

Left-Sided Breast Radiotherapy and Its Impact on Oncologic Dermopigmentation: Technical Considerations for Nipple–Areola Complex Reconstruction

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ABSTRACT

Oncological dermopigmentation enables the reconstruction of the nipple-areola complex following breast cancer treatment. In patients with left-sided breast cancer, the heart's anatomical proximity influences radiotherapy planning, potentially resulting in specific tissue characteristics that affect subsequent pigmentation. Alterations in vascularization, fibrosis, elasticity, skin thickness, hyperpigmentation, and scarring can modify pigment implantation and retention, necessitating adaptations to the conventional technique. This study analyzes the physiological response of left breast skin following radiotherapy and its impact on oncological dermopigmentation, considering parameters such as depth, pressure, speed, and the number of passes. The objective is to establish specific technical criteria for adapting the procedure to the characteristics of the irradiated tissue, thereby facilitating a safe, predictable, and clinically reproducible reconstruction of the nipple-areola complex.

Keywords

Left-Sided Breast Radiotherapy, Oncologic Dermopigmentation, Nipple–Areola Complex Reconstruction, Radiation-Induced Skin Changes, Pigment Retention.

Introduction

Medical reconstructive dermopigmentation of the nipple-areola complex (NAC) is the final step in the physical and psychological restoration of breast cancer survivors. However, skin that has undergone radiotherapy is not a normal biological canvas. Actinic damage permanently alters tissue structure, microcirculation, and skin barrier function. When treatment involves the left breast, these physical alterations intersect with extremely complex dosimetric planning decisions aimed at avoiding cardiac damage, which directly influences the cutaneous irradiation patterns of this specific area.

Why does radiotherapy for the left breast differ from that for the right breast?

The fundamental difference between irradiating the left breast and the right breast lies almost exclusively in the anatomical proximity of critical intrathoracic organs, primarily the heart and the left anterior descending (LAD) artery [1].

The heart is incidentally exposed to ionizing radiation during left-sided treatment [1]. Key clinical studies (such as that by Darby, et al.) have determined that the relative risk of experiencing a major coronary event (myocardial infarction, need for revascularization, or death from ischemic heart disease) increases linearly by 7.4% for every Gray (Gy) of mean heart dose (MHD) delivered - (*Mean Heart Dose*) [2].

Due to this linear risk, the German Society of Radiation Oncology (DEGRO) establishes a very strict recommended limit for the mean

heart dose, which must be < 2.5 Gy [3]. This compels physicists and oncologists to design left-breast treatment plans that prioritize cardiac preservation above all else—a requirement that does not apply to the right breast.

If the patient requires irradiation of the left internal mammary node (IMN) chain due to nodal involvement, the challenge is multiplied [2]. Adding the left IMN drastically increases the mean cardiac dose (increasing from a standard average to MHD values of 6.9 to 8.3 Gy of MHD) [4], thereby significantly increasing late cardiovascular mortality. This necessitates modulating beams in a much more complex manner and closer to the left anterior chest wall.

Radiotherapy techniques used for the left breast

To meet the required cardiac and pulmonary dose limits, advanced technological techniques are employed that substantially modify the radiation trajectory and the volume of healthy tissue exposed:

Deep Inspiration Breath Hold (DIBH - *Deep Inspiration Breath Hold*)

This is the standard technique of choice for heart-sparing purposes. It involves the patient performing a controlled deep inspiration and holding their breath during radiation beam delivery.

- Mechanism: Lung expansion generates a physical-mechanical displacement that moves the heart away from the anterior chest wall and the breast target volume.
- Anatomic consequence: It drastically minimizes the dose received by the cardiac apex and the LAD artery. However, DIBH shifts the position of the axillary lymph nodes anteriorly and cranially, thereby reducing the unwanted incidental dose they receive.

Intensity-Modulated Radiotherapy (IMRT) and Volumetric Modulated Arc Therapy (VMAT)

These techniques employ computerized systems to vary radiation beam intensity during delivery, thereby shaping the dose distribution around the heart with high precision.

