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GERICO-03 phase II trial of accelerated and partial breast irradiation in elderly women: Feasibility, reproducibility, and impact on functional status

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ABSTRACT

PURPOSE: To analyze the feasibility, reproducibility, and impact on functional status of postoperative accelerated and partial breast irradiation (APBI) using interstitial high-dose rate-brachytherapy in women older than 70 years.

METHODS AND MATERIALS: From July 2004 to April 2008, 46 patients were screened for enrollment in a nationwide prospective Phase II trial. A total of 40 patients were eligible according to the inclusion criteria (aged >70 years, T1–2 <30 mm, and pN0). The total delivered dose was 34 Gy of 10 fractions for 5 days. Feasibility and reproducibility were evaluated using a Quality Index (QI) defined as (V_{100}% − clinical target volume)/V_{100}%. Skin toxicity was reported using *Common Terminology Criteria for Adverse Events* version 3.0. ABPI impact on functional dependence was evaluated using the Activity of Daily Living and Instrumental Activity of Daily Living scales. Reproducibility and feasibility were assessed with the optimal two-stage design of Simon.

RESULTS: Median age was 74 years (70–87 years). All patients were treated according to the protocol. Median Quality Index calculated for the 40 eligible patients was 13.3% (1–70%). It was considered acceptable, partially acceptable, and nonacceptable in 10, 28, and 2 patients, respectively. Within 12 months after APBI, overall rates of toxicity were 59%, 28%, and 2% for Grade 1, 2, and 3 events, respectively. Twelve months after APBI, 35 patients (87%) achieved excellent/good cosmetic result. Compared with baseline values, Activity of Daily Living and Instrumental Activity of Daily Living scores remained unchanged 6 and 12 months after APBI.

CONCLUSIONS: APBI by means of high-dose rate-brachytherapy is a feasible/reproducible technique without significant impact on functional dependence in the treatment of elderly women with early breast cancer.

Keywords: Elderly; Breast cancer; Partial breast irradiation; Brachytherapy; Functional status

Introduction

Management of early breast cancer in the elderly has become a societal and medical concern both in North America and Western Europe, where the number of women affected by the disease is continuously increasing in all age

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categories, with a higher prevalence in women aged 65 years or older (1). Breast conservative treatment (BCT), defined as a postlumpectomy whole-breast radiotherapy (WBRT), followed by adjuvant endocrine therapy, has definitively emerged as the gold standard for patients aged 50 years and older presenting with an early breast cancer and favorable prognostic factors (i.e., tumor size <3 cm, negative lymph node dissection, and positive estrogen/progesterone receptor status) (2). Although focusing on a highly selected subset of patients regarding local recurrence prognostic factors (T1, pN0, without extensive intraductal component, and/or lymphatic vessel involvement), postoperative WBRT remains necessary to reduce the risk of local recurrence (3).

The therapeutic approach in the elderly differs from the one in the younger patients. Elderly patients are indeed prone to geriatric frailty characterized by a limited life expectancy and comorbid conditions different from breast cancer that increase with age in incidence and severity. These factors can limit the ''visibility'' of the expected long-term benefits theoretically brought by standard adjuvant treatments (4). Difficulty of compliance is also an issue to take into account in elderly breast cancer management (5). Because of uneasy transportation from home to radiation therapy facility (RTF), many elderly women fear that WBRT currently available will reduce their mobility and impact negatively on their quality of life. In the United States, the distance from RTF has been correlated with the decreased likelihood that women living far from RTF would undergo BCT with, as a consequence, their preference for radical mastectomy (6). Taken all together, these findings led the International Society of Geriatric Oncology to recommend the development of radiation therapy regimen specifically adapted to the elderly patients (7).

Can a compromise be reached between a WBRT treatment lasting 5–6 weeks and the omission of irradiation? The American Society of Radiation Oncology (ASTRO) and European Society for Radiotherapy and Oncology (ESTRO) conferences have proposed that accelerated and partial breast irradiation (APBI) should be considered as an adapted therapeutic alternative for the subgroup of patients with low-risk breast cancer (8, 9) and more specifically for the elderly (10).

GERICO (standing for GERIatrie onCOlogie) is a French multidisciplinary group founded in 2002 under the auspices of UNICANCER (Fédération Nationale des Centers de Lutte Contre le Cancer). It is dedicated to clinical research in geriatric oncology and focuses its interest on investigating the impact of cancer treatment on functional status, mostly with systemic strategies (11). The GERICO-03 Phase II program applied the same concept and methodology to the question of local treatment (BCT), namely APBI, for early breast cancer in elderly women. We report here the results for the primary endpoint (feasibility and reproducibility) and functional status. Medicoeconomic data will be reported later.

Methods and materials

Study design

GERICO-03 was a nationwide multicentric prospective open-label nonrandomized Phase II trial evaluating the APBI technique by means of postoperative interstitial high-dose-rate brachytherapy (IHDRB). The protocol was reviewed and approved by the ethical committee (Comité de Protection des Personnes, Ile de France Vii, Kremlin-Bicetre, Kremlin-Bicêtre 94270). The study was conducted according to the Declaration of Helsinki and the Good Clinical Practice requirements.

Patient eligibility

Women aged 70 years and older with a Karnofsky index of 70% or higher, presenting with an operable early breast cancer and no clinically involved axillary node, were screened for participation. Systematic workup included bilateral mammogram, abdominal CT scan or liver ultrasonography, bone scan, and chest X-ray. Patients were definitely included after checking pathology inclusion criteria, such as (*1*) histologically proven invasive noninflammatory and nonlobular breast cancer, (*2*) tumor sized 30 mm or less, (*3*) at least six nodes in the axillae clearance, (*4*) malignancy-free excision margins measuring 2 mm or more, and (*5*) at least three clips placed within the excision cavity during lumpectomy. Written informed consent was obtained preoperatively. Exclusion criteria included: *in situ* lobular/ductal carcinoma, multicentric tumor, peritumoral lymphatic emboli, any preoperative treatment for the same tumor, previous history of breast plastic surgery and of other malignant tumors, and delay of 6 weeks or more between lumpectomy and first day of irradiation.

Aims of the study and endpoint assessment

The primary endpoint was the feasibility and reproducibility of ABPI using IHDRB. The secondary endpoints included the following: (*1*) APBI impact on functional status, (*2*) local recurrence- and distant metastasis-free survivals and specific survival, (*3*) adverse effects and cosmetic results, (*4*) quality of life, and (*5*) economic impact of APBI.

Feasibility and reproducibility assessment

Because the brachytherapy process highly depends on the geometry of catheter placement in the tumor bed and the delineation of the clinical target volume (CTV), feasibility and reproducibility assessments were based on a quantitative analysis of the implant quality. The *quality index* (QI*) was defined as follows:

$$\mathrm{QI}* = \frac{|V_{100} - \mathrm{CTV}|}{V_{100}} \times 100$$

where V_{100} is the volume receiving 100% of the prescribed dose and V_{CTV} is the outlined volume.