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Original article

Intensity modulated radiation therapy with simultaneous integrated boost in early breast cancer irradiation. Report of feasibility and preliminary toxicity

Radiothérapie conformationnelle avec modulation d'intensité avec boost *simultané dans le cancer du sein de stade T1-2, N0-1, M0. Faisabilité et toxicité*

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ABSTRACT

Purpose. – To investigate the feasibility and tolerance in the use of adjuvant intensity modulated radiation therapy (IMRT) and simultaneous integrated boost in patients with a diagnosis of breast cancer after breast-conserving surgery.

Patients and methods. – Between September 2011 to February 2013, 112 women with a diagnosis of early breast cancer (T1-2, N0-1, M0) were treated with IMRT and simultaneous integrated boost after breast-conserving surgery in our institution. A dose of 50 Gy in 25 fractions was prescribed to the whole breast and an additional dose of radiation was prescribed on the tumour bed. A dose prescription of 60 Gy in 25 fractions to the tumour bed was used in patients with negative margins after surgery, whereas if the margins were close (< 1 mm) or positive (without a new surgical resection) a dose of 64 Gy was prescribed. All patients were followed with periodic clinical evaluation. Acute and late toxicity were scored using the EORTC/RTOG radiation morbidity score system. Both patient and physician recorded cosmetic outcome evaluation with a subjective judgment scale at the time of scheduled follow-up.

Results. – The median follow-up was 28 months (range 24–40 months). The acute skin grade toxicity during the treatment was grade 0 in 8 patients (7%), grade 1 in 80 (72%), grade 2 in 24 cases (21%). No grade 3 or higher acute skin toxicity was observed. At 12 months, skin toxicity was grade 0 in 78 patients (70%), grade 1 in 34 patients (30%). No toxicity grade 2 or higher was registered. At 24 months, skin toxicity was grade 0 in 79 patients (71%), grade 1 in 33 patients (29%). No case of grade 2 toxicity or higher was registered. The pretreatment variables correlated with skin grade 2 acute toxicity were adjuvant chemotherapy ($P = 0.01$) and breast volume $\geq 700\,cm^3$ ($P = 0.001$). Patients with an acute skin toxicity grade 2 had a higher probability to develop late skin toxicity ($P < 0.0001$). In the 98% of cases, patients were judged to have a good or excellent cosmetic outcome. The 2-year-overall survival and 2-year-local control were 100%.

Conclusion. – These data support the feasibility and safety of IMRT with simultaneous integrated boost in patients with a diagnosis of early breast cancer following breast-conserving surgery with acceptable acute and late treatment-related toxicity. A longer follow-up is needed to define the efficacy on outcomes.

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RÉSUMÉ

Objectif de l'étude. – Étudier la faisabilité et la tolérance d'une radiothérapie conformationnelle avec modulation d'intensité (RCMI) et *boost* simultané pour des cancers du sein après chirurgie conservatrice.
Patientes et méthodes. – Entre septembre 2011 et février 2013, 112 patientes atteintes d'un cancer du sein de stade T1-2, N0-1, M0 ont reçu une RCMI avec *boost* simultané après chirurgie conservatrice. Une dose de 50 Gy en 25 fractions a été prescrite dans le volume cible prévisionnel mammaire, ainsi qu'un *boost* dans le lit tumoral, pour atteindre 60 Gy en 25 fractions en cas de marges d'exérèse saines et 64 Gy en cas de marges étroites (moins de 1 mm) ou d'atteinte des tranches de section. Les patientes ont été régulièrement suivies, et la toxicité aiguë et tardive évaluée selon la classification de l'European Organization for Research and Treatment of Cancer (EORTC) et du Radiation Therapy Oncology Group (RTOG). Le résultat esthétique a été évalué subjectivement à la fois par la patiente et le médecin à la fin du suivi.
Résultats. – Le suivi a été en médiane de 28 mois (24–40). La toxicité cutanée aiguë a été de grade 0 chez huit patientes (7 %), 1 chez 80 (72 %), 2 chez 24 (21 %) et 3 chez aucune. À 12 mois, la toxicité cutanée était de grade 0 chez 78 (70 %), 1 chez 34 (30 %), 2 ou plus chez aucune, à 24 mois 0 chez 79 (71 %), 1 chez 33 (29 %), 2 ou plus chez aucune. Il y avait une corrélation entre la toxicité cutanée de grade 2 et la chimiothérapie adjuvante ($p = 0{,}01$) et un volume mammaire 700 cm^3 ou plus ($p = 0{,}001$). La toxicité tardive s'est avérée plus fréquente en cas de toxicité aiguë de grade 2 ($p < 0{,}0001$). Le résultat esthétique était bon ou excellent dans 98 % des cas. La probabilité de survie à 2 ans était de 100 %.
Conclusion. – La RCMI avec *boost* simultané s'est avérée faisable et sure après chirurgie conservatrice chez les patients atteintes d'un cancer du sein de stade T1-2, N0-1, M0. Un suivi plus long est requis pour tirer des conclusions définitives.
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1. Introduction