- Low-dose spill issue: Although they succeed in reducing high-dose volumes within the heart, this comes at the cost of spreading a "penumbra" of low doses to adjacent healthy structures, such as the ipsilateral lung, the contralateral breast, and the total cardiac volume. This leads to a moderate increase in the mean lung dose (MLD) to the left lung and the peripheral skin dose in adjacent areas.

Prone Positioning

This method utilizes gravity to allow the left breast to "hang" away from the chest wall, naturally distancing breast tissue from the heart and lungs. However, this technique is applicable only when irradiation of regional lymph node chains (RNI) is not required—cases where cardiac dose levels are typically already within acceptable limits.

Accelerated Partial Breast Irradiation (APBI)

For very low-risk tumors, the option exists to treat only the tumor bed (rather than the entire breast). The use of much smaller

planning volumes significantly reduces cardiac exposure, though some studies associate this approach with higher rates of long-term late skin toxicity compared to whole-breast irradiation.

Physiological and Structural Consequences at the Cutaneous level

Ionizing radiation directly attacks the DNA of rapidly growing cells (such as those of the epidermis) and skin appendages through the formation of free radicals, causing short- and long-term effects that irreversibly alter the structure of the skin where dermopigmentation is to be performed:

A. Microcirculatory Alteration and Subclinical Vascular Damage

- Linear reactive hyperemia: Cutaneous microcirculatory blood flow (quantitatively measured via laser Doppler flowmetry—LDF) increases in a strictly linear fashion as the administered radiation dose accumulates.
- Peak and delayed stabilization: Microvascular blood flow reaches its peak perfusion level immediately upon completion of the 3-week radiotherapy course. Although it progressively decreases, approaching baseline levels around 3 months post-treatment, the vessels sustain permanent sequelae.
- Persistent subclinical damage: LDF monitoring demonstrates that even in patients clinically classified as having "Grade 0" visible toxicity (with no observable redness or erythema), there is a statistically significant internal inflammatory increase in the microcirculation. Furthermore, the irradiated microvasculature suffers a permanent functional loss in its vasodilatory capacity in response to thermal stress, due to microvascular endothelial damage and arteriolar alteration.

Glandular Atrophy and Skin Barrier Instability

Radiation destroys and induces irreversible atrophy in the dermal adnexal glands:

- Loss of sebaceous and sweat glands: 78.62% of patients report total or partial loss of sweating (anhidrosis) in the irradiated area. As the glands secreting sweat and sebum (lipids) are destroyed, the skin loses its natural epicutaneous emulsion.
- Xerosis and hyperkeratosis: 80.76% of patients suffer from extreme skin dryness (xerosis) secondary to this lack of lubrication. Biologically, this is accompanied by hyperkeratosis (thickening of the outer stratum corneum) and thickening of the epidermis, along with a progressive loss of subcutaneous collagen fibers.
- "Radiation-irritated skin": This develops into a chronic condition (manifesting 90 days or more post-treatment) characterized by dry skin, constant itching (pruritus), and a severely compromised protective barrier. This skin is hypersensitive and prone to contact dermatitis or recurrent eczema (present in 18.05% of patients).

C. Melanocytic Activation and Hyperpigmentation

- Reactive melanogenesis: Ionizing radiation abnormally and persistently activates melanocytes in the basal layer of the epidermis, promoting the overproduction of melanin that is deposited in the keratinized layers of the skin.

- Persistent hyperpigmentation: Approximately 79.81% of survivors exhibit pigmentary deposits (ranging from mild to severe hyperpigmentation) in the irradiated area. This darkening permanently alters the baseline color tone of the treated breast compared to the healthy contralateral breast.

