EVALUATION OF THE EFFICACY OF ATLANTIA ALOE VERA PRODUCTS IN BREAST CANCER PATIENTS WITH RADIOTHERAPY-INDUCED RADIODERMATITIS

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INTRODUCTION

Radiotherapeutic Oncology is one of the basic treatment for breast cancer and, together with surgery and systemic treatments (Chemotherapy and Hormone Treatment) constitutes one of the main therapeutic weapons. The vast majority (more than 90% of patients diagnosed with breast cancer) will require radiotherapy at some point in the process. This percentage may increase if we count palliative treatments.

Radiotherapy is given in sessions and the usual protocol is 25 sessions from Monday to Friday. It is completely painless and involves just a few minutes in treatment Units (linear accelerators).

In spite of the fact that it is painless, it is not without toxicity and the most frequent radiotherapy-related toxicity is skin toxicity, radiodermatitis, which may vary from erythema to necrosis in the worst case scenario.

Ionising radiation causes a reduction in the base layer of the dermis and its rate of cell recovery. The epidermal layer becomes thinner and may disappear completely unless its normal desquamation is replaced by dermal layers that have lost their capacity to proliferate (sic). Breaking this balance between damage-repair-replacement means that on occasions the epidermis disappears completely as a result of cell depletion due to non-renewal.

Some degree of skin toxicity is inherent in the treatment and may be considered inevitable. This toxicity presents in the form of reddening, pruritis, dry desquamation, and in the most severe cases, wet desquamation, pain, burning, etc. Loss of quality of life is well-documented in these advanced cases. We need to consider that we are talking about extensive RDT treatment fields in highly sensitive areas such as the breast. Pain may be so severe that in addition to altering body image it also causes very severe discomfort, hinders wearing certain items of clothing and may even make it difficult to sleep.

Tissue radiobiology (the effect of therapeutic radiation) makes it inadvisable to suspend RDT treatment. In most cases our patients are advocated to continue with RDT, living with their lesions. Our nursing care consists of preventing early the onset, and in turn rapid development of radiodermatitis. Our care is based on a whole battery of preventive measures, in the knowledge that it is virtually impossible to have the skin return to normal before treatment ends. The main objective of skincare during RDT is to minimise side effects.

In the healthcare setting skin toxicity associated with external RT is measured using subjective scales (EORTC, OMS, SQL).

The present evaluation of the efficacy of ATLANTIA aloe vera products is aimed at making an objective QUANTIFICATION of skin changes in relation to specific parameters. One of the usual measurement tools used in cosmetic dermatology is used for the purposes of quantification. The aim is to measure accurately changes in skin properties and how these are affected by the use of ATLANTIA products. This study will collate the data of 14 patients who received external radiotherapy during the summer of 2012.

The skin properties to be measured are:

- **ELASTICITY:** Many physiological variants affect skin viscoelasticity: age, sex, skin area, phototype, ethnicity, hormone cycles, etc.

  As already stated, ionising radiation damages important proteins such as collagen and elastin, which play a direct role in elasticity. The impairment of new cell production in the basal layer of the dermis brings about a reduction in these proteins. It is essential to find topical agents to prevent impairment and even favour the production of these proteins, and therefore to limit the impairment of this biomechanical characteristic of the skin as far as possible.

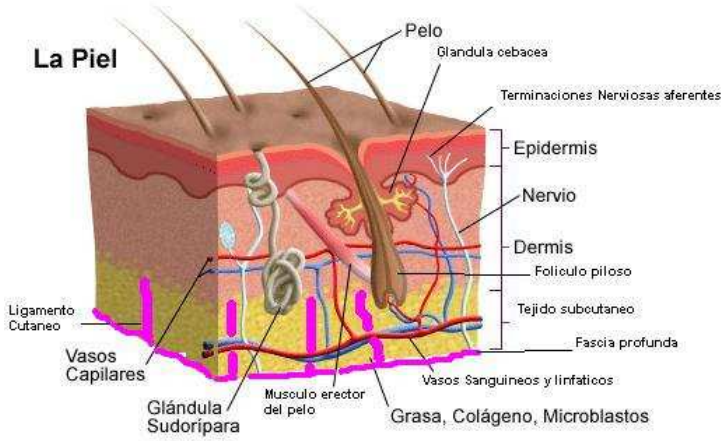
- **PIGMENTATIÓN:** Melanin (from "melas", black) is a blackish brown intracellular pigment. Melanin has two main functions: to protect against radiation and to quench cytotoxic free radicals. The number of melanocytes in the skin per unit area is similar throughout the various races. Skin colour depends basically on the number and distribution of melanin cells in the surface layers of the epidermis. So-called melanin or pigmentary incontinence occurs mainly in the case of post-inflammatory melanosis, particularly following forms of dermatitis that present with lesions of the basal layer of the epidermis.

