. Technologic advances in the planning and delivery of radiotherapy (RT) have enabled significant progress in the accuracy and conformality of radiation treatment. Four-dimensional CT and image-guided RT improve the accuracy of radiation treatment. Three-dimensional RT and intensity-modulated RT allow increased conformality of radiation dose distribution, sparing of normal organs, and providing opportunity for dose escalation. Initial clinical experience with these technologies shows favorable tolerance and outcomes. (*JNCCN* 2010;8:428–436)

Medscape: Continuing Medical Education Online

Accreditation Statement

This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of Medscape, LLC and *JNCCN – The Journal of the National Comprehensive Cancer Network*. Medscape, LLC is accredited by the ACCME to provide continuing medical education for physicians. Medscape, LLC designates this educational activity for a maximum of 0.50 *AMA PRA Category 1 Credits*™. Physicians should only claim credit commensurate with the extent of their participation in the activity. All other clinicians completing this activity will be issued a certificate of participation. To participate in this journal CME activity: (1) review the learning objectives and author disclosures; (2) study the education content; (3) take the post-test and/or complete the evaluation at **www.medscapecme.com/journal/jnccn**; (4) view/print certificate.

Learning Objectives

Upon completion of this activity, participants will be able to:

- Review locoregional recurrence rates for gastric cancer after surgery alone
- List the limitations of radiation therapy for gastric cancer
- Describe survival for gastric cancer associated with adjuvant chemotherapy added to radiation therapy
- List the factors that determine outcomes of the dosimetry approach to radiation therapy for gastric cancer
- Compare toxicities associated with different advanced radiation therapy techniques in patients with gastric cancer

From the Department of Radiation Oncology, Mayo Clinica Arizona, Scottsdale, Arizona.

Submitted November 11, 2009; accepted for publication December 18, 2009.

Correspondence: Matthew D. Callister, MD, Department of Radiation Oncology, Mayo Clinic Arizona, 13400 East Shea Boulevard, Scottsdale, AZ 85259. E-mail: callister.matthew@mayo.edu

EDITORS

Kerrin G. Robinson, MA, Medical/Scientific Editor, Journal of the National Comprehensive Cancer Network

Disclosure: Kerrin G. Robinson, MA, has disclosed no relevant financial relationships.

AUTHORS AND CREDENTIALS

Matthew D. Callister, MD, Department of Radiation Oncology, Mayo Clinic Arizona, Scottsdale

Disclosure: Matthew D. Callister, MD, has disclosed no relevant financial relationships.

Leonard L. Gunderson, MD, Department of Radiation Oncology, Mayo Clinic Arizona, Scottsdale

Disclosure: Leonard L. Gunderson, MD, has disclosed no relevant financial relationships.

CME Author

Désirée Lie, MD, MSEd, Clinical Professor, Family Medicine, University of California, Irvine, Orange, California; Director of Research and Patient Development, Family Medicine, University of California, Irvine, Medical Center, Rossmoor, California

Disclosure: Désirée Lie, MD, MSEd, has disclosed the following relevant financial relationship: Served as a nonproduct speaker for: "Topics in Health" for Merck Speaker Services.

Adjuvant Chemoradiation in Gastric Cancer

The rationale and benefit of radiotherapy (RT) for managing nonmetastatic gastric and gastroesophageal junction (GEJ) cancers have been well defined by analysis of locoregional failure patterns and clinical trials of its use. Clinically detected locoregional recurrence after surgical resection alone generally exceeds 25%.[1,2] However, as shown by the University of Minnesota reoperation series, local and regional recurrence rates after resection significantly exceed reported rates of clinical recurrence.[3] In this study, 107 patients who had undergone surgery with curative intent underwent reoperation to identify early locoregional relapse and attempt surgical resection and salvage. Local disease relapse was seen in 67% of patients, and 88% of these had a component of local or regional failure. In addition, 50% of peritoneal failures were localized to the original tumor bed rather than diffuse throughout the abdomen. High failure rates at the gastric resection bed (54%), anastomosis (26%), or regional nodes (42%) have been corroborated by autopsy series.[4,5]

Intergroup 116, a randomized phase III trial of adjuvant postoperative upper abdominal RT and 5-fluorouracil (5-FU)/leucovorin-based chemotherapy for gastric cancer, showed that patients who underwent locoregional cancer therapy had improved overall and disease-free survival (OS/DFS) versus those who underwent surgery alone (3-year OS, 50% vs. 41%; $P = .005$, and 3-year DFS, 48% vs. 31%; $P = .001$).[6] In addition, multiple randomized trials of preoperative chemoradiotherapy (CRT) for esophageal cancer that included tumors of the GEJ[7–9] and a trial exclusively of GEJ tumors[10] have shown improvement in patient survival with locoregional therapy.

