

# Use of Gentian Violet in the Treatment of Severe Radiodermatitis Secondary to Adjuvant Radiotherapy in Breast Cancer

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*Adjuvant radiotherapy is indicated for patients with conservatively or radically operated breast cancer, demonstrating the benefit of this type of treatment for local recurrence rate and survival. Radiodermatitis are radiation-induced skin reactions, a significant side effect of cumulative ionizing radiation in significant doses at the skin level during the treatment of various tumor localizations. This study presents aspects regarding prevention and treatment of radiodermatitis in patients with adjuvant irradiated breast cancer treated in the Regional Institute of Oncology Iasi. In the study group, use of gentian violet has helped to alleviate these side effects of irradiation, both in intensity and duration, with an important impact on the quality of life of the patients.*

*Key words: radiotherapy, radiodermatitis, gentian violet, breast cancer*

Radiotherapy is the treatment using ionizing radiation for malignant neoplasms and, more rarely, for some benign conditions. Radiotherapy can be curative, healing, or palliative, for symptom relief without increasing survival.

Adjuvant radiotherapy consists of irradiation of the breast after conservative surgical treatment or of the thoracic wall and the regional lymph nodes after radical mastectomy with axillary lymphadenectomy.

External radiotherapy is administered with linear accelerators of high energy (6-15MV), which operate dually, having both X-ray and electron-mode.

Irradiation of the entire breast after conservative surgery for in situ ductal carcinoma lowers the risk of local recurrence with survival rates equal to those resulting from mastectomy (level of evidence I, A). Adjuvant radiotherapy in conservatively operated invasive breast cancer reduces the risk of locoregional and distant recurrence by 15% to 10 years and breast cancer mortality by 4% at 15 years (17 randomized trials, 10,801 patients). Additional irradiation with 10-16Gy of the tumor bed (boost) provides a further reduction in the relapse rate in patients who have unfavorable risk factors (level of evidence I, A).

In radically operated invasive breast carcinoma in patients with positive lymph nodes, adjuvant radiotherapy reduces the risk of locoregional recurrence and at a distance of 10% to 10 years and the risk of mortality by 8% at 20 years.

Adjuvant radiotherapy is always recommended for patients with breast cancer at high risk of recurrence:  $\geq 4$  positive axillary lymph nodes and T3-T4 tumors independent of lymph node status, and recent trials also indicate benefits for patients with 1-3 positive axillary lymph nodes (level of evidence I, A).

Almost all cancer patients receiving radiation therapy will develop a radiodermatitis form of varying degrees, from erythema, dry desquamation (grade I) to severe wet desquamation and ulceration (grade II-IV) [1,2].

Radiation-induced skin side effects have been recognized and reported scientifically since the beginning of the 20th century [3,5]. These lesions can lead to a decrease in quality of life, local discomfort, pain, aesthetic appearance change, decreased treatment compliance,

sometimes discontinuation of treatment with a decrease in therapeutic effect by increasing the overall duration of treatment [4].

The first visible cutaneous change is erythema, which occurs in more than 90% of patients irradiated, followed by desquamation in more than 30% of patients [6]. Sometimes after several years of treatment, heavier reversible lesions of chronic radiodermatitis (fine, dry skin, atrophy, fibrosis, telangiectasia, pigmentation changes) occur.

The intensity of radiation-induced skin reactions depends on numerous risk factors that have been categorized in the literature as being related to the patient (intrinsic), treatment (extrinsic), or mixed [7,8]. Intrinsic risk factors include age, gender, smoking, poor nutritional status, obesity, comorbidities (diabetes), hormonal status, exposure to ultraviolet radiation (UV). Treatment-related factors include the total radiation dose, dose fractionation mode, fractional dose, type of radiation used, radiosensitizers, chemotherapy or concomitant biological therapies, irradiated target volume, use of boluses [1,2,7,9-11]. The severity and duration of radiation induced skin reactions in cancer patients treated with the intensity modulated radiotherapy (IMRT) are lower compared to conformational 3D radiotherapy [12-14].

To prevent and reduce the intensity of radiodermatitis, moisturizing creams, topical corticosteroids, proteolytic enzymes, zinc or silver sulfadiazine are used but there is no consensus on the recommended standard [15-19].

Methyl violet belongs to the aryl-methane colorants category, being a mixture of tetramethyl, pentamethyl, hexamethyl pararosaniline. Depending on the percentage of the three dyes, different color shades can be obtained (fig. 1, 2, 3).

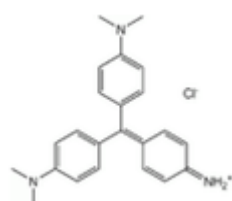


Fig.1. Methyl violet 2B

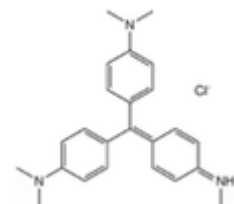


Fig.2. Methyl violet 6B (gives a darker shade compared to tetramethyl)

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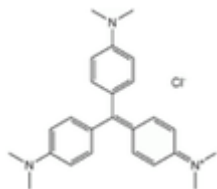


Fig.3. Methyl violet 10B (provides an intermediate hue, darker than 2B, but lighter than 6B)

Hexamer 10B (gentian violet) has antibacterial and antifungal properties. The 1% gentian violet, 96% ethyl alcohol, and distilled water solution for external use is used as a local disinfectant and antiseptic.

