



Radiation therapy (RT) is commonly used in the treatment of older cancer patients. RT may be used as definitive therapy for benign or malignant tumours, as adjuvant therapy with surgery and/or chemotherapy, as palliative therapy when cure is no longer possible, and as alternative to surgery in patients with multiple comorbidities. However, RT is often not given to older patients who might benefit from it, due to biases, misapprehensions about potential toxicity, and social factors particular to this patient population. The preponderance of data suggest that RT is well tolerated in older adults and treatment decisions should be based on prognostic factors irrespective of age. Emerging RT technologies may particularly benefit aged patients by reducing potential toxicities, shortening treatment times, and improving tumour control.

Key words: age, radiation therapy, toxicity, cancer, procedures

Radiation Therapy in Older Adults

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Introduction

Radiation therapy (RT) is commonly used in the treatment of cancer. Given the increasing incidence of most malignancies with advancing age,¹ it is not surprising that RT is often administered in older adults. The purpose of this review is to provide a general overview of RT in aging patients. Particular attention is devoted to the issue of RT-related toxicities and methods for their reduction, particularly novel technologies and treatment approaches. The published literature regarding RT in older adults is also reviewed.

Radiation Therapy

The first cancer patient was treated with radiation in 1896, within months of Roentgen's discovery of x-rays.² Today RT is used to treat tumours arising from virtually every organ system. While frequently used as definitive treatment, RT is also used as adjuvant therapy in combination with surgery and/or chemotherapy. It also offers a means of palliating symptoms when cure is no longer possible. It is estimated that 50–60% of all cancer patients will receive RT at some time during the course of their disease.³

The therapeutic benefit of RT derives from the induction of DNA damage and cellular death in tissues exposed to ionizing radiation.⁴ Treatment is commonly administered in the form of high-energy photons and electrons, delivered using a linear accelerator (external beam RT). Treatment typically requires four to seven weeks of daily therapy. At select centres, heavy particle

beams (e.g., protons, neutrons) are used.^{5–6} Alternatively, RT can be delivered using radioactive sources (brachytherapy) placed within a cavity (intracavitary) or within the tumour itself (interstitial). Brachytherapy may be delivered over several minutes (high-dose-rate, or HDR) or several days (low-dose-rate, or LDR).

General Issues and Concerns

Although RT is highly effective, multiple studies have noted that aged cancer patients are less likely to receive RT than younger patients.^{7–9} This is due in part to the fact that older cancer patients are less likely to undergo any treatment, irrespective of their disease extent.^{10–11} Other contributing factors include misapprehensions about radiation toxicity, myths and biases about its use in older adults, and barriers arising from social or cognitive issues.

Toxicity

RT is often thought to be poorly tolerated or too toxic for older adults. However, as is discussed below, the preponderance of published data do not support the view that toxicity is more frequent or severe in older patients. The decision to give (or withhold) RT should instead be based on the health and performance status of the patient.^{9–11} Studies specifically comparing outcomes across age groups have generally shown equivalent outcomes following RT for young and old patients when equivalent treatment is given.^{12–14} Older adults have also been noted to be able to complete treatment as often as younger



Figure 1 A. Gamma Knife Unit. Courtesy of Elekta Corporation, Stockholm, Sweden.

patients,^{15–19} even combined modality protocols.^{20–21}

Myths and Biases

Myths regarding the use of RT in older adults are additional barriers. These patients and / or their providers may consider RT a “treatment of last resort” or believe that once cancer is diagnosed, it is “too late.”²² However, RT frequently offers the only curative approach when surgery is not possible.²² Older patients are often considered to be less compliant with RT, when

quite the opposite is true.²² Tumours in aged patients are also sometimes considered less aggressive, when in fact data suggest that they can present with more aggressive disease.^{23–25}

Social Considerations

Multiple social factors provide further barriers to RT. Older adults who drive are four times more likely to undergo RT than those who depend on others for transportation.⁹ Unfortunately, one-third of cancer patients over 65 (and two-thirds over 85) are dependent on others for transportation.²⁶ Moreover, patients who live alone (namely, a quarter of older cancer patients) are less likely to undergo RT.²⁶ Admission to a long-term care facility to facilitate daily transportation for RT may be particularly helpful for older patients who are otherwise unable to obtain transportation to and from the clinic.

