

Hypoesthesia, pain and disability of upper limb after adjuvant radiotherapy for breast cancer*

Hipoestesia, dor e incapacidade no membro superior após radioterapia adjuvante no tratamento para câncer de mama

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SUMMARY

BACKGROUND AND OBJECTIVES: Surgery and radiotherapy (RT) may induce upper limb (UL) pain, functional disorder and daily life activities impairment. This study aimed at evaluating and comparing superficial sensitivity (SS) on the dermatome corresponding to the intercostobrachial sensory nerve (ICBN), pain and disability of UL ipsilateral to surgery before and after adjuvant RT.

METHOD: Twenty females submitted to surgery including axillary lymphadenectomy (AL) were evaluated before and immediately after adjuvant RT (25-30 sessions). The following tools were used to evaluate SS, pain and disability: esthesiometry, McGill Pain Questionnaire (MPQ), Pain Rating Index and shoulder disability (SPADI). Two measures were obtained from

MPQ: number of words chosen (NWC) and pain rating index (PRI). Wilcoxon Signed Rank Test for paired samples was used for intragroup comparison, considering significant $p < 0.05$.

RESULTS: There has been significant SS decrease after RT by increased esthesiometer pressure from 1.9 ± 0.2 to 2.8 ± 0.2 ($p = 0.004$) indicating hypoesthesia. There has been no difference in contralateral UL. NWC and PRI scores have significantly increased ($p = 0.005$ and $p = 0.006$) after RT. There has been significant total SPADI score increase after RT ($p = 0.0001$), with increased disability from 24.6 ± 5.7 to 39.2 ± 5.7 ($p = 0.001$) and pain from 26.3 ± 6.4 to 48.4 ± 7.1 ($p = 0.001$).

CONCLUSION: Hypoesthesia was identified in the ICBN pathway, in addition to UL pain and disability after adjuvant RT.

Keywords: Breast cancer, Hypoesthesia, Mastectomy, Pain, Physical therapy, Radiation therapy.

RESUMO

JUSTIFICATIVA E OBJETIVOS: Tratamento cirúrgico e radioterapia (RT) podem provocar dor no membro superior (MS), distúrbio funcional e prejuízo nas atividades de vida diária. O objetivo deste estudo foi avaliar e comparar a sensibilidade superficial (SS) no dermatomo correspondente ao nervo sensitivo intercostobraquial (NICB), a dor e a incapacidade do MS homolateral à cirurgia antes e após RT adjuvante.

MÉTODO: Vinte mulheres submetidas à cirurgia incluindo linfadenectomia axilar (LA) foram avaliadas antes e imediatamente após a RT adjuvante (25-30 sessões). Para avaliar a SS, dor e incapacidade foram utilizadas: a estesiometria, o Questionário de Dor McGill (MPQ) e o Índice de Dor e Incapacidade no ombro (SPADI).

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Duas medidas foram obtidas através do MPQ: número de palavras escolhidas (NWC) e índice de dor (PRI). Para comparação intragrupo, adotou-se teste de *Wilcoxon Signed Rank Test* para amostras pareadas, $p < 0,05$.

RESULTADOS: Após a RT houve redução significativa da SS pelo aumento da pressão exercida pelo estesiômetro de $1,9 \pm 0,2$ para $2,8 \pm 0,2$ ($p = 0,004$) indicando hipoestesia. No MS contralateral não houve diferença. Escores do NWC e do PRI aumentaram significativamente ($p = 0,005$ e $p = 0,006$) após a RT. Observou-se aumento significativo do escore total do SPADI após a RT ($p = 0,0001$), com aumento da incapacidade de $24,6 \pm 5,7$ para $39,2 \pm 5,7$ ($p = 0,001$) e a dor de $26,3 \pm 6,4$ para $48,4 \pm 7,1$ ($p = 0,001$).

CONCLUSÃO: Foi identificada hipoestesia no trajeto do NICB, dor e incapacidade no MS após a RT adjuvante.

Descritores: Dor, Fisioterapia, Hipoestesia, Mastectomia, Neoplasias da mama, Radioterapia.

INTRODUCTION

Breast cancer (BC) is the tumor of highest incidence among females being in Brazil the major cause of death by malignant diseases among females. For 2012 it is estimated that there will be 52680 new BC cases¹. In spite of the evolution in diagnosis and the possibility of using the sentinel lymphnode technique, radical or conservative surgical treatments still prevail. Axillary lymphadenectomy (AL) is most commonly used for disease staging and orientation about the choice of adjuvant therapy. In addition to surgery, complementary treatments such as chemotherapy (CT), radiation therapy (RT) and/or hormonotherapy may be used.