## Experimental part

### Materials and methods

The study was conducted in the Radiotherapy Laboratory at the Regional Institute of Oncology. For all patients, the treatment plan was performed by simulation using a SOMATOM DEFINITION Siemens CT scanner. The patient is positioned on an inclined board with an adjustable angle, markers are placed on the chest, the area of interest is scanned, followed by delineation of target volumes and organs at risk, followed by dosimetry and determination of treatment parameters (fig. 4).



Fig.4. Patient positioning for CT simulation

The Eclipse treatment plan system was used, and irradiation was performed with photons with 6MV/10MV energies at the Clinac IX linear particle accelerator (fig. 5).



Fig.5. Positioning the patient for treatment, to the accelerator

The study included 78 breast cancer patients aged 32-81, stages I-III, 19 patients (24.36%) operated conservatively, 59 patients (75.64%) operated radically, who received adjuvant radiotherapy at doses total of 42.56Gy / 16 fractions / 2.66Gy / fraction / 22 days for 47 patients (60.25%) and 50Gy / 25 fractions / 2Gy / fraction / 33 days for 31 patients (39.75%), 10Gy boost for 4 patients (5.12%). For 20 patients (25.64%) a bolus of 5mm or 10mm thickness was used. The two types of fractionation are equivalent in terms of local control rate and toxicity, but, for radiobiological reasons, the hypofraction scheme is preferred to the conventional one [20].

Classification of radiodermatitis was performed according to the 2010 RTOG criteria (Radiation Therapy Oncology Group). In order to prevent severe radiodermatitis, patients have used moisturizing creams daily after each irradiation session, 2-3 times a day, in the first 10-15 days of treatment, followed by topical corticosteroids alternatively with moisturizing creams. The gentian violet solution was administered topically only to patients who experienced wet desquamation injuries. Patient monitoring on the occurrence and evolution of

radiodermatitis was performed weekly during treatment and post-treatment for patients with severe radiodermatitis, subsequently 3-6 months for 2 years.

## Results and discussions

In the first week of treatment, no skin side effects were reported, 72 patients (92.3%) had grade I radiodermatitis (moderate erythema, as illustrated in fig. 6) at the end of the second treatment week. At the end of treatment 3 patients (3.84%) presented grade I radiodermatitis, 50 patients (64.1%) experienced grade II radiodermatitis (intense erythema, dry desquamation, pruritus, pain), 23 patients (29.48%) presented grade III radiodermatitis (wet desquamation, pain), 2 patients (2.56%) had grade IV radiodermatitis (ulcers, pain).



Fig.6. Grade I radiodermatitis

The radiation doses to which radiodermatitis occurred were 20-30Gy for erythema, 30-40Gy for dry desquamation, over 40Gy for wet desquamation.

In conservatively treated patients, grade III radiodermatitis was recorded in 12 patients (63.15%), of whom 2 patients with bulky breasts, 3 patients with boost (60Gy total dose of radiation), 2 patients with diabetes, one patient with concomitant biologic treatment (Trastuzumab).

Grade III radiodermatitis in radically operated patients was recorded in 11 patients (18.64%), of whom 5 bolus patients (3 boluses of 10 mm and 2 boluses of 5 mm), 3 patients with diabetes and 2 patients with concomitant biologic treatment (Trastuzumab).

Among patients with grade IV radiodermatitis, a patient was conservatively operated and irradiated with boost and a patient was radically operated and a bolus of 10 mm was used to adequately irradiate the thoracic wall. We mention that the acute skin side effects recorded did not cause the interruption of irradiation.

Since the occurrence of wet desquamation injuries, no moisturizing creams or topical corticosteroids were applied, and the patients used 1% gentian violet solution, 3-4 daily applications, on average for two weeks. Applying this dye reduced the pain sensation in all patients, has favored reepithelization and complete remission of radiation-induced lesions.

Of late skin effects, fibrosis in a patient (1.28%) and discreet pigmentation changes were observed in 4 patients (5.12%).

The results obtained are consistent with those in the literature, which indicate the occurrence of erythema in more than 90% of treated patients and desquamation in more than 30% of the irradiated patients, remitting acute cutaneous lesions in 3-4 weeks after the end of treatment [6,21].

## Conclusions

Acute radiodermatitis occurs frequently in patients following radiotherapy, following cytokine-mediated inflammation and radiation-induced DNA damage.

Maintaining an adequate degree of skin hydration reduces the severity of radiodermatitis, the use of topical corticosteroids and antibacterial and antifungal solutions prevents overinfection of these lesions with better results in repairing acute lesions and reducing the incidence of chronic lesions.

Recent technical advances in radiotherapy have been able to partially improve skin adverse reactions, but these remain significant in some patients, which motivates future studies on new therapies for the prevention and treatment of radiodermatitis in order to increase the quality of life of the oncological patient.

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