Cognitive and Functional Status

Impaired functional and cognitive status have been shown to be major factors predicting failure to receive RT in older adults.⁹ While clearly a prolonged treatment course would be inappropriate in

a patient with severely compromised cognitive or functional status, mild-to-moderate impairments should not be considered a contraindication. Patients with minor cognitive deficits such as memory loss may benefit from writing down or repeating instructions.²⁷ Helping patients anticipate potential sequelae, and encouraging them to discuss their concerns and feelings openly, are important quality-of-life aspects of treating aging cancer patients as well.²⁷

Published Studies

In this section, published studies focusing on the older patient in a number of tumours sites treated with RT are presented. In addition to the sites discussed below, RT may be used to treat a number of tumours and conditions prevalent in older adults, including skin cancer, macular degeneration, heterotopic ossification, and in-stent restenosis in patients with coronary artery disease.

Breast Cancer

Older breast cancer patients are less likely to undergo surgery and more likely to receive RT alone.²⁸ When surgery is performed, however, they are less likely than younger women to receive adjuvant RT,²⁹ despite its proven benefits.^{30–32} In a review of 128 stage I–II patients, Kantorowitz *et al.* found that adjuvant RT was delivered in 82% of women age <60 versus 40% of those >60.³³ The percentage receiving RT ages 60–70, <70, and >80 were 45%, 36%, and 24%, respectively. Withholding RT increased the risk of tumour recurrence, with recurrence in 46%, 38% and 20% of patients age 60–70, >70, and >80 years, respectively. Corresponding rates were 0%, 6%, and 0% in patients treated with adjuvant RT.

Most investigators have not observed worse toxicity^{18,34} or cosmesis^{35–36} in older breast cancer patients treated with RT. However, some have reported worse cosmesis³⁷ and shoulder mobility.³⁸ Interestingly, the risk of brachial plexopathy may decrease with increasing age.³⁹



Figure 1B. Head ring used for stereotactic radiosurgery. During treatment, the ring is secured to the treatment couch to minimize patient movement. Courtesy of John M. Buatti, M.D., University of Iowa, Iowa City, IA.

Genitourinary Tumours

Multiple investigators have noted no correlation between advanced age and rectal or bladder sequelae in irradiated prostate cancer patients.^{40–42} Liu *et al.* found that maximal symptoms may develop earlier in older men, but the severity and frequency are similar, except for mild urinary dysfunction.⁴³ Results of treatment and quality of life studies are, however, generally similar for older and younger men,⁴⁴ supporting the use of RT in the older prostate cancer patients.⁴⁵

Aggressive combined modality approaches have been shown to be well tolerated in appropriately selected aged bladder cancer patients.^{20–21,46–47} In medically inoperable or locally advanced patients, favourable results have been reported in those older patients treated with chemoradiotherapy alone.^{47–48}

Lung Cancer

Schild *et al.* evaluated outcomes in 246 locally advanced non-small-cell lung cancer (NSCLC) patients undergoing aggressive chemoradiotherapy.⁴⁹ While toxicity (predominantly hematologic) was more common in patients age >70, survival rates were equivalent, supporting the use of aggressive approaches in appropriately selected older patients. Others have noted that RT alone^{50–51} or combined with weekly taxotere⁵² is well-tolerated in older patients. Radiation pneumonitis is not more likely in older adults, but when it does occur, it may be more severe.^{53–54} Poor surgical candidates with early stage disease may be safely irradiated with curative intent.⁵⁵

Gastrointestinal Cancers

Two investigators have found that RT is well tolerated and effective in older esophageal cancer patients.^{56–57} In rectal cancer patients, most studies do not show a correlation between age and frequency or severity of toxicity, including long-term function.^{58–59} Despite this, and improved outcomes associated with adjuvant 5-fluorouracil and RT,^{60–61} increasing age is associated with decreased utilization of adjuvant combined modality therapies for stage II–III rectal cancer.⁶²

Central Nervous System

Excellent control and low adverse sequelae rates following RT have been reported in multiple series, comprised predominantly of aged patients.^{63–64} In glioblastoma multiforme (GBM), outcome is worse in older patients, particularly those with a poor performance status,⁶⁵ supporting the use of supportive care alone. Increasing attention is focused on short-course RT regimens in older GBM patients.⁶⁶ However, improved outcomes have been reported in older patients with a good performance status following aggressive combined treatment.⁶⁷ Though most sequelae rates are similar, older patients may show slower cognitive improvement following cranial RT.⁶⁸