- **HYDRATION:** Radiation damages the basal layer of the skin by dehydrating and disrupting the homeostatic balance of the skin (water-sodium cell transmembrane balance) and these biomechanical changes also impair its repopulation. It is an essential factor in caring for irradiated skin.

- **ERYTHEMA:** Erythema is "reddening" of the skin due to inflammatory or immunological processes. Erythema may be caused by many things. The skin's exposure to high doses of ionising radiation causes lymphocytes to accumulate in the layers of this, due to the effects of cell death, and finally the development of erythematous alterations in the skin. It is similar to sunburn.

LESION GRADING W.H.O. SCALE	
GRADE 0	No change.
GRADE 1	Mild erythema and dry desquamation.
GRADE 2	Tight or shiny erythema and patchy wet desquamation.
GRADE 3	Confluent wet desquamation other than skin folds.
GRADE 4	Ulceration and necrosis.

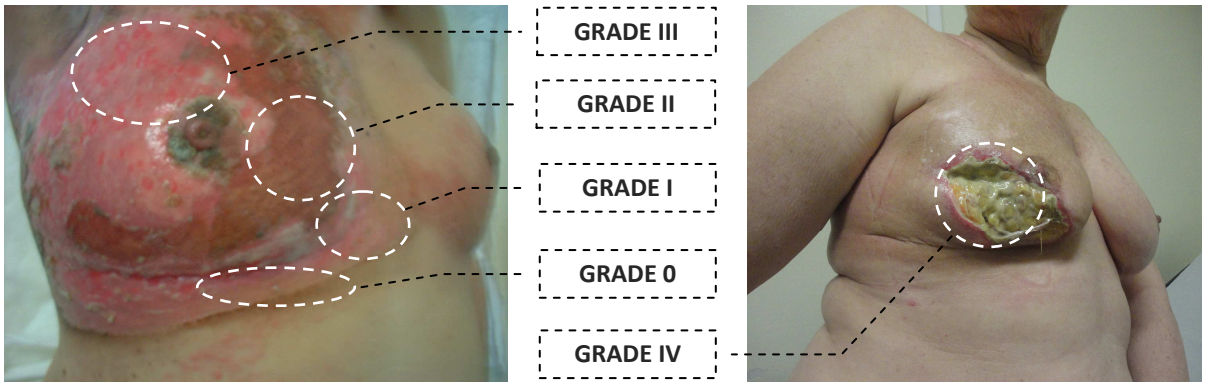
CLINICAL SYNDROMES	
EARLY ONSET	LATE ONSET
ERYTHEMA	ATROPHY
PIGMENTATION	TELANGIECTASIA
DEPILATION	FIBROSIS
DRY DESQUAMATION	NECROSIS
WET DESQUAMATION	
NECROSIS	



The loss of basal cells starts at doses of 20-25 Gy and is at its maximum at 50Gy.

- **ERYTHEMA:** Vasodilation or hyperaemia of the dermal microvasculature, with inflammatory response (80-90% of patients).
- **DRY DESQUAMATION:** This reflects the superficial loss of cells by the epidermis.
- **WET DESQUAMATION:** This is the result of rupture of the epidermis and exposure of the dermis, having greater effect on the basal layer's capacity to repopulate (10-15% of patients).