Although BC surgery brings several benefits, there may be complications, such as local infections, skin necrosis, scar complications, movement amplitude disorders, lymphedema, functional changes, nervous injuries, pain and sensitivity disorders in the upper limb (UL) ipsilateral to the operated breast. It is believed that AL is one of the major justifications for postoperative complications and morbidities, exactly due to the resection of lymphnodes, the location and extension of the surgical approach¹⁻⁵.

RT may be used as adjuvant or neoadjuvant therapy for surgery. It is a method that destroys local tumor cells with ionizing radiation beams produced by devices or emitted by natural radioisotopes. A pre-calculated radiation dose, expressed in centigray (cGy) or gray (Gy) is applied for a certain time and in a certain volume of tissue^{4,5}. Radiation also affects normal tissues causing side effects such as pain, fatigue, sensory and skin changes,

such as radiodermatitis. Approximately 90% of patients may experience some dose-dependent skin reaction^{4,5}.

RT-induced skin changes may interfere with the superficial sensitivity (SS) of the irradiated region, but it is believed that the major cause of sensory changes is total or partial injury of the sensory intercostobrachial nerve (ICBN) during surgery⁶. ICBN is derived from lateral cutaneous branches of the second and third intercostal nerves and its injury is responsible for frequent complaints of discomfort or unpleasant sensation, that is, it may induce disesthesia of the postero-medial border of upper arm, axilla and/or chest wall of the affected side. In the literature as well as in the clinical practice, several females may complain of hypoesthesia, anesthesia, burning, punctiform pain and even hyperesthesia^{6,7}.

The association of factors triggered by surgical treatment and RT may negatively interfere in the daily life of these females, causing UL pain, functional disorder and impairment of their daily activities^{8,9}, in addition to the possibility of such symptoms getting worse after RT⁷. Clinical complaint of sensitivity changes is very common, but many professionals do not value it, because it is a persistent symptom caused by sensory nerve injury. Recognizing the different aspects of sensitivity, in addition to the presence of some type of disability is indeed important for future healing and preventive actions to decrease physical, emotional and social impact of BC and its adjuvant treatments.

This study aimed at evaluating and comparing superficial sensitivity in the dermatome corresponding to ICBN, as well as pain and disability of the upper limb ipsilateral to surgery in females submitted to axillary lymphadenectomy before and after RT.

METHOD

This was an observational and longitudinal study carried out from August to October 2011, in the Radiation Therapy and Physical Therapy Sector of the Urgency Hospital of Sergipe (HUSE) and in the Beneficence Foundation Surgery Hospital (FBHC), Aracaju, SE, and all participants have signed the Free and Informed Consent Term.

Inclusion criteria were females submitted to surgery associated to AL to treat BC and who would start adjuvant therapy. Those submitted to bilateral surgery, breast reconstruction or breast prosthesis implant were excluded, in addition to neoadjuvant RT, presence of UL lymphedema, active infectious processes, morbid obesity, neuropathic diseases and/or sensitivity changes existing before surgery, presence of open wounds in the

ICBN pathway, orthopedic changes, those having undergone UL physical therapy during the research period and those with understanding difficulties or mental confusion to perform physical tests and answer to questionnaires. Initially, personal and oncologic information was collected with the following information: age, marital status, profession, body mass index (BMI), associated diseases, surgical history (type and time elapsed after surgery, side, adjuvant treatment and associated diseases), among others.

RT was performed during five or six weeks (depending on the dose) with daily applications on breast or breastplate, and axilla and clavicular fossa, however in lower doses. Before starting RT and in the last session, superficial sensitivity (SS) on ICBN pathway on upper limbs (UULL)¹⁰ was evaluated, upper limb pain was characterized by McGill pain Questionnaire (MPQ)¹¹ and UL disability was evaluated by the Shoulder Pain and Disability Index (SPADI)¹². Final evaluations were carried out in the last or one before last session due to practical service questions and the availability of patients' transportation. SS was evaluated by an esthesiometer made up of pairs of six Semmer Weinstein (Sorri[®]) monofilaments with increasing tensile strengths, previously calibrated in a precision analytic scale (CKA[®]). Pressure strength values in grams (g) after calibration were attributed to each filament as follows: green (0.05 g), blue (0.2 g), violet (2.6 g), dark red (3.6 g), orange (9.4 g) and magenta red (107.9 g).