Randomized trials of neoadjuvant[11] or perioperative chemotherapy[12] without RT have also shown survival improvement compared with resection alone. However, given the modest long-term survival among patients treated with either strategy, the respective gains associated with neoadjuvant chemotherapy or CRT strategies probably present an opportunity to integrate approaches (rather than compete) to improve outcomes, as shown by at least one randomized trial for GEJ cancer.[10]

Irradiation Field Design and Delivery

Over the past decade, significant technologic improvements have been made in RT plan design and delivery that are applicable to gastric cancer and show promise in improving patient tolerance and efficacy. Given the large RT target volumes required for treating gastric cancer, the proximity of vital organs in the upper abdomen and lower thorax, and tissue movement from respiration, RT for this disease is both technically and clinically challenging. Intergroup 116, conducted between 1991 and 1998, delivered RT generally using 2-dimensional treatment planning techniques, frequently with opposed anteroposterior/posteroanterior (AP-PA) fields, based on radiographic landmarks and boundaries.[6,13]

Although treatment was associated with improved survival, 41% and 32% of patients experienced grade 3 or 4 toxicity, respectively, with 17% unable to complete therapy because of poor tolerance. Minor or major errors in field design were discovered in 35% of patients during preirradiation quality assurance (QA) review. The upfront QA allowed most of the major or minor deviations to be corrected before the start of irradiation, and resulted in only a 6.5% final major deviation rate. Use of upfront QA may have been a key factor in achieving a positive survival advantage for adjuvant CRT in Intergroup 116. Improvements in treatment accuracy and conformality of RT dose present a significant opportunity in the field of radiation oncology to further advance patient outcome.

Improved Accuracy

The results of Intergroup 116 not only showed a benefit in adjuvant CRT for patients with resected gastric cancer but also highlighted that many radiation oncologists are unfamiliar with treating large upper abdominal fields. As a result, the investigators published multiple excellent reviews and articles educating the radiation oncology community on proper field design based on pathways of tumor spread and recurrence patterns in addition to limitations of normal organ exposure.[13–17] Over the past decade, a shift has occurred toward more sophisticated treatment techniques that use multiple and often non-coplanar beams, such as 3-dimensional conformal RT (3DRT) and intensity-modulated RT (IMRT), to treat most cancers, including gastric and GEJ cancer. Increased emphasis has also been placed on accurate 3-dimensional target delineation based on CT anatomy[18] rather than only 2-dimensional field design.

In addition to refinements in RT target definition based on CT-planning, technologic advances have allowed study of and solutions for variability in target and normal organ location during a treatment course (day-to-day interfraction variability) and actual treatment (intrafraction variability caused by respiration). Interfraction variability in stomach location can be substantial, particularly among patients treated with neoadjuvant CRT, because of daily variations in gastric filling.[19,20] Intrafraction changes in target shape (deformation) and location are asymmetric and mainly from respiratory motion. Movement, particularly in the cranial-caudad dimension, frequently exceeds 1 to 1.5 cm.[19–21]

To account for this inter- and intrafraction variability, some investigators have suggested treatment margins of up to 3 to 5 cm, depending on the dimension, to accommodate the wide range of variability seen among studied patients.[19] Although using larger treatment margins may ensure more consistent treatment of the intended volumes, they are associated with additional toxicity from excessive coverage in many patients. Image-guided RT (IGRT) allows overexpansion of treatment margins to be minimized through use of daily imaged-guidance (ultrasound, kilovoltage x-ray, or cone-beam CT) to optimize patient setup and therefore accuracy of treatment delivery. Initial experiences with IGRT for gastric cancer were with ultrasound (B-mode acquisition and targeting)[22,23] using upper abdominal vasculature and kidneys and liver for treatment localization. Although not widely adopted, this technique was found to be more accurate than the traditional use of skin marks and to have improved treatment accuracy in most patients.[23]

Daily kilovoltage radiograph matching has also been described[24] but only improves daily alignment based on boney anatomy rather than organ or nodal location. Perhaps the most significant advance in IGRT technology for the upper abdomen is cone-beam CT. At the time of treatment, a CT is generated by the actual treatment machine, thereby allowing corrections to be made in treatment delivery based on CT anatomy.[23]

In addition to daily IGRT to account for interfraction changes in target volumes, intrafraction changes from respiration can be individually accounted for by 4-dimensional CT (4DCT) at the time of simulation. A 4DCT images the patient in all phases of respiration rather than during a single breath-hold. The multiple image sets can then be reconstructed to view and measure tumor and organ motion from respiration (similar to fluoroscopy, but using CT). Target volumes are adjusted during treatment planning to account for their movement range during the complete respiratory cycle. Thus, this technique leads to an increase in the average tumor volume compared with static imaging.[21] However, given the high variability in target location and movement among individuals, this technology may decrease the irradiated area compared with treatment planning without 4DCT, when large margins are generally applied to account for the range in movement among groups of patients.