[Legends to figure: La Piel = The Skin; Pelo = Hair; Glandula cebacea = Sebaceous gland; Epidermis = Epidermis; Nervio = Nerve; Dermis = Dermis; Foliculo piloso = Hair follicle; Tejido subcutaneo = Subcutaneous tissue; Fascia profundis = Fascia profundis; Vasos sanguineos y linfaticos = Blood and lymph vessels; Grasa, Colageno, Microblastos = Fat, Collagen, Microblasts; Musculo erector del pelo = Hair erector muscle; Glandula sudoripara = Sweat gland; Vasos capilares = Capillary vessels; Ligamento cutaneo = Skin ligament]



ATLANTIA PRODUCTS USED

The various products that **ATLANTIA** offers us**:**

MOISTURISING BODY MILK		Aqua, aloe barbadensis gel, paraffinum liquidum, caprylic/capric triglyceride, helianthus annus seed oil, glycerin, cetyl alcohol, persea gratissima oil, ceteareth-12, ceteareth-20, glyceryl stearate, caprylyl glycol, dimethicone, carbomer, ascorbyl palmitate, lecithin, tocopherol, ascorbic acid, sodium hydroxide, disodium edta, parfum.
ALOE MOISTURISING GEL		Aloe barbadensis gel, aqua, glycerin, polysorbate 20, caprylyl glycol, carbomer, sodium hydroxide, parfum, disodium edta, amyl cinnamal, hexyl cinnamal, limonene , citronellol, geraniol, CI 42051, CI 15985.
SUPERDEFENSE		Aqua, aloe barbadensis gel, paraffinum liquidum, caprylic/capric triglyceride, isohexadecane, glyceryl stearate, glycerin, potassium cetyl phosphate, cetyl alcohol, dimethicone, butyrospermum parkii butter, stearic acid, sorbitan stearate, tocopheryl acetate, parfum, phenoxyethanol, carbomer, acrylates/vinyl isodecanoate crosspolymer, methylparaben, disodium EDTA, sodium hydroxide, butylparaben, ethylparaben, linalool, butylphenyl methylpropional, hexyl cinnamal, tocopherol, propylparaben, isobutylparaben, citronellol, alpha-isomethyl ionone, limonene, hidroxyisohexyl 3-cyclohexene carboxaldehyde, geraniol, ascorbyl palmitate, lecithin, eugenol.
PURE ALOE VERA GEL		Aloe barbadensis, glycerine, carbomer, caprylyl glycol, sodium hydroxide. Components of aloe vera: Polysaccharides (acemannan, galacturonic acid). Sugars (glucose, mannose, galactose, ...). Organic acids (glutamic acid, malic acid, citric acid, ...) Enzymes (cellulase, carboxypeptidase, catalase, ...) Amino-acids (valine , methionine, lysine, etc) B vitamins Minerals (copper, iron, potassium, magnesium)

PROTOCOLISED CARE PLAN

Protocolised care plan - Institut Catala d´Oncologia (I.C.O. L´Hospitalet Ll.)

- Our patients must wash with soapy water and keep their skin dry; the use of deodorants on the underarm area is not recommended (particularly those containing alcohol and/or aluminium).
- The use of colognes and perfumes is discouraged.
- Shaving with an electric razor is recommended for hair removal rather than depilatory creams, wax, manual razors, etc.
- Patients may swim; a shower taken immediately afterwards is recommended in order to remove chlorine and chemical products. Dry the skin immediately, avoid lengthy contact of wet swimwear with the skin and apply a moisturiser
- Exposure to the sun must be avoided. The area must be covered as far as possible and a factor 50+ sun cream must be used.
- Avoid massage, skin scratches, adhesive plasters, etc. It is best not to wear a bra and clothing made from cotton or natural fibres is recommended.
- The recommended creams must be applied after the daily session and at most 2-3 hours before this.

CARE	**BEFORE STARTING**	Moisturise with Moisturising Milk once/day
	GRADE 0	**When treatment starts**, Moisturise 1-2 times/day.
	GRADE 1	Increase frequency of moisturisation to 3 times/day. Start to apply creams containing Aloe vera 1-2 times/day. Comfortable with pruritis, thyme water cold compresses.
	GRADE 2	All of the above - care with medicated ointments may need to be started (Blastoestimulina, Claral, Synalar Gamma, Silvederma). In case of oozing, apply hydrogel dressings.
	GRADE 3	Daily nursing care

In the absence of any prior experience, we have adapted our Care plan to the various products supplied by ATLANTIA. One very positive factor was the possibility of obtaining different products and concentrations of active ingredient in order to use the most appropriate one at all stages of the process and skin evolution.