The third violet filament (2.6 g) was considered as normality value after calibration based on the control limb. Above this value, sensitivity was considered decreased, and below this value, sensitivity was considered preserved. The following markings were made to standardize the esthesiometric test: the distance between the coracoid process and the medial epicondyle was divided in three equal spaces, considering three points: proximal (P1), distal (P2) and medium (P3), which corresponds to the medium point between P1 and P2. As from P1, a point was marked 3 cm below toward the posterior arm; as from P3, a point was marked at 2.5 cm; and as from P2, another point was marked at 2 cm. Esthesiometry was performed exactly on those points (Figure 1).

To evaluate SS, patients remained with their eyes closed and in the supine position, with the shoulder abducted 90 degrees, external rotation and with the forearm flexed in 90 degrees. The monofilament was perpendicularly applied to skin, mildly pressing until the initial filament curvature, and then it was removed. Measure was duplicated and incremental with regard to pressure, considering as skin sensory threshold the filament where patients reported feeling the touch. Measure was repeated twice



Figure 1 – Points to evaluate superficial sensitivity on the dermatome of intercostobrachial sensory nerve (ICBN).

and result was recorded as from the sum and the mean. Both UULL were evaluated, being the ipsilateral to surgery considered affected and the contralateral adopted as control limb. The lower the sensitivity, the higher the pressure, thus higher value in grams of the esthesiometric measurement.

The ICBN dermatome also involves the axillary region, but this region was not evaluated because complaints of discomfort are in general related to UL and also to mastectomy scar, which may prolong to the axilla impairing sensory response.

The Brazilian version of McGill Pain Questionnaire (Br-MPQ) was used in the form of interview to characterize pain. Br-MPQ has two indices: number of words chosen (NWC) and pain report index (PRI), being made of 68 descriptors distributed in four categories (sensory, affective, evaluative and mixed) and of 20 subcategories.

Each subcategory has from 2 to 5 words. Females were oriented to choose between zero and 20 words for each subcategory most similar to their perceived pain. Each chosen word has a value and the sum of them generates total PRI. Additionally for each PRI category a score may be calculated. NWC refers to the number of selected descriptors on the tool corresponding to words chosen to explain pain, with a minimum value of zero and maximum of 20. For both, PRI and NWC, the higher the score the more severe the pain.

Shoulder Pain and Disability Index (SPADI) questionnaire was also applied as interview and the Brazilian version consists of 13 items distributed in the disability scale (eight items) and the pain scale (five items), being each item scored from zero to 10. Final score varies between zero and 100 and the higher the score, the worse the shoulder disorder¹².

Data were analyzed by the BioEstat 5.0 program and results were described in absolute frequencies, percentages, means and standard deviation of means. Wilcoxon Signed Rank Test for paired samples was used to compare superficial sensitivity and shoulder pain and disability questionnaire scores before and after RT, with significance level of 95% ($p < 0.05$).

This study was approved by the Ethics Committee for Research with Human Beings, Teaching Hospital, Federal University of Sergipe (CAAE 0087.0.107.000-2011).

RESULTS

Participated in this study 25 females but five were discontinued from the study for interrupting RT by medical orientation. From 20 included females, mean age was 52.7 ± 11.2 years, mean BMI was $26.2 \text{ kg/m}^2 \pm 2.7$, 13 females were married, four single and three widows. With regard to occupation, six were housewives, two were peasants, five were retired and seven had different activities (autonomous). Most prevalent surgery was mastectomy (60%) and the number of RT sessions has varied from 25 to 30. Mean fractionated doses were 186.7 ± 23.2 cGy, varying between 100 and 215 cGy. Mean total RT dose corresponded to $4947 \text{ cGy} \pm 734.8$, varying from 2500 to 6020 cGy (Table 1).

Table 1 – General and clinical-surgical characteristics of patients (n = 20).