Finally, further reductions in the target volume can be accurately devised by using respiratory gating.[25] Rather than expanding target volume to account for full respiratory range, this technique accurately limits the irradiated volume to a more stationary phase of the respiratory cycle (usually end-expiration).

The clinical benefit of these technologic advances in treatment accuracy have not been and may not be prospectively compared with conventional 2-dimensional RT, as used in the Intergroup 116 trial. Regardless, the true locoregional control rate is arguably still suboptimal with traditional doses (45 Gy) and techniques. Adjuvant CRT is associated with 15% to 19% clinical local failure rates (often as first site of failure).[6,26,27] Although these rates are an improvement compared with 22% to 29% local recurrence among patients treated with surgery alone in the same series, both rates probably greatly underestimate the locoregional component of disease relapse for which RT impacts on patient outcome. Detection of locally recurrent disease is likely underappreciated in clinical trials and continues to be challenging in the postoperative patient, even with improved imaging. These advances in treatment accuracy are anticipated to continue to contribute to reductions in locoregional failure. In addition, patient tolerance of therapy may improve through reducing unnecessary exposure of normal organs to RT.

Improved Dosimetry

In addition to solutions to improve the accuracy of RT for gastric cancer, advances in the delivery of radiation have enabled significant improvements in the distribution of radiation dose (dosimetry) that conforms to the target volume while reducing exposure to adjacent normal tissues (lung, heart, liver, spinal cord, bowel, and kidneys). Two-dimensional treatment planning, usually with opposed AP-PA fields, can expose a significant volume of kidney to therapy. At least 2 series have described a gradual decline in renal function occurring at least 18 to 24 months after postoperative RT for gastric cancer.[28,29] Although the detected decline in renal function with limited follow-up was not clinically significant, long-term renal function among gastric cancer survivors has not been reported, and improvements in renal sparing may allow delivery of more aggressive chemotherapy regimens or nephrotoxic drugs (e.g., cisplatin). In addition, the total dose using 2-field techniques is limited to a fairly moderate adjuvant dose of only 45 Gy because of spinal cord and small bowel limitations.

Using 3DRT, a patient's abdominal and thoracic anatomy (target and normal structures) are reconstructed in 3 dimensions after CT imaging, allowing optimal field shape, orientation, and relative weighting to be devised virtually. Multiple studies comparing 3DRT techniques with standard 2-field treatment show significant reduction in kidney exposure to radiation (especially the left) and in spinal cord dose, and improved radiation coverage of the intended target volume (see Table 1).[30–33]

IMRT represents a further advance in the delivery of highly conformal RT to the upper abdomen. This technique builds on the advantages of 3DRT but incorporates differentially modulated subportions of each beam to further improve dose conformality and gradients. Initially implemented for small target volumes (e.g., prostate cancer), significant dosimetric gains can be made with this modality for the large and complex volumes associated with gastric cancer (see Figure 1). An initial potential disadvantage of IMRT in the upper abdomen was dose inhomogeneity leading to potential "hot spots," possibly in bowel.[34] This limitation is more easily resolved with newer IMRT planning systems.

Multiple comparative dosimetric studies have been conducted comparing IMRT with 2-field plans and 3DRT.[35–37] IMRT is consistently associated with a significant reduction in dose to the highest exposed kidney (usually the left).[25,34,38–41] In addition, reductions in dose to the liver,[34,37,42] heart,[36] lung,[43] and spinal cord[39,41] have been reported with IMRT compared with 2-field plans and 3DRT. Furthermore, a comparison study of 3DRT and IMRT treatment plans performed by blinded radiation oncologists showed preference for IMRT 89% of the time, with 90% concordance in choice among physicians.[36] Finally, there is further promise of improved radiation dose conformality with the most recent advances in IMRT delivery, such as volumetric modulated arc therapy or helical tomotherapy, in which dose is delivered with a modulated RT beam in a rotational arc. At least one study has shown improved target coverage and dose homogeneity with tomotherapy compared with IMRT with static beam configurations.[44]

With all of these treatment planning systems, especially IMRT, the dosimetric outcomes are highly dependent on not only the technology but also the planner's complex prioritization of the often-competing goals of dose homogeneity, conformality of dose to the target, and limits to normal organ exposure. Thus, the overall reported benefit of these advanced technologies in each study depends on not only technologic advancements but also preferences in how these tools are used to develop an optimal plan. Regardless, the literature shows a stepwise improvement in dose delivery and sparing of abdominal organs with the progressive implementation of these advanced treatment systems.

Though objective evidence of organ sparing has been consistently reported, the clinical significance of these improvements, especially for the kidneys, has been challenged, especially for patients with adequate functional reserve.[39] However, the potential benefit of these techniques in sparing normal organs is probably not yet fully appreciated, because Intergroup 116 and most dosimetric studies presented in this article involve patients treated with only 45 Gy of radiation. Although this dose is associated with improvement in patient OS, presumably through reduction in locoregional recurrence, 45 Gy is certainly at the lowest level used in the neoadjuvant or adjuvant treatment of almost all carcinomas and sarcomas.