Critical implications for the dermopigmentation technique

For the professional performing reconstructive dermopigmentation, these physiological and dosimetric alterations of the left breast necessitate substantial changes to the technique and safety of the procedure:

From physiological alteration to pigmentary response: observations derived from clinical experience

The previously described changes take on clinical significance when analyzing pigment behavior during and after dermopigmentation. Experience with previously irradiated patients shows that the pigmentary response of these tissues is less predictable than that observed in skin not subjected to radiotherapy, both during implantation and throughout the subsequent healing process.

This clinical observation aligns with existing literature. Prior radiotherapy has been identified as a factor associated with a greater need for repigmentation of the areola-nipple complex. Studies included in recent reviews report difficulties with pigment retention in up to 70% of previously irradiated patients, while independent clinical analyses have identified a history of radiotherapy as a significant risk factor for requiring additional pigmentation sessions.

Based on our clinical experience, we propose that this reduced predictability should not be addressed by immediately increasing the intensity of implantation. Instead, it indicates that the tissue requires a progressive treatment strategy, taking into account its baseline condition, its response during the procedure, and its evolution between sessions.

Pigment retention and the healing process

A recurring observation is the apparent greater loss of pigment during the healing process in certain irradiated skin types—specifically those exhibiting xerosis, scaling, or significant alterations to the skin surface.

Following dermopigmentation, a local inflammatory response occurs, succeeded by re-epithelialization. A portion of the superficially implanted pigment may be eliminated during this process, whereas the fraction that is adequately deposited and stabilized remains within the tissue. For this reason, the appearance immediately after the procedure does not reflect the final pigment outcome.

In clinical practice, irradiated skin with marked xerosis may exhibit more pronounced scaling and irregular pigment evolution once surface repair is complete. This can manifest as areas of lower color density, partial color loss, or uneven pigment distribution.

Consequently, pigment retention should be assessed once the healing process has concluded, rather than during the initial days following the procedure. The need for a second intervention should not necessarily be viewed as a complication or technical failure; instead, it may be an expected aspect of the progressive management of irradiated tissue.

Skin preparation as a preliminary stage to dermopigmentation

Based on the cases analyzed, it is proposed that dermopigmentation reconstruction should not begin directly with pigment implantation. For patients with skin sequelae following radiotherapy, there must be a preliminary stage aimed at determining whether the tissue is in a suitable condition for the procedure.

This stage constitutes pre-procedure skin conditioning, defined as the set of measures intended to optimize the tissue's surface conditions prior to pigment implantation.

Irradiated Skin Alteration	Impact on the Dermopigmentation Technique	Clinical Measures and Recommendations
Xerosis and Hyperkeratosis	The thickened and dry stratum corneum decreases skin elasticity, hindering smooth needle penetration and increasing epidermal resistance.	Requires prior protocols of prolonged deep hydration with emollients. The use of large-gauge needles that tear the rigid tissue must be avoided.
Barrier Damage and Hypersensitivity	Greater susceptibility to bacterial infections and an elevated 18% risk of eczema or reactive contact dermatitis to pigment components.	Performing patch tests prior to the procedure with the selected pigments is mandatory. Strict use of sterile and hypoallergenic medical-grade pigments.
Loss of Elasticity and Collagen Atrophy	Higher risk of pathological scarring or the skin "spitting out" the pigment due to the alteration of the supporting dermal collagen.	The pigment must be deposited with extreme precision in the upper dermoepidermal junction. Work with low voltages and minimal passes so as not to saturate or injure the atrophic dermis.
Active Baseline Hyperpigmentation	The chromatic background of the irradiated left breast is typically darker and more grayish/brownish than that of the healthy contralateral breast due to melanocyte activation.	Color selection for the artificial areola cannot be an exact copy of the healthy breast. Color theory must be employed to neutralize the cool and dark baseline tones of the irradiated skin.
Unstable and Subclinical Microcirculation	Microvascular instability can generate more profuse bleeding or lymphatic exudate than normal during tattooing (even in normal-looking skin), washing out the pigment before it fixes.	Dermograph pressure must be moderated. The waiting period post-radiotherapy must be an absolute minimum of 3 to 6 months (ideally when microcirculation stabilizes near the baseline level).