Characteristics	Mean \pm SD
Age (years)	52.7 ± 11.2
Body mass index (kg/m^2)	26.2 ± 2.7
Number of resected lymphnodes	9.3 ± 8.5
Types of surgery	n (%)
Radical (mastectomy)	12 (60)
Conservative (quadrantectomy, tumorectomy)	8 (40)
Side of surgery	
Right	10 (50)
Left	10 (50)
Time after surgery	
< 6 months	9 (45)
\geq 6 months	11 (55)
Adjuvant treatment	
Chemotherapy (CT)	15 (75)
Radiation therapy (RT)	
Number of sessions	26.4 ± 1.7
Fractionated doses	186.7 ± 23.2

Before RT, superficial sensitivity on the ICBN pathway corresponded to 1.9 ± 0.2 g on the ipsilateral limb and 1.0 ± 0.2 g on the contralateral limb, both within criteria adopted as normality (third filament – 2.6 g). After RT there has been significant superficial sensitivity decrease in all evaluated points on the ipsilateral limb, shown by increased esthesiometer pressure from 1.9 ± 0.2 g to 2.8 ± 0.2 g ($p = 0.004$), indicating hypoesthesia. There has been no significant difference in SS of contralateral UL when measures before and after RT were compared.

Table 2 – Superficial sensitivity on upper limbs ipsilateral and contralateral to surgery before and after radiation therapy (n = 20).

Superficial Sensitivity	Before	After	p
Ipsilateral limb			
Point 1	1.9 ± 0.2	2.8 ± 0.2	0.004*
Point 2	1.9 ± 0.2	2.8 ± 0.2	0.004*
Point 3	1.9 ± 0.2	2.8 ± 0.2	0.004*
Control limb			
Point 1	1.1 ± 0.2	1.0 ± 0.2	0.499
Point 2	1.1 ± 0.2	1.0 ± 0.2	0.674
Point 3	1.1 ± 0.2	1.0 ± 0.2	0.612

Calibration of each filament with precision analytic scale (CKA®): Green (0.05 g), blue (0.2 g), violet (2.6 g), dark red (3.6 g), orange (9.4 g) and magenta red (107.9 g).

* $p < 0.05$ Wilcoxon Signed Rank Test.

Pain evaluated by Br-MPQ has shown, in general, that total PRI and NWC have significantly increased ($p = 0.006$ and $p = 0.005$, respectively) after RT (Table 3). Sensory PRI and PRI have also shown significant increase ($p = 0.014$ and $p = 0.043$). In the sensory category, major descriptors were: pain “that comes and goes”, “spread in circles”, “stings like a needle prick”, “lacerating”, “pinching”, “jerking”, “heating”, “itching”, “tingling”, “numb” and “hurting”. In the affective category, distributed in five sub-categories, most mentioned were: “tiring”, “frightful”, “punishing” and “nagging”. In the evaluative category, with just one sub-category, most common descriptors were: “mild” and “annoying”. In the mixed category, with four sub-categories, major descriptors were: “tight”, “increases and decreases” and “stressing”. After RT, in addition to mentioned descriptors, the following sensations were emphasized: “pulsing”, “radiating”, “stinging”, “pressing” (sensory), “dull” (affective) and “stabbing” (mixed).

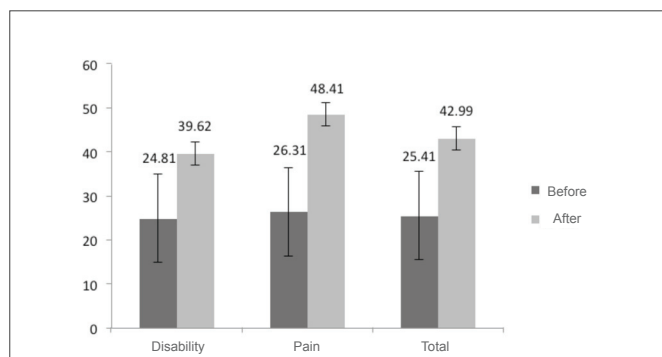
With regard to SPADI (Graph 1) there has been significant total score increase after RT ($p = 0.001$).

Table 3 – Pain index and number of words chosen from the McGill pain questionnaire before and after RT (n = 20).

	Before	After	p
PRI			
Sensory	6.7 ± 1.7	11.5 ± 1.5	0.014*
Affective	2.0 ± 0.6	3.7 ± 0.6	0.043*
Evaluative	1.2 ± 0.6	1.3 ± 0.3	0.443
Mixed	1.1 ± 0.1	2.2 ± 0.4	0.072
Total	11.1 ± 2.9	19.4 ± 2.2	0.006*
NWC	6.1 ± 1.5	11.1 ± 1.1	0.005*

Values in mean ± standard-deviation, *p < 0.05 = Wilcoxon Signed Rank Test; PRI = Pain Report Index; NWC = number of words chosen.

