Novel eradicative high-dose rate brachytherapy for internal mammary lymph node metastasis from breast cancer

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Abstract

AIM: To develop a method of delivering an eradicative high radiotherapeutic dose safely preserving the surrounding skin in the treatment of internal mammary lymph node metastasis (IMLNM) of breast cancer.

METHODS: We report a 38-year-old female patient with a solo IMLNM showing no response to 60 Gy in 2.5 Gy fractions of external beam radiotherapy. To eradicate this tumor, a boost brachytherapy plan was created after percutaneous insertion of an applicator needle into the IMLNM lesion avoiding the pleura and vessels under ultrasound monitoring. According to the dose distribution, the required thickness of a spacer between the skin and the tumor was determined, and hyaluronic gel was injected up to this thickness under ultrasound monitoring. We evaluated skin doses, target doses and clinical outcome.

RESULTS: All procedures were performed easily. Sixteen Gy (34.7 Gy equivalent in 2 Gy fractions calculated by the linear quadratic model at α/β = 10: EQ̄D2, α/β = 10, cumulative total was 101.9 Gy EQ̄D10) to 100% of the target volume was irradiated with cumulative maximum skin dose of 70 Gy EQ̄D2, α/β = 3 which was 98.7 Gy EQ̄D2, α/β = 3 without spacer. No procedure related- or late complications and no local recurrence at the treated site were observed for three years until expiration.

CONCLUSION: We consider that this procedure will provide an eradicative high-dose irradiation to IMLNM of breast cancer, preserving skin from overdose complications.

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Key words: Brachytherapy; Hyaluronate; Internal mammary lymph node; Metastasis; Skin preservation; Breast cancer; Organ at risk

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INTRODUCTION

Metastasis to the internal mammary lymph nodes (IMLN) is one of the characteristic conditions in breast cancer. Although the incidence is rare in early stage[1], IMLNM
was found in 13.8% of patients with clinical N2 or N3 locally advanced disease, of which 27.9% were refractory to chemotherapy and 11% were refractory to both chemotherapy and radiotherapy of 50 Gy to 72 Gy. Dose escalation is a key to overcome radioresistance. However, high dose treatment is generally limited by low tolerability of the surrounding normal tissues. The calculated dose causing necrosis or ulceration in 5% of 10 cm² of irradiated skin in five years was reported to be 70 Gy\(^{[3]}\). This is recommended to ensure the safety of these tissues in high dose eradication treatment to radioresistant tumors. One practical solution is to obtain a safe distance by using a spacer. Recently, high-dose radiotherapy using various spacers has been developed\[^{[4-9]}\]. Of these spacers, high-molecular-weight hyaluronate is a safe intrinsic substance in the human body and when used as an injectable spacer is temporarily successful during high dose rate brachytherapy (HDRBT)\[^{[5,9,10-12]}\]. HDRBT with a spacer may facilitate safe and effective dose delivery to IMLNM. We report a patient with an IMLNM as a sole recurrence.

**MATERIALS AND METHODS**

**Patient**

A 38-year-old female patient was referred for radiotherapy of a sole IMLNM of 2 cm in diameter. Eight years before, she underwent right mastectomy for stage II breast cancer of 5 cm in size, histologically proved as invasive ductal carcinoma with estrogen receptor overexpression. She received postoperative intravenous chemotherapy consisting of Cyclophosphamide 500 mg/body weight (1.5 μ³), Adriamycin 50 mg/body and 5-fluorouracil 500 mg/body on day 1, repeated every 3 wk for a total of eight courses (six courses and an additional two courses); and per oral treatment with tamoxifen, 20 mg/body daily for 5 years. The patient was followed up regularly for 3 years. No postoperative radiotherapy was performed.

In August of the 6th year after surgery, the patient began to feel occasional pain in her anterior chest wall. X-ray computed tomography (CT) examination revealed a parasternal spherical mass, and this was histologically confirmed as ductal carcinoma with estrogen receptor overexpression. She received postoperative intravenous chemotherapy consisting of Cyclophosphamide 500 mg/body weight (1.5 μ³), Adriamycin 50 mg/body and 5-fluorouracil 500 mg/body on day 1, repeated every 3 wk for a total of eight courses (six courses and an additional two courses); and per oral treatment with tamoxifen, 20 mg/body daily for 5 years. The patient was followed up regularly for 3 years. No postoperative radiotherapy was performed.