- **THERAPY PLANNING CT:** At the point when the planning of External Radiotherapy treatment commences. In addition to the interview and welcome protocol, the Nursing Interview must also focus on preventive skin care as a priority.

- **STARTING RADIOTHERAPY:** At the Nursing Interview we start the care that we will recommend during Radiotherapy.

- **HALF OF THE TREATMENT SESSIONS:** Weekly follow-up is provided and when the patient has undergone 12 to 14 sessions, we consider that care needs to be adapted to the dose received and to be tailored to the condition of the skin.

- **END OF TREATMENT:** When treatment ends, the care recommended to the patient is adapted to the state of their skin and they are advised to continue with this at home until their radiodermatitis is completely resolved.

ACTION	RECORD	ASSESS	DELIVER	FREQUENCY
THERAPY PLANNING CT	YES	YES	*START: Moisturising body milk*	Once/day
START OF TREATMENT	YES	YES	*START: Superdefense* *Moisturising gel*	Twice/day Once/day
HALF-WAY THROUGH TREATMENT	YES	YES	*START: PURE Aloe Vera gel*	Once/day
END OF TREATMENT	YES	YES	*Maintain until skin recovers* – *Superdefense* – *Moisturising gel* – *PURE Aloe vera gel*	Twice/day Once/day Once/day

AIM AND STUDY METHODOLOGY

<table>
<tr><td rowspan="3">AIM</td><td colspan="2">Since prevention is one of the basic aims in seeking to prevent radiodermatitis during radiotherapy, we wished to evaluate the efficacy of ATLANTIA aloe vera-based products in a group of breast cancer patients treated with RDT.</td></tr>
<tr><td><u>GENERAL</u></td><td>– To quantify skin changes occurring during treatment and how ATLANTIA products help to minimise these.
– To assess whether these products would be effective in preventing Radiodermatitis.</td></tr>
<tr><td><u>SPECIFIC</u></td><td>– To record lesion grades using the WHO scale.
– To quantify how Erythema is affected.
– To quantify how Elasticity is affected.
– To quantify how Hydration is affected.
– To quantify how Melanin is affected.</td></tr>
<tr><td>VARIABLES</td><td colspan="2">Lesion grades:
• Erythema.
• Hydration.
• Pigmentation.
• Skin elasticity.</td></tr>
<tr><td>METHDOLOGY</td><td colspan="2">• Descriptive observational study in women with breast cancer undergoing RDT treatment.
• Patients who, in our experience, are at greatest risk of developing radiodermatitis are selected.
• The time of year is the worst in terms of heat (May to September 2012).
• Obesity is a risk factor for breast cancer, also due to anatomical configuration (large breasts), reflecting an increased risk of developing radiodermatitis.
• 14 patients were selected who complied with these characteristics and were capable of understanding and maintaining the recommended care regime.
• These patients (14 in total) were recruited from the moment of the doctor's decision to start treatment and when treatment planning started.
• Cosmetic dermatology technology is used to quantify changes in variables using harmless probes capable of measuring the different parameters when in contact with the skin.
• Measurements are recorded on a scale of 0-99.
• At the first measuring session (CT) both breasts are measured in order to provide information on the baseline skin of the other breast also, for comparison purposes; the application of moisturising body milk starts. In the first instance they are instructed in the order in which to apply the various products.
• At the weekly follow-up visits measurements are carried out on the treated breast. It is checked and placed on record that the proposed care is being followed and that the products are being applied correctly.
• Patients are provided with the recommended products, supplied by the ATLANTIA laboratory.</td></tr>
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CHARACTERISTICS OF SELECTED PATIENTS

AVERAGE AGE	AGE RANGE		
56 YEARS	FROM 47 TO 79 YEARS	40-49	5 PEOPLE
		50-59	3 PEOPLE
		60-69	4 PEOPLE
		70 A MÁS	2 PEOPLE

SITE	NUMBER OF PATIENTS
LEFT BREAST	10
RIGHT BREAST	4
TOTAL PATIENTS	14

As stated above, people with large breasts are, in our experience, more likely to suffer from radiodermatitis, particularly in the submammary skin fold.