Head and Neck Tumours

In a review of oropharyngeal cancer patients, Chin *et al.* noted that although aging patients are able to tolerate RT with outcomes similar to younger patients, older patients are often prescribed and receive lower doses, regardless of their disease extent.¹⁶ Pignon and coworkers examined a cohort of 1,307 patients with head and neck cancer, including 408 patients over age 65. No differences were observed across age groups in survival, acute mucosal reactions, or weight loss, suggesting that age per se should not be considered in the therapeutic decision process.⁶⁹ Others have reached similar conclusions.^{17,70}

Gynecologic Malignancies

Studies of irradiated cervical cancer patients have generally shown equivalent likelihood of survival, pelvic recurrence, and toxicity across age groups.^{71–77} The higher prevalence of comorbidities in older cervical cancer patients tends to explain differences in tolerance of RT, and equivalent treatments lead to equivalent outcomes irrespective of age alone.⁷⁶ Of note, investigators who have reported higher complication rates have treated with unconventional fractionation schemes.⁷⁸



Figure 2A. Anterior-posterior radiograph of the pelvis in a patient treated with LDR permanent prostate brachytherapy, illustrating seeds within the prostate gland. Courtesy of Douglas A. Kelly, M.D., Cancer Treatment Centers of America, Tulsa, OK.

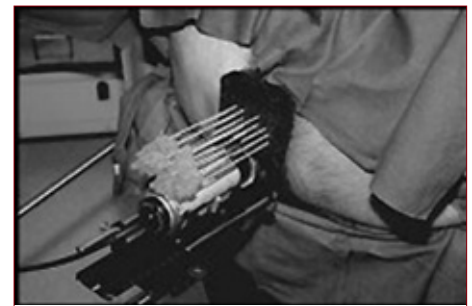


Figure 2B. High-dose-rate prostate brachytherapy. Needles are inserted transperineally under ultrasound guidance and after-loaded with HDR Ir192. Courtesy of Douglas A. Kelly, M.D., Cancer Treatment Centers of America, Tulsa, OK.

Some⁷⁹ but not all⁸⁰ studies have suggested that aged endometrial cancer patients undergoing RT have worse outcomes compared to younger women. Age has been associated with an increased risk of RT-related sequelae.⁸¹ Of note, older endometrial cancer patients have more adverse pathologic features^{25,79} and are at risk for pelvic recurrence following surgery alone.²⁵ Adjuvant RT lowers this risk²⁵ and is indicated in older patients with adverse pathologic features. Medically inoperable patients can receive definitive RT; in these women, disease-free survival appears to be comparable in older and younger patients.⁸²

Other Malignancies

Age has been associated with worse prognosis in Hodgkin's disease following RT in some⁸³ but not all⁸⁴ studies. However, older patients able to



Figure 3A. MammoSite Radiation Therapy System. Courtesy of Proxima Therapeutics, Alpharetta, GA.

tolerate definitive RT have relatively high survival rates.⁸³ Connors *et al.* studied 78 non-Hodgkin's lymphoma patients (median age, 64 years) and concluded that RT was highly successful with acceptable toxicity.⁸⁵ A study of 20 older African patients with Kaposi's sarcoma showed that RT was associated with excellent symptomatic relief with minimal side effects.⁸⁶

Special RT Procedures Stereotactic Radiosurgery

Stereotactic Radiosurgery (SRS) is a specialized external beam technique whereby a large, single dose of radiation is delivered to a small, intracranial volume with high precision. Treatment is administered with either a dedicated Cobalt-60 unit (Gamma Knife, Elekta Corporation, Stockholm, Sweden) (Figure 1A) or a modified linear

accelerator. Multiple beams (or arcs) conform the dose to the target lesion(s); rapid-dose falloff results in sparing of surrounding normal tissues. Immobilization is ensured with the aid of surgical pins in the patient's skull or with a relocatable head frame (Figure 1B).