The benefits of improved organ-sparing with 3DRT, and especially IMRT, may be more apparent with the use of more aggressive chemotherapy regimens. With more advanced radiation techniques, acceptable toxicity has been reported with the concurrent use of oxaliplatin and capecitabine,[41] cisplatin and 5-FU,[45] or adjuvant cisplatin, taxol, and 5-FU before CRT (with 5-FU).[29]

Table 1 Dosimetric Comparisons of Advanced Radiotherapy Techniques in the Postoperative Management of Gastric Cancer (45 Gy)

	n	Techniques	Kidney	Liver	Spinal Cord	Heart	Target
Weiland et al.[34] 2004	15		NTCP:*	NTCP:	Max dose:		
		2F	31	2.5	31		
		3F (3D)	69	0.5	47		
		IMRT	< 1	1.2	40		
		IMRT (tomotherapy)	< 1	1.3	31		
Leong et al.[31] 2005	15		D66:	Mean dose:	D33:		Coverage:
		2F	L 40, R 35	14	45		93%
		6F (3D)	L 18, R 18	22	17		99%
Ringash et al.[36] 2005	20		D80:	D50:	Max dose:	D50:	Mean dose:
		5F (3D)	L 12, R 8	28	46	16	45
		IMRT	L 12, R 3	17	37	13	46
Milano et al.[38†] 2006	6		Mean dose:	Mean dose:			Mean dose:
		2F	L 32, R 12	21			51
		3F (3D)	L 24, R 13	34			52
		IMRT	L 19, R 10	22			53
Wals et al.[32] 2006	26		NTCP:	NTCP:	NTCP:		
		2F	L 16, R 3	7.2	1.7		
		4F (3D)	L 2, R 0	0.5	0.5		
van der Geld et al.[25] 2007	5		Mean dose:				
		3F (3D)	L 20, R 33				
		IMRT	L 15, R17				
Soyfer et al.[33] 2007	19		Mean dose:*	Mean dose:	Max dose:		
		2F	25	16	51		
		4F	21	27	39		
		4F (3D)	19	24	38		
Chung et al.[42] 2008	10		Mean dose:	Mean dose:	Max dose:		Coverage:
		3-4F (3D)	L 15, R 13	26	30		72%
		IMRT	L 14, R 11	23	30		95%
Alani et al.[39] 2009	14		Mean dose:*	Mean dose:	Max dose:		
		4F (3D)	26	25	39		
		IMRT	13	31	24		
Dahele et al.[44] 2009	5		Mean dose:	Mean dose:			Mean dose:
		2F	L 27, R 25	24			48
		5F (3D)	L 25, R 26	31			48
		IMRT	L 17, R 15	27			48
		Helical tomotherapy	L 18, R 14	27			46

Mean doses are in Gy.
Abbreviations: 3D, 3-dimensional radiotherapy; D, dose to a percent of organ (e.g., D50, dose to 50% of organ); F, field; IMRT, intensity-modulated radiotherapy; L, left; Max, maximum; NTCP, normal tissue complication probability (%); R, right.
*Higher dose kidney.
†50.4 Gy.

Irradiation Dose Escalation

Given the likely higher micrometastatic burden remaining in the gastric bed and lymphatics in this disease compared with many other cancers, a reasonable argument can be made that the current standard dose of 45 Gy is likely the minimum effective dose. Therefore, therapeutic gain may be possible through careful dose escalation to selected areas of the target volume, while sparing dose-limiting organs or structures with 3DRT or IMRT techniques. Again, based on the high rates of recurrent locoregional disease in the University of Minnesota experience,[3] local control probably has not been convincingly maximized in this disease even with adjuvant CRT. Because conventional techniques have been limited to 45 Gy, dose escalation can be evaluated using IMRT for