As first radiotherapy to the IMLNM, a three-dimensional plan of 60 Gy in 2.5 Gy fractions (67.2 Gy-EQD\(_2\), \(\alpha/\beta = 10\)) by external beam radiotherapy (EBRT) was prescribed (Figure 1). Doses in the skin were 36 Gy (32.4 Gy EQD\(_2\), \(\alpha/\beta = 3\)) at 0.1 mm depth as an epidermis reference point (RP), 48 Gy (48 Gy-EQD\(_2\), \(\alpha/\beta = 3\)) at 2.5 mm depth as a dermis RP, and 54 Gy (57.1 Gy-EQD\(_2\), \(\alpha/\beta = 3\)) at 5 mm depth as a subdermis RP. Pulmonary V\(_{20}\) (the volume of lung receiving at least 20 Gy) was 6.3%.

However, the tumor showed no significant reduction in size at 1 mo after radiotherapy (Figure 2). It was the only lesion. Following the patient’s desire for local cure by radiotherapy, we planned an immediate boost brachytherapy. Informed consent was obtained from the patient prior to treatment, which was performed with standard institutional approval. The entire procedure was performed at our outpatient clinic.

**Preparation and needle deployment**

Hyaluronic gel mixture was prepared by mixing 50 mg sodium hyaluronate with a median molecular weight of 3.4 million Daltons (Suvenyl, Chugai/Roche, Tokyo, Japan) with saline, to produce a volume of 50 mL. The patient was sedated but awake. Under monitoring with ECG, PaO\(_2\), respiration, and blood pressure, and under ultrasound and X-ray CT (SCT-7000, Shimadzu, Kyoto, Japan) guidance, a brachytherapy applicator needle (1.1 mm outer diameter; 16 cm length) was inserted in the target, avoiding vascular and pulmonary injury (Figure 2A and B). Then, 3 mm-pitch CT images were acquired and transferred to the treatment planning computer (PLATO, Nucletron, Veenendaal, Netherlands).

**Treatment planning, gel injection and irradiation**

We created a 3D brachytherapy treatment plan prescribing 16 Gy (34.67 Gy-EQD\(_2\), \(\alpha/\beta = 10\)) to 100% of the planned target volume. Calculated skin dose to the epidermis RP at 0.1 mm depth was 9.3 Gy (22.9 Gy-EQD\(_2\), \(\alpha/\beta = 3\)), the dermis RP at 2.5 mm depth was 8 Gy (17.6 Gy-EQD\(_2\), \(\alpha/\beta = 3\)) and to the subdermal RP at 5 mm depth was 12.5 Gy (41.6 Gy EQD\(_2\), \(\alpha/\beta = 3\)) (Figure 2C, Table 1); each cumulative dose was 62.9, 65.6 and 98.7 Gy EQD\(_2\), \(\alpha/\beta = 3\) respectively. Tentatively we tried to keep the maximal skin dose below 70 Gy EQD\(_2\), \(\alpha/\beta = 3\) and the maximal dose to subdermal tissue was calculated below 6.7 Gy (12.9 Gy-EQD\(_2\), \(\alpha/\beta = 3\)). Thus, the calculated minimum spacer thickness was 6.9 mm (total skin

| Skin point | Epidermis | Dermis | Subdermis |
|------------|-----------|--------|-----------|
| Reference  | Depth from the skin | 0.1 | 2.5 | 5 |
| EBRT       | Dose (cGy) | 36 | 48 | 54 |
| BT without | Equivalent dose* - a | 40 | 48 | 57.1 |
| spacer     | Equivalent dose* - b | 22.9 | 17.6 | 41.6 |
| BT with    | Dose (cGy) | 1.8 | 4.4 | 6.7 |
| spacer     | Equivalent dose* - c | 1.73 | 6.51 | 12.9 |
| Ratio of dose reduction in equivalent dose* - c/b | 1/13.2 | 1/2.7 | 1/3.22 |

*EQD\(_2\), \(\alpha/\beta = 1\); EBRT: External beam radiotherapy; BT: Brachytherapy.
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Before irradiation, hyaluronic gel was injected into the subcutaneous tissue using a 21-gauge needle. The created thickness of the skin was confirmed by ultrasonography with a 10 MHz transducer before and immediately after irradiation (Figure 3). The planning data were sent to an I-192 remote after-loader system (Microselectron HDR Ir-192, Nucletron) and irradiation was started. After irradiation, the needles were promptly removed and the patient was allowed to rest; she left the clinic, when ready, on foot. The patient was followed-up regularly at our clinics.