SRS is an appealing approach in older adults as it provides a less invasive alternative to surgery. Excellent control rates with low toxicity have been reported in many brain tumours undergoing SRS.^{87–89} SRS also provides an effective, low risk, non-invasive means of treating metastatic lesions in patients with lung, breast, and other malignancies, with control rates in most series exceeding 85%.^{90–92} SRS may be used alone or as a “boost” in conjunction with whole brain RT.⁹³ Recent interest has focused on its use in extracranial sites, including the lung⁹⁴ and spine.⁹⁵

Prostate Brachytherapy

Prostate brachytherapy is a form of interstitial brachytherapy that involves the placement of radioactive “seeds” (I125 or Pd103) within the prostate gland. Seeds with a short half-life can be placed permanently, delivering treatment as they decay. Prostate brachytherapy is an important treatment modality in the older adults, for it provides an alternative to both surgery and external beam RT. Reported control rates have been comparable to both surgery and external beam RT in early stage patients, with low rates of toxicity^{96–98} apart from transient acute bladder symptoms.⁹⁹

In the past, prostate brachytherapy was an invasive procedure with seeds placed under direct vision at the time of pelvic lymphadenectomy. Results were disappointing, however, due to inadequate coverage of the prostate. Today, seeds are placed using a transperineal approach under transrectal ultrasound guidance, ensuring accurate positioning and improved dose coverage (Figure 2A). Some centres perform prostate brachytherapy using HDR techniques (Figure 2B).¹⁰⁰

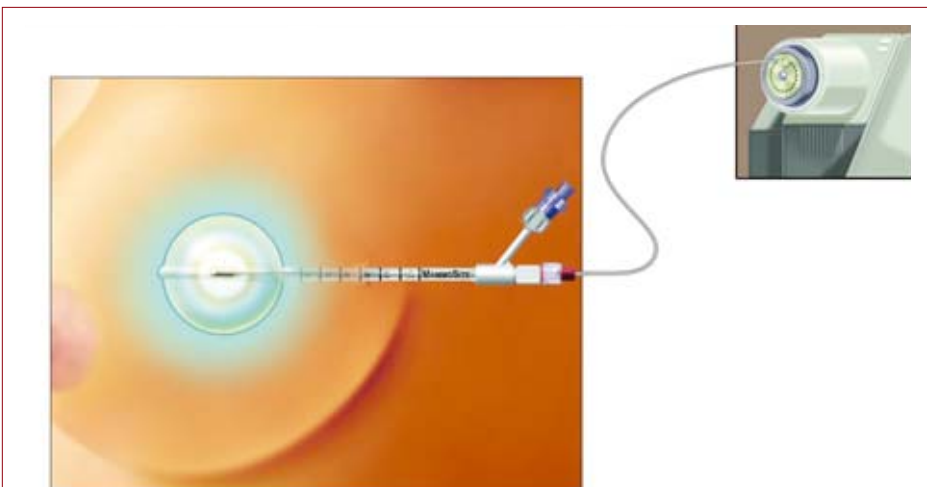


Figure 3B. An illustration of the MammoSite device within a lumpectomy cavity in a patient undergoing breast conservation. Courtesy of Proxima Therapeutics, Alpharetta, GA.

MammoSite®

MammoSite® (Proxima Therapeutics, Alpharetta, GA) is an intracavitary brachytherapy approach whereby treatment is delivered to the lumpectomy cavity in women undergoing breast-conserving surgery (Figure 3A). At surgery, a balloon catheter is placed within the lumpectomy cavity. Once in place, the balloon is inflated and a HDR Ir192 source is inserted, delivering treatment in a few minutes, typically twice daily over five days (Figure 3B).

MammoSite® is an appealing approach in the older breast cancer patient since it avoids a protracted course of external beam RT. Treatment is also delivered directly to the lumpectomy site, minimizing exposure of surrounding normal tissues (and thus potential sequelae). While initial published reports have been promising,^{101–103} most include small numbers with short follow-up times. Larger, prospective trials are needed to assess the full benefits and risks of this approach, in particular the risk of tumour recurrences elsewhere in the breast.

Intensity-Modulated Radiation Therapy

Intensity-modulated RT (IMRT) is a novel approach to the planning and

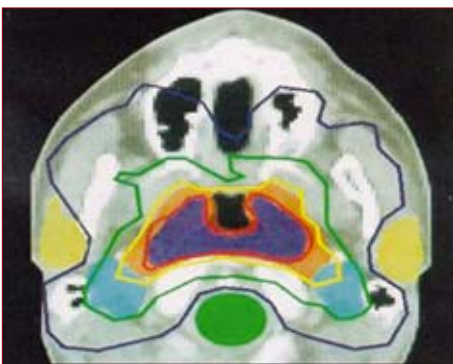


Figure 5. IMRT dose distribution superimposed on an axial computerized tomography slice of a patient with head and neck cancer. High-dose isodose lines conform to the target tissues, reducing dose to the bilateral parotid glands and the risk of xerostomia. Courtesy of James Mogavero, Long Island Jewish Medical Center, New Hyde Park, NY.