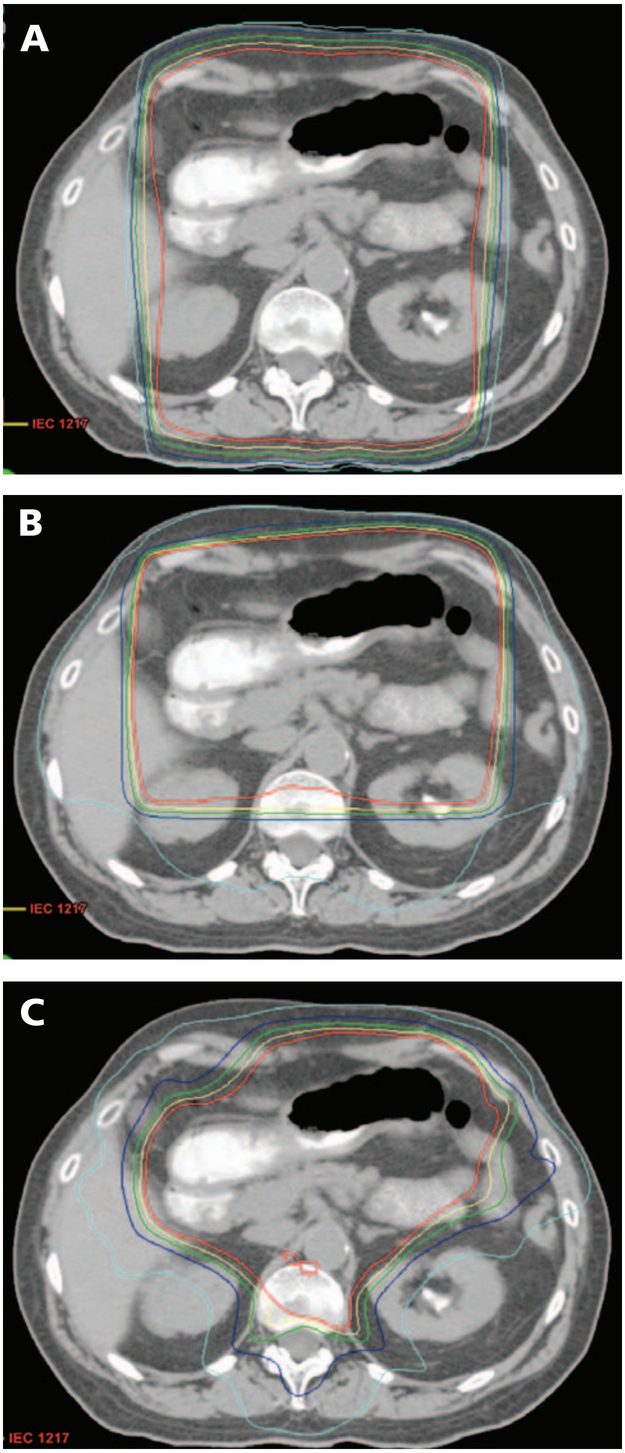

Figure 1 Dosimetric comparison between 2-field (A), 3-dimensional radiotherapy (B), and intensity-modulated radiotherapy plans (C) in a patient receiving neoadjuvant chemoradiotherapy. Colored lines represent 45- (red), 43- (yellow), 40- (green), 35- (blue), and 25-Gy (cyan) isodose lines.

patients with highest risk for microscopic residual after resection (e.g., positive margins, extensive nodal involvement, limited nodal dissection).

At least 2 series have reported evidence of improved locoregional control with dose escalation in the postoperative setting. A retrospective review of 63 patients treated with postoperative CRT at the Mayo Clinic Rochester noted higher locoregional control with doses of RT greater than 50 Gy.[46] Another encouraging study was reported by Arcangeli et al.,[47] describing the outcome of 40 patients treated postoperatively with hyperfractionated RT (1.1 Gy twice daily) to an escalated dose of 55 Gy with concurrent 5-FU. Acute grade 2 or higher hematologic toxicity, nausea and vomiting, or diarrhea was only experienced in 23%, 23%, and 3% of patients, respectively, with no significant late toxicity observed. With a median follow-up of more than 5 years, the in-field recurrence rate was only 7.5%, and 52% of patients were alive. Although neither institution used IMRT in their series, these data support the premise that increase doses of RT beyond 45 Gy may improve patient outcome. The dosimetric advantages of IMRT certainly facilitate the further investigation this strategy.

Clinical Outcomes with Advanced Technologies

Although prospective randomized studies have not been performed to compare advanced radiation techniques versus traditional techniques, and likely will not, multiple single-institution series have observed improved tolerance of gastric RT and favorable clinical outcomes with these newer techniques. In the clinical series from Mayo Clinic Rochester, grade 4/5 complications were observed in 22% of patients treated with a 2-field technique (AP-PA) compared with only 4% among patients whose treatment included 4 or more fields (3DRT; $P = .045$).[46] Another series of 82 patients treated with 3DRT (5-field with concurrent 5-FU) from the Princess Margaret Hospital reported similar toxicity and outcomes to Intergroup 116 with 57% of patients experiencing a grade-3 or more toxicity.[45]

In their initial clinical experience with IMRT in the postoperative treatment of gastric cancer, Milano et al.[38] treated 6 patients with 50.4 Gy with 5-FU and saw no acute grade 3 toxicity. In a subsequent larger series, Boda-Heggemann et al.[41] compared a 27-patient cohort who received 3DRT with

5-FU and leucovorin with 33 patients treated with IMRT and capecitabine and oxaliplatin. Patients treated with IMRT had a higher completion rate of treatment, less rise in serum creatinine in the year after therapy, and a 20% absolute improvement in 2-year OS.