RESULTS

Procedural results

Figures 2C and 4 show irradiation of 100% volume of the planning target volume by 16 Gy in one fraction (32.4 Gy-EQD$_2$, $\alpha/\beta = 10$). Pulmonary tissue volume receiving more than 20 Gy-EQD$_2$, $\alpha/\beta = 3.07$ [13] was 7.8 cc. The thickness of the gel injected skin did not show significant change before and after the irradiation (C). Slight decrease in the thickness might be due to compression by the probe. A low echogenic gel area is seen in the mid zone of the subcutaneous tissue including bright spots of air bubbles (B and C). Asterisk: Skin surface (epidermis); White arrow: Range of skin including epidermis, dermis and subdermis; Curved arrow: A gel layer between the surface of the skin and the ultrasonography probe (top), which surface gel was for a precise measurement avoiding compression.

Figure 3 Measurement of skin thickness: The skin thickness from the epidermis to the bottom of the subdermis was approximately 7 mm before the gel injection (A), approx. Fourteen mm after gel injection (B) and the thickness almost remained the same after irradiation (C). Slight decrease in the thickness might be due to compression by the probe. A low echogenic gel area is seen in the mid zone of the subcutaneous tissue including bright spots of air bubbles (B and C). Asterisk: Skin surface (epidermis); White arrow: Range of skin including epidermis, dermis and subdermis; Curved arrow: A gel layer between the surface of the skin and the ultrasonography probe (top), which surface gel was for a precise measurement avoiding compression.
the total treatment time was 10 min and 2.5 h, respectively. There were no procedure-related complications, and no additional medication was required.

**Clinical outcome**

Four weeks later, a marked reduction in tumor size was observed and the CEA level decreased from 18.6 μg/mL to 10.0 μg/mL. One year later, the patient developed another IMLNM 7 cm cranial to the previous one. This second lesion was treated with a single brachytherapy dose of 20 Gy (92 Gy EQD2, α/β = 3) with the maximal skin dose of 5 Gy (Figure 4). The needle was inserted passing through the cartilage. The subdermal dose was decreased to 1/3.25 by gel injection. Two years after this treatment there was no evidence of the tumor on X-ray CT imaging, and no pulmonary or skin damage (Figure 5). Both local lesions were cured without complications. The patient died 3 years later due to liver metastasis.

**DISCUSSION**

**IMLNM and radiotherapy**

Treatment of IMLNM has long been a delicate balance as there are tradeoffs between elective surgery for metastatic tumors and survival benefit[14] and between prophylaxis to relapse and radiation toxicity to the lungs and heart[15,16]. Increased non-breast-cancer mortality including cardiac events in post-surgically irradiated women[17,18] is thought to be related to involvement of these normal organs. The incidence of adverse radiation effects is higher in meta-analyses on older trials with larger fields[15,19]. Thus, older radiation techniques with deep tangents or direct fields on IMLN have been abandoned from the current standard. However, there is still a need for prophylaxis of IMLNM. Recent studies with electron boost to IMLN[20], and even with tangential field irradiation[15], found no increase in these risks. It is necessary to balance the cost, risk and benefit of these prophylaxes. The present approach may provide a countermeasure to prophylaxis failure.

**Adjuvant brachytherapy in breast cancer treatment**

In adjuvant radiotherapy, surgical margin-intensive treatments including IMRT or brachytherapy[21] such as 5-d treatment with MammoSite[22] were developed based on an incidence map of ipsilateral breast recurrence[23,24]. This type of accelerated partial breast irradiation (APBI) is time-saving, has cosmetic advantages, and enables preservation of normal organs such as heart and lungs. The use of APBI brachytherapy is consistently increasing. In contrast, a retrospective study on Medicare beneficiaries found an association between APBI brachytherapy and a higher rate of later mastectomy (4.0% vs 2.2%), increased toxicities, and post-operative complications, compared to traditional radiation therapy[25]. Large randomized trials comparing APBI brachytherapy to whole breast irradiation are ongoing.
Reirradiation brachytherapy