Our specially selected patients have the following characteristics:

PHYSICAL BUILD	HEIGHT	WEIGHT	BMI	OVERWEIGHT
AVERAGE	1.58 m	76.5	30.5	Type 1 obesity

- The average Body Mass Index (BMI) of our patients is 30.5, which may be classified as Type 1 obesity according to the scales used.
- Using to the formula applied in corsetry, the average measurement in centimetres of the breast contours (measured around the fullest point of the breasts and under the breasts) gives us an average bra size of 115 cm.

TREATMENTS RECEIVED			
CONSERVATIVE SURGERY		14 patients	100%
CHEMOTHERAPY	YES	7 patients	4 Neo-adjuvant chemotherapy
	NO	7 patients	
TAMOXIFEN		9 patients	

- 100% of our patients underwent conservative surgery, i.e. lumpectomy.
- Half of them had received Chemotherapy, this factor representing a major risk for presenting with radiodermatitis since not enough time has elapsed since the last cycle in order for the patient to be recovered fully.

SKIN PHENOTYPE	III	IV	V
	3	4	7
PHENOTYPE	III	IV	V

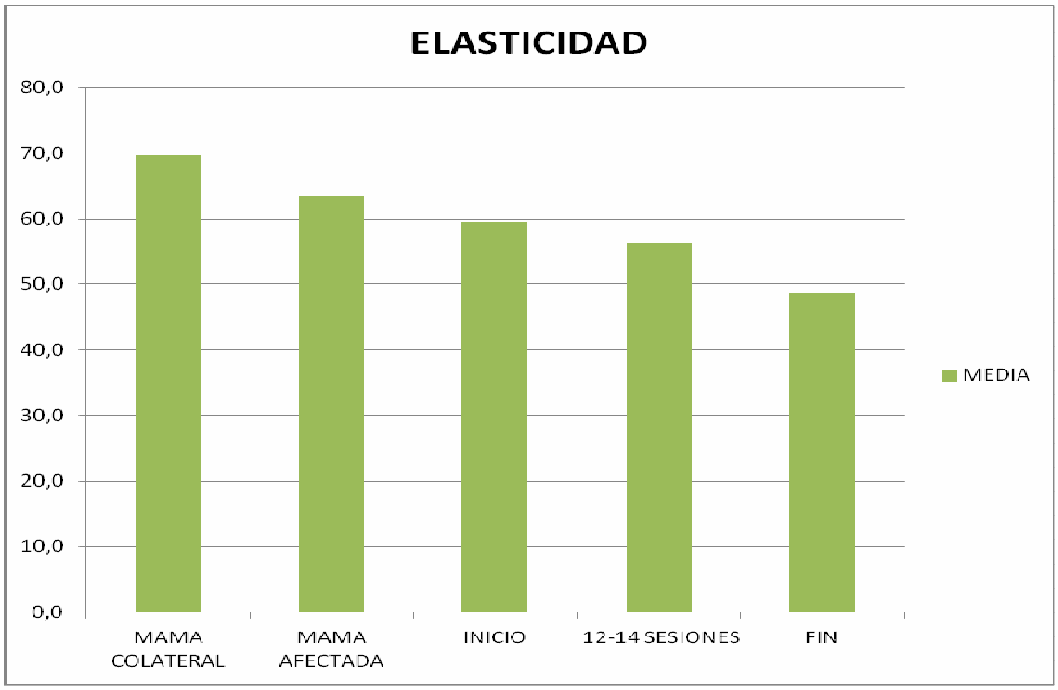
- The phenotype of the patients varies and all are Caucasian, from the Mediterranean region.

GRAPHS AND COMMENTS ON RESULTS

- When treatment ended all of our patients presented with moderate to severe Grade 1 lesions affecting virtually the whole of the breast. This outcome falls within the parameters of minimum anticipated iatrogenic lesions. We think that 100% of the dose of radiation is administered very close to the skin in order to cover the whole of the breast tissue.
- 6 patients (42%) presented with mild Grade II lesions located in the usual risk zones between the underarm and the inframammary fold. Blastoestimulina twice/day was recommended to 3 of these patients. No additional care was needed.