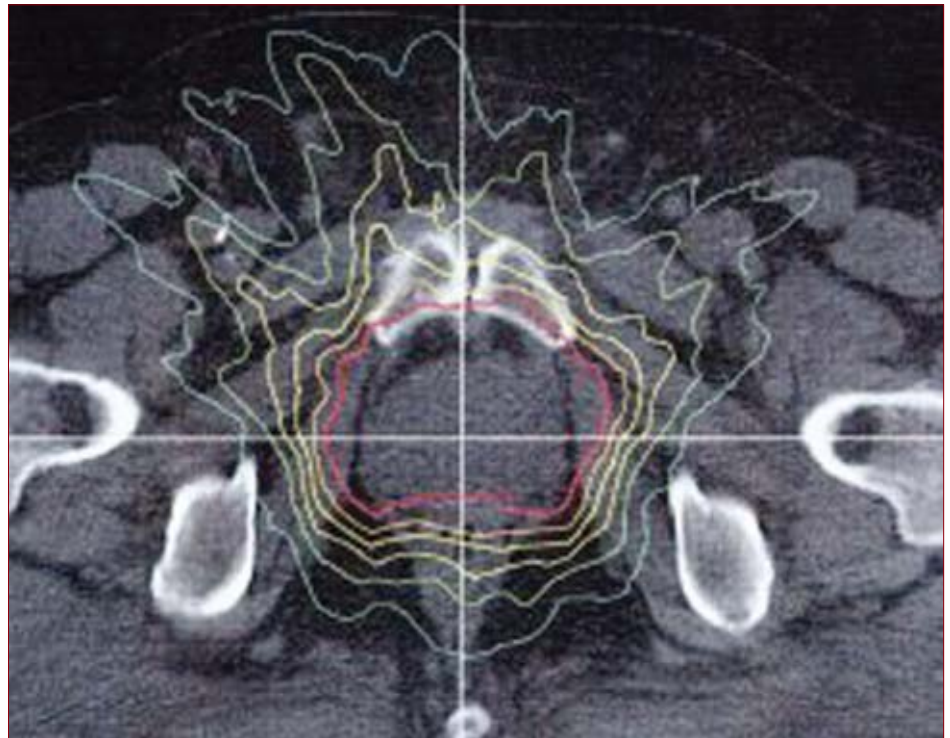


Figure 4. Axial computerized tomography slice illustrating an IMRT plan in a patient with prostate cancer. Note that the high-dose isodose curves conform to the shape of the prostate, sparing the rectum and reducing the risk of proctitis and rectal bleeding. Courtesy of Douglas A. Kelly, M.D., Cancer Treatment Centers of America, Tulsa, OK.

delivery of RT. Unlike conventional RT, IMRT conforms the prescription dose to the shape of the target tissues in three dimensions, thereby reducing the volume of normal tissues exposed to high doses. Using an “inverse” planning process, modulated beams are designed using sophisticated computerized optimization software. When cast into the patient, highly conformal dose distributions are achieved.

Until recently, IMRT was performed at only a few centres. With the proliferation of commercial systems, IMRT is now widely available.¹⁰⁴ Multiple investigators have demonstrated the benefit of IMRT planning in nearly all tumour sites. Outcome studies have been promising, including in tumours common in older adults, e.g., brain,¹⁰⁵ prostate,¹⁰⁶ head and neck,¹⁰⁷ and gynecologic¹⁰⁸ tumours. Example IMRT plans are shown in Figures 4 and 5.

IMRT has considerable potential in older adults. Sparing of normal tissues may reduce the risk and severity of RT-related toxicities, improving patient qual-

ity of life. Highly conformal plans may also allow the safe delivery of higher than conventional doses, improving tumour control.¹⁰⁶ IMRT may also allow treatment courses to be shortened without increasing toxicity.^{109–110}

Conclusion

RT is beneficial and generally well-tolerated in the aging. However, these patients encounter particular barriers to receiving RT in many clinical situations when it is appropriate. Awareness of these issues is an important aspect of caring for the older cancer patient. Newer therapeutic technologies may also provide a means to circumvent some of these barriers and improve these patients' quality of life.