In general, reirradiation or boost irradiation is increasing in importance for the treatment of relapsed and/or refractory cancer\textsuperscript{[26,27]}. The clinical rationale of local eradication is thought to be high for oligometastasis\textsuperscript{[28]}\textsuperscript{[28]}. Brachytherapy has advantages for selective intensive treatment of a small target\textsuperscript{[29]}\textsuperscript{[29]}, and its usefulness is reported in the treatment of ipsilateral recurrence\textsuperscript{[30]}\textsuperscript{[30]}. However, reirradiation is often limited by normal organs, especially closely surrounding organs such as skin. Skin protection during intensive brachytherapy was achieved by injectable spacers such as hyaluronate\textsuperscript{[31]}\textsuperscript{[31]}. This spacing technique can be used to protect the intestines\textsuperscript{[12,30]}\textsuperscript{[12,30]}, and rectum\textsuperscript{[11,31]}\textsuperscript{[11,31]}, as well as other organs\textsuperscript{[30]}\textsuperscript{[30]}. The present report is an extension of these critical organ preservation procedures to eradicative reirradiation of IMLNM by brachytherapy.

Rationale of the present technique

Although local eradication may be expected with combined chemotherapy and EBRT to breast cancer-IMLNM, some are refractory\textsuperscript{[3].} Dose escalation may be effective for overcoming radioresistance, but is generally associated with an increased likelihood of normal tissue complications\textsuperscript{[4]}. Even when recently developed technologies are employed, the inability to avoid risk organs close to the target remains a weak point. In combination with HDRBT, the creation of an artificial space between the target and risk organs in a minimally invasive procedure may provide an effective solution.

Advantage of the subvolume effect in brachytherapy

Unlike EBRT, by its nature interstitial brachytherapy delivers an additional dose to the tumor subvolume. Kim et al\textsuperscript{[34]} calculated that significant increases in tumor control probability (from 50% to 75%) would be achieved for a small increase in the risk of necrosis, when a substantial portion of the tumor volume (60%-80%) could be boosted up to 130%. In the present case, the dose distribution and dose-volume histograms show that the tumor subvolume received significant intensive doses. Further research should be performed to examine the subvolume effect in brachytherapy.

Gain in therapeutic ratio

To date, there are no generally accepted safety limits for small skin areas based on dose volume relationship, except for the area based data for 10 cm\textsuperscript{2} and larger\textsuperscript{[5]}. Though a small degree of skin necrosis may not be a serious matter, it should be avoided if possible. Using gel injection, the therapeutic ratio of the target dose and skin dose in the present case was improved by 3.25-4.17. It may be said that the gel spacing procedure can provide a significant improvement in the therapeutic ratio that safely promotes high dose radiotherapy required for local eradication.

Feasibility and safe practice

The percutaneous intercostal needle approach can be performed safely by ultrasound and/or X-ray CT guidance, even penetrating the cartilage as in the second lesion, avoiding injury to arteries or high flow veins. Because this method with gel injection is a short-time single session therapy, this may also be useful in treating multiple lesions at the same time on an outpatient basis.

Skin dose estimation in the future

Even in the case of reirradiation, it is necessary to avoid skin perforation by radiotherapy. Of the three layers of the skin (epidermis, dermis and subdermis), the thickness of each differs widely according to site and species. We can observe these delicate structures by high frequency ultrasound imaging\textsuperscript{[33]}. Although the biological response to radiation differs by skin layer, available dose-complication probabilities are calculated for the whole skin\textsuperscript{[3]}. We have complied with the published recommendations.

In the clinical situation, these considerations cause difficulties in accurate dose calculation and in measurement of thin layers, especially in EBRT. The use of explicit setup, irradiation techniques, Monte-Carlo calculation, and detailed skin information using high-precision ultrasound examination will promote more accurate estimations.

We think that brachytherapy with the hyaluronate gel injection procedure, via the percutaneous intercostal approach, can provide safe and eradicative high-dose irradiation with skin preservation for IMLN metastasis from breast cancer.

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The patient’s consent for publication (http://www.wjgnet.com/1949-8470office/eximage/2sign.jp) of the results was obtained before submission of the manuscript.
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Peer review
This paper is a clinical report on using high-dose rate brachytherapy to treat internal mammary lymph node metastasis of breast cancer. Using the authors' reported technique (spacer and EQD calculations), they concluded that their procedure can provide the breast cancer treatment with good skin sparing and therapeutic ratio. This paper is well organized and comprehensive.