  We start out on the assumption that these patients had high potential for developing lesions, based on their characteristics:

  - Half of them had received chemotherapy, a factor that complicates cellular regeneration since in the main they are vitamin deficient as a result of difficulty eating and generally normalised defence mechanisms, but only just.
  - Half of the patients had a BMI of 30.5, i.e. were overweight (Type 1 obesity).
  - They are patients with large breasts having an average bra size of 115, namely having a marked inframammary skin fold which, as we have already said, is considered a high-risk area.
  - The study was conducted during the hottest months (May to September 2012), considering this to be a factor of risk and complication.

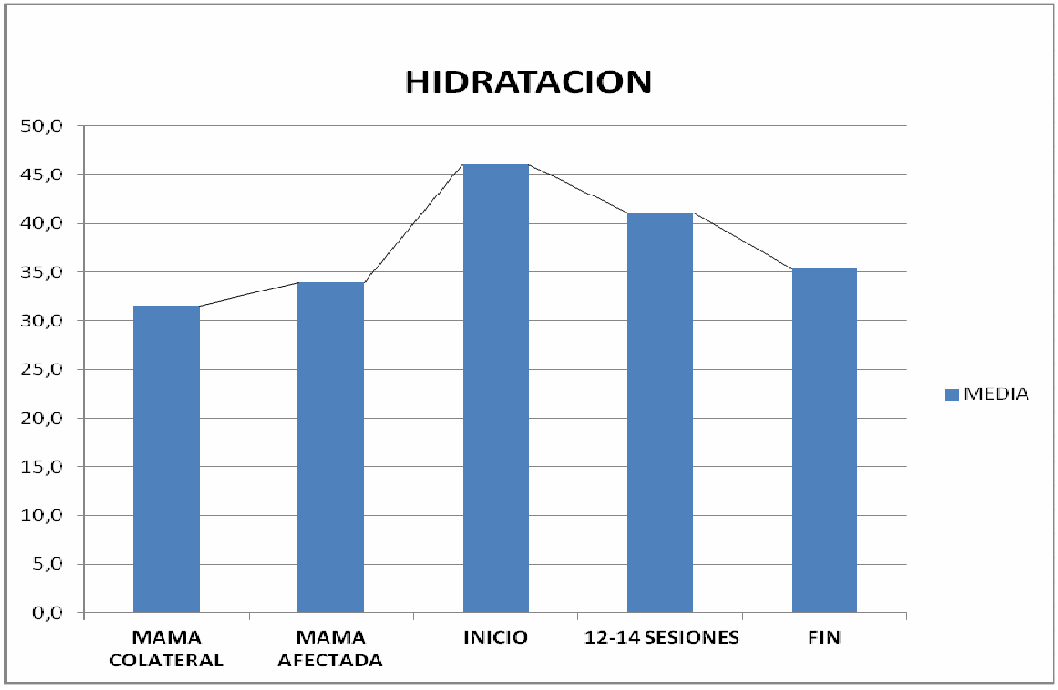


[Legends to graph: ELASTICIDAD = ELASTICITY; MAMA COLATERAL = COLLATERAL BREAST; MAMA AFECTADA = AFFECTED BREAST; INICIO = START; SESIONES = SESSIONS; FIN = END; MEDIA = AVERAGE]

	COLLATERAL BREAST	AFFECTED BREAST	START	12-14 SESSIONS	END
AVERAGE	69.6	63.5	59.6	56.4	48.8

→ **ELASTICITY:**

- This is an important factor, clearly, but more in terms of medium-term cosmetic outcome.
- It is interesting that on average patients lost less than 25% elasticity at the end of treatment, and future studies should quantify whether this is 100% recoverable and over what time period.
- The greatest loss occurs in the last sessions. This would be a factor to take into account in order to emphasise the importance of more specific care from the viewpoint of elasticity.



[Legends to graph: HIDRATACION = HYDRATION; MAMA COLATERAL = COLLATERAL BREAST; MAMA AFECTADA = AFFECTED BREAST; INICIO = START; SESIONES = SESSIONS; FIN = END; MEDIA = AVERAGE]