Conclusions

Although significant progress has been made in improving the outcome of patients with resectable gastric or GEJ cancer using adjuvant chemotherapy and radiation, long-term survival rates and toxicity from therapy are not yet satisfactory. Technologic improvements in the accuracy of RT delivery through CT-based treatment planning with well-defined target volumes, 4-dimensional treatment planning, and IGRT have shown improvement over traditional techniques used only a decade ago. In addition, the improved conformality of dose delivery with 3DRT and IMRT has been shown to reduce the dose to critical organs such as the kidney, liver, spinal cord, and heart, possibly reducing morbidity and facilitating intensification of chemotherapy and chemoradiation regimens. Furthermore, these advances in both accuracy and dose delivery afford the opportunity of radiation dose escalation to maximize locoregional control. As these advances in treatment accuracy and delivery continue to emerge and be refined, their clinical application warrants continued study.

References

1. Landry J, Tepper JE, Wood WC, et al. Patterns of failure following curative resection of gastric carcinoma. Int J Radiat Oncol Biol Phys 1990;19:1357–1362.
2. Papachristou DN, Fortner JG. Local recurrence of gastric adenocarcinomas after gastrectomy. J Surg Oncol 1981;18:47–53.
3. Gunderson LL, Sosin H. Adenocarcinoma of the stomach: areas of failure in a re-operation series (second or symptomatic look) clinicopathologic correlation and implications for adjuvant therapy. Int J Radiat Oncol Biol Phys 1982;8,1–11.
4. Mc NG, Vandenberg H Jr, Donn FY, et al. A critical evaluation of subtotal gastrectomy for the cure of cancer of the stomach. Ann Surg 1951;134:2–7.
5. Thomson FB, Robins RE. Local recurrence following subtotal resection for gastric carcinoma. Surg Gynecol Obstet 1952;95:341–344.
6. Macdonald JS, Smalley SR, Benedetti J, et al. Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction. N Engl J Med 2001;345:725–730.
7. Tepper J, Krasna MJ, Niedzwiecki D, et al. Phase III trial of trimodality therapy with cisplatin, fluorouracil, radiotherapy, and surgery compared with surgery alone for esophageal cancer: CALGB 9781. J Clin Oncol 2008;26:1086–1092.
8. Walsh TN, Noonan N, Hollywood D, et al. A comparison of multimodal therapy and surgery for esophageal adenocarcinoma. N Engl J Med 1996;335:462–467.
9. Nygaard K, Hagen S, Hansen HS, et al. Pre-operative radiotherapy prolongs survival in operable esophageal carcinoma: a randomized, multicenter study of pre-operative radiotherapy and chemotherapy. The second Scandinavian trial in esophageal cancer. World J Surg 1992;16:1104–1109; discussion 1110.
10. Stahl M, Walz MK, Stuschke M, et al. Phase III comparison of preoperative chemotherapy compared with chemoradiotherapy in patients with locally advanced adenocarcinoma of the esophagogastric junction. J Clin Oncol 2009;27:851–856.
11. Boige V, Pignon J, Saint-Aubert B, et al. Final results of a randomized trial comparing preoperative 5-fluorouracil (F)/cisplating (P) to surgery alone in adenocarcinoma of stomach and lower esophagus (ASLE): FNLCC ACCORD07-FFCD 9703 trial [abstract[. J Clin Oncol 2007;25(Suppl 1):Abstract 4510.
12. Cunningham D, Allum WH, Stenning SP, et al. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. N Engl J Med 2006;355:11–20.
13. Smalley SR, Gunderson L, Tepper J, et al. Gastric surgical adjuvant radiotherapy consensus report: rationale and treatment implementation. Int J Radiat Oncol Biol Phys 2002;52:283–293.
14. Tepper JE, Gunderson LL. Radiation treatment parameters in the adjuvant postoperative therapy of gastric cancer. Semin Radiat Oncol 2002;12;187–195.
15. Gunderson LL. Gastric cancer-patterns of relapse after surgical resection. Semin Radiat Oncol 2002;12:150–161.
16. Gunderson LL, Tepper JE. Clinical Radiation Oncology. Philadelphia: Churchill Livingston/Elsevier; 2007.
17. Gunderson LL, Donohue JH, Alberts SR. Cancer of the stomach. In: Abeloff MD, Armitage JO, Lichter AS, et al., eds. Clinical Oncology. Philadelphia: Churchill Livingstone/Elsevier; 2008:1431–1464.
18. Matzinger O, Gerber E, Bernstein Z, et al. EORTC-ROG expert opinion: radiotherapy volume and treatment guidelines for neoadjuvant radiation of adenocarcinomas of the gastroesophageal junction and the stomach. Radiother Oncol 2009;92:164–175.
19. Watanabe M, Isobe K, Takisima H, et al. Intrafractional gastric motion and interfractional stomach deformity during radiation therapy. Radiother Oncol 2008;87:425–431.
20. Wysocka B, Kassam Z, Lockwood G, et al. Interfraction and respiratory organ motion during conformal radiotherapy in gastric cancer. Int J Radiat Oncol Biol Phys 2009; in press.
21. Zhao KL, Liao Z, Bucci MK, et al. Evaluation of respiratory-induced target motion for esophageal tumors at the gastroesophageal junction. Radiother Oncol 2007;84:283–239.
22. Fuss M, Salter BJ, Cavanaugh SX, et al. Daily ultrasound-based image-guided targeting for radiotherapy of upper abdominal malignancies. Int J Radiat Oncol Biol Phys 2004;59:1245–1256.
23. Boda-Heggemann J, Mennemeyer P, Wertz H, et al. Accuracy of ultrasound-based image guidance for daily positioning of the upper abdomen: an online comparison with cone beam CT. Int J Radiat Oncol Biol Phys 2009;74:892–897.
24. Willis DJ, Kron T, Hubbard P, et al. Online kidney verification using non-contrast radiographs on a linear accelerator with on