Disability score has significantly increased from 24.6 ± 25.7 to 39.2 ± 25.4 (p = 0.001) and pain score has increased from 26.3 ± 28.5 to 48.4 ± 31.7 (p = 0.001)



Graph 1 – Comparison of disability, pain and total score before and after radiation therapy. Values in mean ± standard error; Wilcoxon Signed Rank Test, p = 0.001 in all comparisons.

DISCUSSION

Surgery is still the primary BC treatment, especially in more advanced staging. In our sample, 60% were submitted to radical techniques, such as mastectomy with AL. Lymphnodes resection is still the procedure inducing more postoperative complications, especially related to sensory disorders, pain and decreased UL mobility^{4,6}. Our study has observed that before RT, females had already decreased superficial sensitivity on the affected UL as compared to contralateral limb, which has already been evidenced by the literature using esthesiometry^{3,10}. However this is expected since surgery itself may determine such change^{6,7}.

There has been hypoesthesia on the ICBN pathway of the UL ipsilateral to irradiated region, as compared to values of the same limb before RT and to contralat-

eral UL. Since adjuvant RT should be used in all five working days of the week for five to six weeks, it is common the presence of skin reactions in the irradiated area, associated to neuropathies caused by fibrosis and local nervous tissue ischemia¹⁰. This may explain decreased SS immediately after the RT period. It is worth highlighting that, although 15 females were also submitted to CT, the literature is clear in stating that CT does not interfere with ICBN pathway sensitivity because it is a systemic therapy unrelated to localized sensory lesions¹³.

UL pain may start immediately after surgery and may last for long periods³. RT may influence pain onset and persistence, generating chronic presentations^{4,5,9}. So, as observed in our study, UL pain was a symptom present soon after surgery, with significant increase of intensity immediately after RT when measured by MPQ.

ICBN is a predominantly sensory nerve and this justifies the fact that females have chosen words representing sensations such as: “pulsating”, “radiating”, “stinging”, “pressing” (sensory category), “dull” (affective category) and “stabbing” (mixed category). In general, pain may be induced by surgery, by scars, by skin reactions and by fear of adequately moving UL. In our study, movement amplitude was not considered a variable, because all females had to have minimum shoulder abduction amplitude in 90 degrees, external rotation and forearm flexed in 90 degrees to be submitted to RT.

Together with increased pain intensity, this study has observed increased functional disability, showing worsening of upper limb functionality after RT. According to SPADI, activities with the highest level of difficulty and pain severity were “placing something in a high shelf with the affected arm” and “when trying to touch the back of the neck with the affected arm”, respectively. The same was reported by other studies referring marked disability, especially during flexion and abduction movements of the affected shoulder after BC treatment, especially when associated with RT^{5,14}. In general, this shows that RT physically triggers slow scar repair and marked tissue necrosis, substantially impairing UL function^{4,5,7,9}.

During initial evaluation, nine females were pain-free; however after RT only two did not report pain, which was confirmed by final PRI, NWC and SPADI pain scale results. As to SPADI disability scale, five patients had initial scores of zero and only one remained with this result after RT. Such findings confirm the possibility of physical-functional complications potentiated by RT^{7,14}.

A Canadian study⁹ has looked for arm morbidity be-

tween six and 12 months, when evaluating 347 patients after surgery and adjuvant RT in 94% of them. Approximately 12% had lymphedema, 39% have reported pain and 50% had movement amplitude limitations. In spite of losses in quality of life (QL) and of daily activities restriction, most females have not shared with health professionals their arm morbidity. This indicates the need for strategies to follow up patients under BC treatment, with objective measures to evaluate and treat UL morbidities, especially those negatively impacting functionality and daily life activities.

A study¹⁵ has followed 55 females in two groups, one control and one with kinesiotherapy during RT to check the effect of physical therapy on QL. Although without significant differences in some evaluated aspects, the group submitted to supervised exercises for BC was benefited after RT and six months later. The importance of physical therapy in the follow up of females being treated with RT has also been shown¹⁴, being exercises valid to improve movement amplitude^{8,14}, QL¹⁵, and to decrease fatigue and pain¹⁴ during and after RT.

It was possible to observe that hypoesthesia, pain and disability are present in females submitted to AL and that these may worsen after RT. Since participants were evaluated immediately after RT, no long term inference was possible. Follow ups including a physical therapy protocol and larger sample size could contribute for the assistance to these females, for oncology health services and for professionals involved with functional recovery.

CONCLUSION

There has been ICBN pathway hypoesthesia, worsening of pain and disability of upper limb ipsilateral to BC surgery immediately after adjuvant RT.

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