Three-Dimensional Conformal or Stereotactic Reirradiation of Recurrent, Metastatic or New Primary Tumors

Analysis of 108 Patients

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Purpose: To analyze the outcome of reirradiation of recurrent/metastatic or new primary tumors with three-dimensional conformal (3D-CRT) or stereotactic (SRT) techniques.

Patients and Methods: 108 patients reirradiated between 01/2002 and 01/2005 at the European Institute of Oncology, Milan, Italy, were analyzed. Primary diagnosis included breast, lung, head/neck, urologic tumors, and other primaries. Curative and palliative intent were applied to 27 (25%) and 81 patients (75%), respectively. 3D-CRT and SRT were employed in 57 (53%) and 48 patients (44%), respectively, up to a mean dose of 23 Gy.

Results: Median follow-up was 7 months (range, 1–50 months). Response, stabilization, and progression were observed in 33%, 36%, and 17% of patients, respectively (15 patients were not evaluable). No severe toxicity was reported. Median overall survival amounted to 32.6 months and was longer in patients treated with curative intent.

Conclusion: A small portion of patients can be cured with a second course of radiotherapy, and in many cases, palliation can be obtained. Low toxicity of reirradiation with use of modern techniques should allow for the delivery of higher doses and, in consequence, lead to an improvement in reirradiation outcome.

Key Words: Reirradiation · Second-course radiotherapy · Retreatment · Recurrent · Second primary

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Introduction

In recent decades, the number of long-term cancer survivors has increased. Improved outcome has been attributed to earlier detection, better staging, treatment modalities, and multidisciplinary approach [20]. In consequence, new primary tumor, nodal/metastatic disease or recurrent tumor may occur in or on the border of the previous radiotherapy field. Only few patients are candidates for curative surgery, and chemotherapy alone provides limited palliation with no long-term survivors [11]. Physicians are often reluctant to offer a second radiotherapy course due to lack of experience and to potential toxicity [22]. Here, we review the experience of one center where, in 3 years, more than 100 patients were retreated using three-dimensional conformal (3D-CRT) or stereotactic radiotherapy (SRT). We analyzed the outcome in terms of tumor response, survival rates, and toxicity. Moreover, we tested the impact of various patient-, tumor-, and treatment-related factors on the outcome.

Patients and Methods

Between 01/2002 and 01/2005, 108 patients underwent reirradiation at the Division of Radiotherapy of the European Institute of Oncology, Milan, Italy. Clinical records and treatment plans of both radiotherapy courses were analyzed. Both treatments were performed with use of external-beam irradiation. Treatment was classified as “reirradiation” when the part of the first and second irradiated volumes overlapped.

There were 44 females and 64 males (Table 1). The doses of the first radiotherapy ranged from 8 to 74.4 Gy (mean, 37 Gy). Conventional or 3D-CRT techniques were used in 95 patients (88%), whereas SRT was employed in 13 patients (12%) for the first radiotherapy course. For the purpose of this study, doses > 45 Gy and 24 Gy for conventionally fractionated and hypofractionated radiotherapy, respectively, were considered curative dose levels. The first radiotherapy course had curative and palliative intent in 56 (52%) and 52 patients (48%), respectively. Reirradiation was performed for nodal/metastatic lesions, recurrent tumor, and new primary in 71 (66%), 35 (32%), and two lesions (2%), respectively. 27 patients (25%) were reirradiated with curative intent, in 81 cases (75%) reirradiation had palliative intent. The treatment schedule had been chosen at the treating physician’s discretion. The main criterion to propose reirradiation was the possibility to deliver a significant (tumoricidal) dose without exceeding the normal-tissue dose constraints. When this was not possible or if the patient had multiple symptomatic metastases, lower (palliative) dose was prescribed. The interval between the first and second radiotherapy course ranged from 8 to 26 months (median, 14 months). The reirradiated sites included bone, brain, head and neck, abdomen/pelvis, and lung in 27%, 22%, 18%, 18%, and 15% of patients, respectively. The reirradiation doses varied from 4 to 60 Gy (mean, 23 Gy) prescribed in the International Committee of Radiation Units (ICRU) reference point [8]. In the majority of patients, hypofractionation was employed for reirradiation (mean dose/fraction 6.4 Gy, range, 1–18 Gy, given at 1- to 2-day interfraction interval).

3D-CRT was used to treat 57 patients (53%), SRT was used in 48 patients (44%), and in three cases high-dose-rate brachytherapy was added to 3D-CRT or SRT (3%). Information from diagnostic computed tomography (CT) scan, positron emission tomography and/or magnetic resonance imaging was used for reirradiation target delineation (image fusion was performed in a few patients).

3D-CRT was performed with 6- to 18-MV photons (linear accelerator). CT-based (3–5 mm slicing) treatment-planning systems were used. Three-dimensional dose calculation taking scatter from adjacent tissues into account was used. Individual immobilization system, simulation of all therapy phases, orthogonal laser beams (to ensure the position reproducibility during simulation, dosimetric CT scan and therapy), beam’s eye views, dose-volume histograms (DVHs) calculation, customized shielding/multileaf collimator, in vivo dosimetry and electronic portal verification (EPID) were employed in all patients.

For SRT, Brainscan treatment-planning system (v.5.31, BrainLAB, Feldkirchen, Germany) was used. In all SRT patients, contrast medium was administered for simulation CT scan (except for parenchymal lung lesions). Treatment plans for cranial lesions consisted of four to five noncoplanar 6-MV conformal dynamic arcs obtained with the micro-multileaf collimator m3 (BrainLAB). Patients were immobilized with the BrainLAB head-and-neck mask and positioned according

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients</th>
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<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>• Male</td>
<td>64 (59)</td>
</tr>
<tr>
<td>• Female</td>
<td>44 (41)</td>
</tr>
<tr>
<td>Agea (years)</td>
<td></td>
</tr>
<tr>
<td>• Mean (range)</td>
<td>59.5 (21–91)</td>
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<td>• 100</td>
<td>20 (18)</td>
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<td>• 90</td>
<td>23 (21)</td>
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<td>• 80</td>
<td>15 (14)</td>
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<tr>
<td>• 70</td>
<td>5 (5)</td>
</tr>
<tr>
<td>• 60</td>
<td>5 (5)</td>
</tr>
<tr>
<td>• Unknown</td>
<td>40 (37)</td>
</tr>
</tbody>
</table>

Primary diagnosis

• Breast cancer 30 (28)
• Lung cancer 22 (20)
• Head-and-neck cancer 18 (18)
• Urologic tumors 10 (9)
• Gynecologic malignancies 8 (7)
• Gastrointestinal malignancies 6 (6)
• Central nervous system malignancies 5 (5)
• Other primaries 9 (8)

*a at reirradiation

Table 1. Patient characteristics. RT: radiotherapy.

Tabelle 1. Patientencharakteristik. RT: Radiotherapie.