board KV x-ray imaging capability. Int J Radiat Oncol Biol Phys 2009;34:293–300.

25. van der Geld YG, Senan S, van Sornsen de Koste JR, et al. A four-dimensional CT-based evaluation of techniques for gastric irradiation. Int J Radiat Oncol Biol Phys 2007;69:903–909.

26. Lim DH, Kim DY, Kang MK, et al. Patterns of failure in gastric carcinoma after D2 gastrectomy and chemoradiotherapy: a radiation oncologist's view. Br J Cancer 2004;91:11–17.

27. Kim S, Lim DH, Lee J, et al. An observational study suggesting clinical benefit for adjuvant postoperative chemoradiation in a population of over 500 cases after gastric resection with D2 nodal dissection for adenocarcinoma of the stomach. Int J Radiat Oncol Biol Phys 2005;63:1279–1285.

28. Jansen EP, Saunders MP, Boot H, et al. Prospective study on late renal toxicity following postoperative chemoradiotherapy in gastric cancer. Int J Radiat Oncol Biol Phys 2007;67:781–785.

29. Welz S, Hehr T, Kollmannsberger C, et al. Renal toxicity of adjuvant chemoradiotherapy with cisplatin in gastric cancer. Int J Radiat Oncol Biol Phys 2007;69:1429–1435.

30. Marcenaro M, Foppiano F, Durzu S, et al. Kidney-sparing radiotherapy by multiple-field three-dimensional technique in the postoperative management of patients with gastric cancer: comparison with standard two-field conformal technique. Tumori 2006;92:34–40.

31. Leong T, Willis D, Joon DL, et al. 3D Conformal radiotherapy for gastric cancer-results of a comparative planning study. Radiother Oncol 2005;74:301–306.

32. Wals A, Contreras J, Macias J, et al. Damage assessment in gastric cancer treatment with adjuvant radiochemotherapy: calculation of the NTCP's from the differential HDV of the organs at risk. Clin Transl Oncol 2006;8:271–278.

33. Soyfer V, Corn BW, Melamud A, et al. Three-dimensional non-coplanar conformal radiotherapy yields better results than traditional beam arrangements for adjuvant treatment of gastric cancer. Int J Radiat Oncol Biol Phys 2007;69:364–369.

34. Wieland P, Dobler B, Mai S, et al. IMRT for postoperative treatment of gastric cancer: covering large target volumes in the upper abdomen: a comparison of a step-and-shoot and an arc therapy approach. Int J Radiat Oncol Biol Phys 2004;59:1236–1244.

35. Knab B, Rash C, Farrey K, et al. Intensity-modulated radiotherapy for neoadjuvant treatment of gastric cancer. Med Dosim 2006;31:292–297.

36. Ringash J, Khaksart SJ, Oza A, et al. Post-operative radiochemotherapy for gastric cancer: adoption and adaptation. Clin Oncol (R Coll Radiol) 2005;17:91–95.

37. Lohr F, Dobler B, Mai S, et al. Optimization of dose distributions for adjuvant locoregional radiotherapy of gastric cancer by IMRT. Strahlenther Onkol 2003;179:557–563.

38. Milano MT, Garofalo MC, Chmura SJ, et al. Intensity-modulated radiation therapy in the treatment of gastric cancer: early clinical outcome and dosimetric comparison with conventional techniques. Br J Radiol 2006;79:497–503.

39. Alani S, Soyfer V, Strauss N, et al. Limited advantages of intensity-modulated radiotherapy over 3D conformal radiation therapy in the adjuvant management of gastric cancer. Int J Radiat Oncol Biol Phys 2009;74;562–566.

40. Verheij M, Oppedijk V, Boot H, et al. Late renal toxicity following post-operative chemoradiotherapy in gastric cancer [abstract]. Presented at the 2005 Gastrointestinal Cancers Symposium; January 27–29, 2005; Miami, Florida. Abstract 2.

41. Boda-Heggemann J, Hofheinz RD, Weiss C, et al. Combined adjuvant radiochemotherapy with IMRT/XELOX improves outcome with low renal toxicity in gastric cancer. Int J Radiat Oncol Biol Phys 2009;75:1187–1195.