REFERENCES

1 Chen L, Gu Y, Leaw S, Wang Z, Wang P, Hu X, Chen J, Lu J, Shao Z. Internal mammary lymph node recurrence: rare but characteristic metastasis site in breast cancer. BMC Cancer 2010; 10: 429
2 Zhang YJ, Oh JL, Whitman GJ, Iyengar P, Yu TK, Tereffe W, Woodward WA, Perkins G, Buchholz TA, Strom EA. Clinically apparent internal mammary nodal metastasis in patients with advanced breast cancer: incidence and local control. Int J Radiat Oncol Biol Phys 2010; 77: 1113-1119
3 Burman C, Kutcher GJ, Emami B, Goitein M. Fitting of normal tissue tolerance data to an analytic function. Int J Radiat Oncol Biol Phys 1991; 21: 123-135
4 Kishi K, Takiëji K, Shirai S, Sonomura T, Sato M, Yamaue H. Brachytherapy technique for abdominal wall metastases of colorectal cancer: ultrasound-guided insertion of applicator needle and a skin preservation method. Acta Radiol 2006; 47: 157-161
5 Kishi K, Sonomura T, Shirai S, Sato M, Tanaka K. Critical organ preservation in reirradiation brachytherapy by injectable spacer. Int J Radiat Oncol Biol Phys 2009; 75: S587-S594
6 Susil RC, McNutt TR, DeWese TL, Song D. Effects of prostate-rectum separation on rectal dose from external beam radiotherapy. Int J Radiat Oncol Biol Phys 2010; 76: 1251-1258
7 Prada PJ, Gonzalez H, Menéndez C, Llanaza A, Fernández J, Santamarta E, Ricarte PP. Transperineal injection of hyaluronic acid in the anterior perirectal fat to decrease rectal toxicity from radiation delivered with low-dose-rate brachytherapy for prostate cancer patients. Brachytherapy 2009; 8: 210-217
8 Pinkawa M, Corral NE, Caffaro M, Piroth MD, Holy R, Djuvik V, Otto G, Schotth F, Eble MJ. Application of a spacer gel to optimize three-dimensional conformal and intensity modulated radiotherapy for prostate cancer. Radiat Oncol 2011; 10: 436-441
9 Kishi K, Shirai S, Sato M, Sonomura T. Computer-Aided Preservation of Risk Organs in Critical Brachytherapy by Tissue Spacing With Percutaneous Injection of Hyaluronic Acid Solution. Int J Radiat Oncol Biol Phys 2007; 69: S568-S569
10 Prada PJ, Gonzalez H, Fernández J, Bilbao P. High-dose rate intensity modulated brachytherapy with external-beam radiotherapy improves local and biochemical control in patients with high-risk prostate cancer. Clin Transl Oncol 2008; 10: 415-421
11 Kishi K, Sato M, Shirai S, Sonomura T, Yamama R. Reirradiation of prostate cancer with rectum preservation: eradication high-dose-rate brachytherapy with natural type hyaluronic injection. Brachytherapy 2012; 11: 144-148
12 Kishi K, Sonomura T, Shirai S, Noda Y, Sato M, Kawai M, Yamaue H. Brachytherapy reirradiation with hyaluronate gel injection of paraaortic lymph node metastasis of pancreatic cancer: paravertebral approach—a technical report with a case. J Radiat Res 2011; 52: 840-844
13 Dubray B, Henry-Amar M, Meerwaldt JH, Noordik EM, Dixon DO, Cosset JM, Thanes HD. Radiation-induced lung damage after thoracic irradiation for Hodgkin's disease: the role of fractionation. Radiother Oncol 1995; 36: 211-217
14 Veronesi U, Marubini E, Mariani L, Valagussa P, Zucali R. The dissection of internal mammary nodes does not improve the survival of breast cancer patients. 30-year results of a randomised trial. Eur J Cancer 1999; 35: 1320-1325