Due to the number of references accompanying this article, we were unable to publish the complete reference list in print.

Please find the complete reference list online at www.geriatricsandaging.ca

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References

1. U.S. Cancer Statistics Working Group. United States Cancer Statistics: 2000 Incidence. Atlanta (GA): Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; 2003.
2. Holsti LR. Development of clinical radiotherapy since 1896. *Acta Oncol* 1995; 34:995–1003.
3. American Society for Therapeutic Radiology and Oncology website (Accessed on August 21, 2004 at www.astro.org/patient/treating_cancer/what_is_radiation_therapy.htm).
4. Hall EJ, Astor M, Bedford J, et al. Basic radiobiology. *Am J Clin Oncol* 1988; 11:220–52.
5. Loeffler JS, Smith AR, Suit HD. The potential role of proton beams in radiation oncology. *Semin Oncol* 1997;24:686–95.
6. Svensson H, Moller TR. Developments in radiotherapy. *Acta Oncol* 2003;42:430–42.
7. Coburn MC, Pricolo VE, Soderberg CH. Factors affecting prognosis and management of carcinoma of the colon and rectum in patients more than eighty years of age. *J Am Coll Surg* 1994;179:65–9.
8. Newschaffer CJ, Penberthy L, Desch CE, et al. The effect of age and comorbidity in the treatment of elderly women with nonmetastatic breast cancer. *Arch Intern Med* 1996;156:85–90.
9. Goodwin JS, Hunt WC, Samet JM. Determinants of cancer therapy in elderly patients. *Cancer* 1993;72:594–601.
10. Smith TJ, Penberthy L, Desch CE, et al. Differences in initial treatment patterns and outcomes of lung cancer in the elderly. *Lung Cancer* 1995;13:235–52.
11. Samet J, Hunt WC, Key C, et al. Choice of cancer therapy varies with age of patient. *JAMA* 1986;255:3385–90.
12. McKenna RJ Sr. Clinical aspects of cancer in the elderly. Treatment decisions, treatment choices, and follow-up. *Cancer* 1994;74(Suppl. 7):S2107–17.
13. Goodwin JS, Samet JM, Hunt WC. Determinants of survival in older cancer patients. *J Natl Cancer Inst* 1996;88:1031–8.
14. Goodwin JS, Samet JM. Care received by older women diagnosed with breast cancer. *Cancer Control* 1994;1:313–19.
15. Wasil T, Lichtman SM, Gupta V, Rush S. Radiation therapy in cancer patients 80 years of age and older. *Am J Clin Oncol* 2000;23:526–30.
16. Chin R, Fisher RJ, Smee RI, et al. Oropharyngeal cancer in the elderly. *Int J Radiat Oncol Biol Phys* 1995;32:1007–16.
17. Huguenin P, Glanzmann C, Lutolf UM. Acute toxicity of curative radiotherapy in elderly patients. *Strahlenther Onkol* 1996;172:658–63.
18. Wyckoff J, Greenberg H, Sanderson R, et al. Breast irradiation in the older woman: a toxicity study. *J Am Geriatr Soc* 1994;42:150–2.
19. Liu L, Glicksman AS, Coachman N, et al. Low acute gastrointestinal and genitourinary toxicities in whole pelvic irradiation of prostate cancer. *Int J Radiat Oncol Biol Phys* 1997;38:65–71.
20. Rotman M, Aziz H, Porrazzo M, et al. Treatment of advanced transitional cell carcinoma of the bladder with irradiation and concomitant 5-fluorouracil infusion. *Int J Radiat Oncol Biol Phys* 1990;18:1131–7.
21. Sauer R, Schrott KM, Dunst J, et al. Preliminary results of treatment of invasive bladder carcinoma with radiotherapy and cisplatin. *Int J Radiat Oncol Biol Phys* 1988;15:871–5.
22. Berkman B, Rohan B, Sampson S. Myths and biases related to cancer in the elderly. *Cancer* 1994;74(Suppl. 7):2004–8.
23. Holmes FF. Clinical evidence for change in tumor aggressiveness with age. In: Balducci L, Lyman GH, Ershler WB, eds. *Geriatric oncology*. Philadelphia: JB Lippincott Company, 1992:86–91.
24. Hakama M, Penttinen J. Epidemiological evidence for two components of cervical cancer. *Br J Obstet Gynaecol* 1981;88:209–14.