42. Chung HT, Lee B, Park E, et al. Can all centers plan intensity-modulated radiotherapy (IMRT) effectively? An external audit of dosimetric comparisons between three-dimensional conformal radiotherapy and IMRT for adjuvant chemoradiation for gastric cancer. Int J Radiat Oncol Biol Phys 2008;71:1167–1174.

43. Chandra A, Guerrero TM, Liu HH, et al. Feasibility of using intensity-modulated radiotherapy to improve lung sparing in treatment planning for distal esophageal cancer. Radiother Oncol 2005;77:247–253.

44. Dahele M, Skinner M, Schultz B, et al. Adjuvant radiotherapy for gastric cancer: a dosimetric comparison of 3-dimensional conformal radiotherapy, tomotherapy and conventional intensity modulated radiotherapy treatment plans. Int J Radiat Oncol Biol Phys, in press.

45. Kassam Z, Lockwood G, O'Brien C, et al. Conformal radiotherapy in the adjuvant treatment of gastric cancer: review of 82 cases. Int J Radiat Oncol Biol Phys 2006;65:713–719.

46. Henning GT, Schild SE, Stafford SL, et al. Results of irradiation or chemoirradiation following resection of gastric adenocarcinoma. Int J Radiat Oncol Biol Phys 2000;46:589–598.

47. Arcangeli G, Saracino B, Arcangeli G, et al. Postoperative adjuvant chemoradiation in completely resected locally advanced gastric cancer. Int J Radiat Oncol Biol Phys 2002;54:1069–1075.

CME Activity: Radiation Techniques for Gastric Cancer

To obtain credit, you should first read the journal article. After reading the article, you should be able to answer the following, related, multiple-choice questions. To complete the questions and earn continuing medical education (CME) credit, please go to **www.medscapecme.com/journal/jnccn.**

Credit cannot be obtained for tests completed on paper, although you may use the worksheet below to keep a record of your answers. You must be a registered user on Medscape.com. If you are not registered on Medscape.com, please click on the New Users: Free Registration link on the left hand side of the website to register.

Only one answer is correct for each question. Once you successfully answer all post-test questions you will be able to view and/or print your certificate. For questions regarding the content of this activity, contact the accredited provider, CME@medscape.net. For technical assistance, contact CME@webmd.net.

American Medical Association's Physician's Recognition Award (AMA PRA) credits are accepted in the US as evidence of participation in CME activities. For further information on this award, please refer to http://www.ama-assn.org/ama/pub/category/2922.html. The AMA has determined that physicians not licensed in the US who participate in this CME activity are eligible for *AMA PRA Category 1 Credits*™. Through agreements that the AMA has made with agencies in some countries, AMA PRA credit is acceptable as evidence of participation in CME activities. If you are not licensed in the U.S. and want to obtain an AMA PRA CME credit, please complete the questions online, print the certificate and present it to your national medical association.

1. A 40-year-old patient with localized, nonmetastatic gastric cancer undergoes surgical resection with curative intent. Without further treatment, which of the following best describes his risk for local disease relapse and peritoneal failures localized to the original tumor bed, respectively?
   A. 67% and 88%
   B. 67% and 50%
   C. 50% and 67%
   D. 67% and 88%
2. Which of the following best describes the likelihood of incomplete radiation therapy (RT) due to poor tolerance in patients with gastric cancer?
   A. 1 in 2
   B. 1 in 3
   C. 1 in 5
   D. 1 in 7
3. A 50-year-old man must decide whether to add chemoradiation therapy after surgery for nonmetastatic gastric cancer. Which of the following best describes absolute risk for local recurrence associated with adjuvant chemoradiation therapy with surgery compared with surgery alone?
   A. Similar
   B. Better by 2%-4%
   C. Better by 7%-10%
   D. Better by 20%-25%
4. Which of the following best describes factors that affect dosimetry outcomes when RT is given for gastric cancer?
   A. Highly dependent on the technology
   B. Conflicting goals of dose homogeneity and exposure to normal organs.
   C. Conflicting goals of target organ conformality and normal organ exposure
   D. All of the above
5. Which of the following best describes the difference in grade 4/5 toxicities seen in patients with gastric cancer treated with 4-field RT or more compared with 2-field advanced radiation techniques?
   A. Similar
   B. 2 times higher
   C. 3 times higher
   D. 4 times higher

1. The activity supported the learning objectives.
   Strongly Disagree ... Strongly Agree
   1 2 3 4 5
2. The material was organized clearly for learning to occur.
   Strongly Disagree ... Strongly Agree
   1 2 3 4 5
3. The content learned from this activity will impact my practice.
   Strongly Disagree ... Strongly Agree
   1 2 3 4 5
4. The activity was presented objectively and free of commercial bias.
   Strongly Disagree ... Strongly Agree
   1 2 3 4 5