The conditioning process does not intend to reverse structural damage caused by radiotherapy, but rather to address modifiable variables that could affect the response to the procedure. The decision to initiate dermopigmentation should be based on the current condition of the tissue, rather than exclusively on the time elapsed since the completion of radiotherapy.

The preliminary clinical assessment must consider:

- Degree of xerosis and scaling;
- Integrity of the skin surface;
- Tissue elasticity and mobility;
- Presence and degree of fibrosis;
- Apparent skin thickness;
- Residual hyper- or hypopigmentation;
- Telangiectasias and visible vascular characteristics;
- Sensitivity of the area;
- Surgical scars within the area to be reconstructed;
- History of healing complications;
- Characteristics of the breast reconstruction performed;
- Presence of implants or other underlying reconstructive elements.

This evaluation allows for the creation of a clinical map of the tissue before determining the procedural parameters.

Conditioning for xerosis and skin barrier function

The presence of significant xerosis is a key factor to address prior to the procedure. From a technical standpoint, working directly on a surface that is excessively dry, rigid, or scaling hinders control over pigment implantation and may increase result irregularities during the healing process.

Therefore, a preliminary conditioning phase is recommended to restore adequate hydration levels and improve barrier function before performing dermopigmentation. The duration of this preparation should be tailored to the severity of the observed abnormalities and the skin's clinical progression.

The criterion for proceeding should not simply be the completion of a set number of preparation days, but rather the achievement of an intact skin surface—free from significant scaling, clinically stable, and capable of tolerating the procedure.

In cases of persistent or severe skin abnormalities, conditioning must be carried out in collaboration with the treating medical team before subjecting the tissue to further trauma.

Pigmentation changes as a pre-procedure variable

Hyperpigmentation secondary to radiotherapy is not merely an aesthetic issue; it is a technical variable in NAC (nipple-areola complex) reconstruction.

Reconstructive dermopigmentation aims to create a three-dimensional color perception on a specific skin substrate. Consequently, the baseline color of the irradiated skin directly influences the final appearance of the implanted pigment.

Clinical experience shows that attempting to compensate for a hyperpigmented background solely by increasing pigment saturation can yield unnatural results while simultaneously causing unnecessary tissue trauma.

Therefore, before selecting the pigment blend, it is essential to determine the stability of the baseline color and assess whether the pigmentation abnormality requires prior treatment. Once the tissue has stabilized, color selection must simultaneously take into account the tone of the contralateral breast, the residual color of the irradiated skin, and the expected behavior of the pigment after healing.

Adaptive dermopigmentation on irradiated tissue

Once the skin reaches suitable clinical conditions, dermopigmentation must be performed using parameters specifically adapted to the irradiated tissue.

The core technical premise derived from our clinical experience is to **minimize trauma per session and progressively build the pigmentary result**.

Irradiated skin should not be treated with the aim of achieving the same color density in a single session as might be attained in non-irradiated tissue. Loss of elasticity, uneven thickness, fibrosis, and microvascular alterations reduce the margin for technical error, making the control of each pass especially critical.

Implantation depth

Implantation depth is one of the critical parameters of the procedure.

Literature on NAC reconstruction via tattooing typically places the pigment within the dermal plane and notes that the optimal depth can vary significantly depending on tissue quality, particularly in patients who have undergone prior radiation therapy.

In this context, the increased resistance offered by fibrotic tissue should not be interpreted as an indication to automatically increase the depth of penetration. Mechanical resistance and skin thickness are not equivalent.

The technique should aim for the minimum effective depth that allows for controlled pigment implantation without causing unnecessary dermal trauma. This depth must be adjusted during the procedure based on the observed response and the characteristics previously identified in the skin map.

Control of mechanical trauma

Each pass of the device constitutes a new mechanical stimulus on tissue whose reparative capacity may be compromised. Therefore, the technique must limit unnecessary repetition over the same area.