25. Citron JR, Sutton H, Yamada SD, et al. Pathologic stage I-II endometrial carcinoma in the elderly: radiotherapy indications and outcome. *Int J Radiat Oncol Biol Phys* 2004;59:1432–8.
26. Goodwin JS, Hunt WC, Samet JM. A population-based study of functional status and social support networks of elderly patients newly diagnosed with cancer. *Arch Intern Med* 1991;151:366–70.
27. Strohl RA. The elderly patient receiving radiation therapy: treatment sequelae and nursing care. *Geriatr Nurs* 1992;13:153–6.
28. Martin LM, le Pechoux C, Calitchi E, et al. Management of breast cancer in the elderly. *Eur J Cancer* 1994;30A:590–6.
29. Truong PT, Wong E, Bernstein V, et al. Adjuvant radiation therapy after breast-conserving surgery in elderly women with early-stage breast cancer: controversy or consensus? *Clin Breast Cancer* 2004;4:407–14.
30. 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;347:1233–41.
31. Overgaard M, Hansen PS, Overgaard J, et al. Postoperative radiotherapy in high-risk premenopausal women with breast cancer who receive adjuvant chemotherapy. Danish Breast Cancer Cooperative Group 82b Trial. *N Engl J Med* 1997;337:949–55.
32. Ragaz J, Jackson SM, Le N, et al. Adjuvant radiotherapy and chemotherapy in node-positive premenopausal women with breast cancer. *N Engl J Med* 1997;337:956–62.
33. Kantorowitz DA, Poulter CA, Sischy B, et al. Treatment of breast cancer among elderly women with segmental mastectomy or segmental mastectomy plus postoperative radiotherapy. *Int J Radiat Oncol Biol Phys* 1988;15:263–70.
34. Larson D, Weinstein M, Goldberg I, et al. Edema of the arm as a function of the extent of axillary surgery in patients with stage I-II carcinoma of the breast treated with primary radiotherapy. *Int J Radiat Oncol Biol Phys* 1986;12:1575–82.
35. Beadle GF, Silver B, Botnick L, et al. Cosmetic results following primary radiation therapy for early breast cancer. *Cancer* 1984;54:2911–8.
36. Steeves RA, Phromratanapongse P, Wolberg WH, et al. Cosmesis and local control after irradiation in women treated conservatively for breast cancer. *Arch Surg* 1989;124:1369–73.
37. Pezner RD, Patterson MP, Lipsett JA, et al. Factors affecting cosmetic outcome in breast-conserving cancer treatment—objective quantitative assessment. *Breast Cancer Res Treat* 1992;20:85–92.
38. Bentzen SM, Overgaard M, Thames HD. Fractionation sensitivity of a functional endpoint: impaired shoulder movement after post-mastectomy radiotherapy. *Int J Radiat Oncol Biol Phys* 1989;17:531–7.
39. Olsen NK, Pfeiffer P, Johannsen L, et al. Radiation-induced brachial plexopathy: neurological follow-up in 161 recurrence-free breast cancer patients. *Int J Radiat Oncol Biol Phys* 1993;26:43–9.
40. Sandler HM, McLaughlin PW, Ten Haken RK, et al. Three dimensional conformal radiotherapy for the treatment of prostate cancer: low risk of chronic rectal morbidity observed in a large series of patients. *Int J Radiat Oncol Biol Phys* 1995;33:797–801.
41. Hanlon AL, Schultheiss TE, Hunt MA, et al. Chronic rectal bleeding after high-dose conformal treatment of prostate cancer warrants modification of existing morbidity scales. *Int J Radiat Oncol Biol Phys* 1997;38:59–63.
42. Vijayakumar S, Awan A, Karrison T, et al. Acute toxicity during external-beam radiotherapy for localized prostate cancer: comparison of different techniques. *Int J Radiat Oncol Biol Phys* 1993;25:359–71.
43. Liu L, Glicksman AS, Coachman N, et al. Low acute gastrointestinal and genitourinary toxicities in whole pelvic irradiation of prostate cancer. *Int J Radiat Oncol Biol Phys* 1997;38:65–71.
44. Huguenin PU, Bitterli M, Lutolf UM, et al. Localized prostate cancer in elderly patients. Outcome after radiation therapy compared to matched younger patients. *Strahlenther Onkol* 1999;175:554–8.