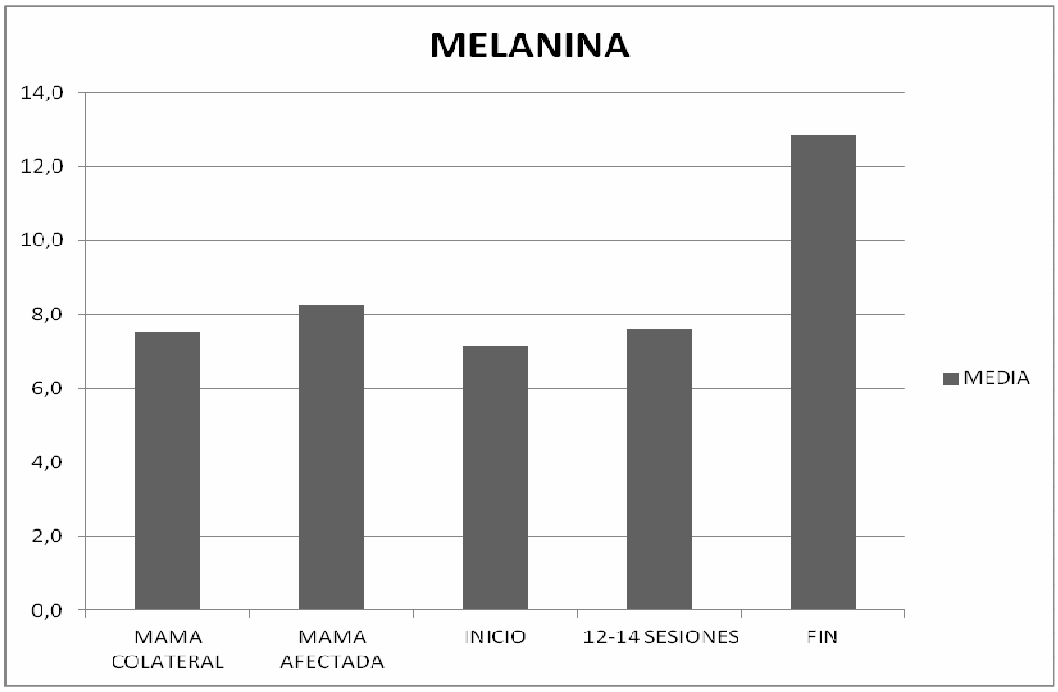
	COLLATERAL BREAST	AFFECTED BREAST	START	12-14 SESSIONS	END
AVERAGE	31.5	34	46.1	41.1	35.4

→ HYDRATION

It is observed that the breast to be treated is more hydrated initially than the contralateral breast as a result of the increased moisturisation recommended following surgery and prior to radiotherapy in order to minimise scarring.

- At the start of treatment the level of hydration is very high as a result of the preventive care carried out since the treatment planning CT at the first nursing consultation. Quantitatively there is an average increase of 12.1 CU, i.e. 35.5% between the CT and the start of treatment.

- It is very noteworthy that when treatment ends, and having received 100% of the radiation dose, **hydration even remains slightly greater than at the start of the treatment** after been subjected to the least favourable conditions of the treatment.



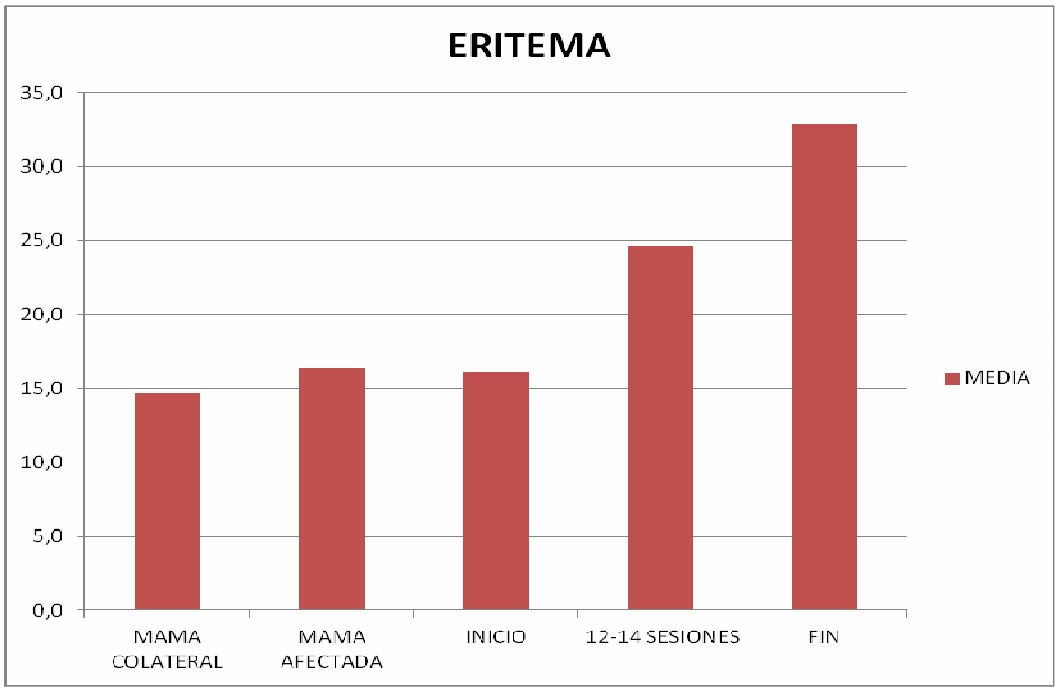
[Legends to graph: MELANINA = MELANIN; MAMA COLATERAL = COLLATERAL BREAST; MAMA AFECTADA = AFFECTED BREAST; INICIO = START; SESIONES = SESSIONS; FIN = END; MEDIA = AVERAGE]