Adjuvant radiotherapy is the standard treatment in patients with a diagnosis of breast cancer after conservative surgery. Several clinical trials reported comparable results in terms of overall survival, local control and a more acceptable cosmetic profile when breast-conserving surgery and adjuvant radiotherapy is used among a radical mastectomy [1–4].

An Early Breast Cancer Trialists' Collaborative Group (EBCTCG) analyses demonstrated a proportional reduction of 70% of local recurrence when adjuvant radiotherapy is used after breast-conserving surgery and a 15-year absolute reduction risk of death corresponding to 5.3% [5,6].

The European Organisation for Research and Treatment of Cancer (EORTC) randomized trial studied, in 5569 patients with a diagnosis of breast cancer, the effect of an additional dose of radiation on the tumour bed, after whole breast irradiation (50 Gy/25 fractions): the addiction of 16 Gy to the surgery cavity reduced the local recurrence from 7.3% to 4.3% at 5 years [3].

As reported in the literature, the use of sequential or concomitant boost with a 3-dimensional conformal radiotherapy approach demonstrated good results in terms of feasibility and cosmetic [7–9].

Technological improvement and introduction in the clinical practice of intensity modulated radiation therapy (IMRT) can lead to new approaches in the treatment of breast cancer after conserving surgery, despite the fact that IMRT is still not considered the standard technique.

In terms of dose distribution, IMRT can decrease the dose on normal tissue (i.e. lung and heart) during whole breast irradiation and guarantee a better dose distribution on the tumour bed boost [10]. Recent experiences did not observe any dosimetric difference in the use of sequential boost or simultaneous integrated boost [11,12].

However, the literature reported a limited number of clinical analyses in the use of IMRT and simultaneous integrated boost.

The purpose of this study was to provide further data of feasibility and safety using IMRT and simultaneous integrated boost in patients with a diagnosis of early breast cancer treated with a conserving surgery.

2. Material and methods

2.1. Patients' selection

Between September 2011 and February 2013,112 consecutive invasive breast cancer patients received an IMRT and simultaneous integrated boost at our institution. Inclusion criteria were: pT1-2 disease, pN0-1 nodes status, no neoadjuvant systemic therapy, non-metastatic disease.

All patients were staged using the American Joint Committee on Cancer (AJCC) 2009 criteria. Before IMRT and simultaneous integrated boost treatment, all patients were generally staged with: clinical examination, mammography, echography (breast and bilateral axilla) and magnetic resonance imaging. In selected cases, a bone scan was requested in order to rule out metastatic disease.

Patients' baseline characteristics are summarized in Table 1. Estrogen receptors were positive in 90% of cases, progesterone receptors in 79%, HER-2 in 10%. All patients receiving adjuvant chemotherapy and/or hormonal treatment were included in the study.

2.2. Treatment procedure

All patients received a breast-conservative surgery and sentinel lymph node biopsy, followed by axillary dissection in the case of positivity. All cases were discussed in a Breast Cancer Board. In patients with a positive surgical margin, defined as extension of the disease within 1 mm of the inked surgical margin, re-excision was strongly recommended.

Adjuvant chemotherapy, hormonal treatment, monoclonal antibodies and regional radiotherapy were prescribed according to the international guidelines [13]. In the current series, adjuvant systemic therapies were administered as follows: chemotherapy in 23 patients (20%), hormonal therapy in 78 (70%), trasuzumab in 11 (10%). Radiotherapy of breast gland started not later than 4 weeks after surgery and/or by the end of chemotherapy.

Patients were immobilized in a supine position with torso raised and arms elevated on Posi-Board frame (Civco Inc.®) and a

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