15 Kajai H, Maunu P. Tangential breast irradiation with or without internal mammary chain irradiation: results of a randomized trial. Radiother Oncol 1995; 36: 172-176
16 Kirova YM. Recent advances in breast cancer radiotherapy: Evolution or revolution, or how to decrease cardiac toxicity? World J Radiol 2010; 2: 103-108
17 Clarke M, Collins R, Darby S, Davies C, Elphinstone P, Evans E, Godwin J, Gray R, Hicks C, James S, MacKinnon E, McGale P, McHugh T, Peto R, Taylor C, Wang Y. 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
18 Giordano SH, Kuo YF, Freeman JL, Buchholz TA, Hortobagyi GN, Goodwin JS. Risk of cardiac death after adjuvant radiotherapy for breast cancer. J Natl Cancer Inst 2005; 97: 419-424
19 Haybittle JL, Brinkley D, Houghton J, A’Hern RP, Baum M. Postoperative radiotherapy and late mortality: evidence from the Cancer Research Campaign trial for early breast cancer. BMJ 1989; 286: 1611-1614
20 Kirova YM, Campana F, Fournier-Bidoz N, Stihart A, Dendale R, Bollet MA, Fouquet A. Postmastectomy Electron Beam Chest Wall Irradiation in Women With Breast Cancer: A Critical Step Toward Conformal Electron Therapy. Int J Radiat Oncol Biol Phys 2007; 69: 1139-1144
21 Arthur DW, Vicius FA, Kuske RR, Wazer DE, Nag S. Accelerated partial breast irradiation: an updated report from the American Brachytherapy Society. Brachytherapy 2003; 2: 124-130
22 Niehoff P, Ballardi B, Polgár C, Major T, Hammer J, Richetti A, Kovács G. Early European experience with the MammoSite radiation therapy system for partial breast brachytherapy following breast conservation operation in low-risk breast cancer. Breast 2006; 15: 319-325
23 Fisher ER, Dignam J, Tan-Chiu E, Costantino J, Fisher B, Paik S, Wolmark N. Pathologic findings from the National Surgical Adjuvant Breast Project (NSABP) eight-year update of Protocol B-17: intraductal carcinoma. Cancer 1999; 86: 429-438
24 Fisher B, Anderson S. Conservative surgery for the management of invasive and noninvasive carcinoma of the breast: NSABP trials. National Surgical Adjuvant Breast and Bowel Project. World J Surg 1994; 28: 63-69
25 Release MAN. APBI Brachytherapy Associated with Higher Rate of Later Mastectomy, Increased Toxicities, and Post-Operative Complications, Compared to Traditional Radiation Therapy in Women with Early Breast Cancer. MD Anderson News Release 2012
26 Zwicker F, Roeder F, Thieke C, Timke M, Münter MW, Huber PE, Debus J. IMRT reirradiation with concurrent cetuximab immunotherapy in recurrent head and neck cancer. Strahlenther Onkol 2011; 187: 32-38
27 Harkenrider MM, Wilson MR, Dragun AE. Reirradiation as a Component of the Multidisciplinary Management of Locally Recurrent Breast Cancer. Clin Breast Cancer 2011; 11: 171-176
28 Lo SS, Fakiris AJ, Teh BS, Cardenes HR, Henderson MA, Forquer JA, Papiez L, McGarry RC, Wang JZ, Li K, Mayr NA, Timmerman RD. Stereotactic body radiation therapy for oligometastases. Expert Rev Anticancer Ther 2009; 9: 621-635
29 Haie-Meder C, Siebert FA, Pötter R. Image guided, accelerated, high dose brachytherapy as model for advanced small volume radiotherapy. Radiat Oncol 2011; 100: 333-342
30 Polgar C, Major T, Sulyok Z, Fröhlich G, Szabó E, Sávolt A, Mátrai Z, Tóth L, Fodor J. [Second breast-conserving surgery for breast cancer]. Radiother Oncol 2010; 52: S568-S569
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31 Kishi K, Mabuchi Y, Sonomura T, Shirai S, Noda Y, Sato M, Ino K. Reirradiation of paraaortic lymph node metastasis by brachytherapy with hyaluronate injection via paravertebral approach: With DVH comparison to IMRT. Brachytherapy 2011 Dec 28 [Epub ahead of print]

32 Kishi K, Mabuchi Y, Sonomura T, Shirai S, Noda Y, Sato M, Ino K. Eradicative brachytherapy with hyaluronate gel injection into pararectal space in treatment of bulky vaginal stump recurrence of uterine cancer. J Radiat Res 2012; 53: 601-607

33 Kishi K, Tamura S, Mabuchi Y, Sonomura T, Noda Y, Nakai M, Sato M, Ino K, Yamanaka N. Percutaneous interstitial brachytherapy for adrenal metastasis: technical report. J Radiat Res 2012; 53: 807-814

34 Kim Y, Tome WA. Is it beneficial to selectively boost high-risk tumor subvolumes? A comparison of selectively boosting high-risk tumor subvolumes versus homogeneous dose escalation of the entire tumor based on equivalent EUD plans. Acta Oncol 2008; 47: 906-916

35 Wortsman X, Wortsman J. Clinical usefulness of variable-frequency ultrasound in localized lesions of the skin. J Am Acad Dermatol 2010; 62: 247-256

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