	COLLATERAL BREAST	AFFECTED BREAST	START	12-14 SESSIONS	END
AVERAGE	7.5	8.2	7.1	7.6	12.9

→ **MELANIN:**

On studying the Melanin graph we can say that melanin is not significantly affected until 65-70% of the total dose to be received has been exceeded. This fact reinforces our idea of increasing the frequency of care when 50% of the dose has been received, with the intention of anticipating changes in the skin.

- The increase is 4.7 Clinical Units on average compared with the start.
- As a percentage, the increase is 57% from the start until the end of the treatment.
- Since this is a small sample no significant link with phenotypes is observed.
- It is noted that the melanin levels of 2 patients quadrupled in terms of CU from start to finish. We see this change as being inherent in the skin of these particular patients, due to their capacity to create granules of melanin. In terms of its impact on the study and due to the small size of the sample, this distorts the average considerably.



[Legends to graph: ERITEMA = ERYTHEMA; MAMA COLATERAL = COLLATERAL BREAST; MAMA AFECTADA = AFFECTED BREAST; INICIO = START; SESIONES = SESSIONS; FIN = END; MEDIA = AVERAGE]

	COLLATERAL BREAST	AFFECTED BREAST	START	12-14 SESSIONS	END
AVERAGE	14.6	16.4	16.1	24.6	32.9

→ ERYTHEMA

- At the end of the treatment our patients presented with moderate to severe Grade I lesions affecting virtually the whole of the breast. A gradual increase is noted, indicating that erythema is directly dose-related.

- The increase in CU is similar, both from the start until half-way and from half-way to the end, although visible reddening (subjective) is more obvious towards the end. This confirms our thought that an objective evaluation (measurement using cosmetic dermatology technology) is more reliable than mere subjective observation of degrees of redness.

  As was to be expected, patients with type V phenotypes present with an average of 18.3 CU compared with 21.4 CU of phenotype III.

CONCLUSIONS

- The final results obtained lead to the conclusion that high-risk patients treated with ATLANTIA products presented with the same problems that could have been presented by patients not at risk (no previous chemotherapy, no heat, not large-breasted).

- **In conclusion, we managed to reduce risk in patients with all adverse characteristics and deemed to be at high risk, to medium-low risk.**

- This reduction in iatrogenic risk, quantified on the basis of the change in the various parameters affected and which add up to the end result of radiodermatitis classified as stated previously, decreased discomfort, reflected in less severe pruritis, less burning, reduced sensitivity, a reduced sensation of tightness, less malaise, improved rest/sleep pattern and a more normal family and social life. **This enables us to venture that we are witnessing a substantial improvement in quality of life**.

- This reduction in grade of radiodermatitis in high-risk patients also has its repercussions in terms of reduced use of healthcare resources (care and equipment, nursing time, etc.).

- In view of the above we can consider that the ATLANTIA Aloe Vera-based products tests are very effective.

According to patients they are pleasant to use and give the impression of being a safe, reliable product. **In our opinion they are to be highly recommended for use throughout Radiotherapy, even under the least favourable conditions.**