Pressure, speed, needle configuration, number of passes, and dwell time at a single point must be understood as interdependent variables. No single parameter determines the degree of trauma;

rather, it results from the cumulative effect of all of them.

Consequently, the proposed technique aims to achieve uniform implantation through controlled movements and a limited number of passes, while continuously re-evaluating the tissue response.

The appearance of a disproportionate tissue response should serve as a criterion for reducing intensity or ceasing work on that area, rather than continuing in an attempt to achieve color saturation.

Needle selection

The choice of needle configuration must be based on the condition and thickness of the tissue, the specific area of the NAC being reconstructed, and the amount of pigment intended for implantation.

In irradiated skin, the goal is not to maximize the amount of pigment deposited per pass, but rather to control the balance between pigment deposition and mechanical trauma.

Configurations that cause excessive trauma to atrophic, thin, or particularly fragile tissues should be avoided. Similarly, the presence of fibrosis requires individual assessment, as increased surface resistance does not, in itself, justify a more aggressive technique.

Building the result through multiple sessions

The need for multiple sessions is particularly significant in patients who have undergone radiation therapy.

Available evidence indicates that prior radiotherapy is associated with a higher likelihood of color loss and the need for re-tattooing. This observation supports the approach derived from our clinical experience: **reconstruction of the irradiated NAC (nipple-areola complex) should be viewed as a process rather than necessarily a single procedure.**

The initial session should establish a conservative pigment base. Once healing is complete, an objective assessment can be made regarding pigment retention, areas requiring correction, and tissue response.

Subsequent sessions allow for the progressive increase of density, correction of irregularities, and color adjustment, without initially subjecting the tissue to excessive trauma at the outset.

In this way, the number of sessions is no longer viewed solely as an indicator of technical efficacy. In irradiated tissue, a greater number of sessions involving less individual trauma can be a deliberate safety strategy.

Pigment selection and chemical safety

The choice of pigment is particularly important when dealing with skin where the barrier function and repair capacity have been previously altered.

The products used must comply with current regulations applicable

to pigments intended for tattooing or permanent makeup and be supported by documentation detailing their composition, traceability, and adherence to restrictions regarding potentially hazardous chemicals.

In the European context, the REACH Regulation establishes specific restrictions for thousands of substances found in tattoo and permanent makeup inks, including limits on certain substances that are carcinogenic, mutagenic, toxic to reproduction, sensitizing, or irritating.

For oncology patients, product selection must be viewed as a matter of clinical safety rather than merely a choice of color. The use of substances with unverified composition, origin, or traceability must be avoided.

Likewise, pigment oversaturation should be avoided. Introducing a larger amount of pigment does not necessarily result in better retention and may increase the local inflammatory response and the trauma caused during the procedure.

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Follow-up evaluation and repigmentation criteria

The outcome of the dermopigmentation procedure must be evaluated once skin healing is complete, rather than immediately after the intervention.

The follow-up evaluation should document, at a minimum, skin integrity, color uniformity, the percentage or degree of pigment retention, the presence of areas of color loss, tone changes, the scarring response, and the occurrence of any complications.

This stage is particularly important for transforming clinical experience into quantifiable data. Standardized photographic documentation—taken before the procedure, immediately afterward, and during follow-up visits—would allow for an objective comparison of pigment evolution and the establishment of response patterns.

The decision to proceed with a new session should be made only after a joint assessment of tissue recovery and the resulting pigmentation.

Proposal for a clinical protocol based on clinical experience

Based on accumulated experience, we propose structuring oncological dermopigmentation on irradiated breast tissue as a sequential process:

Assessment → Conditioning → Conservative dermopigmentation → Healing → Re-assessment → Progressive repigmentation.

This model differs from conventional procedures primarily by incorporating the physiological condition of the tissue as a

determining factor for the technique.

The initial clinical decision does not concern the color or design of the nipple-areola complex (NAC), but rather determines whether the skin is ready to receive pigment. Subsequently, technical parameters are adapted to the observed individual characteristics, prioritizing controlled pigment implantation over immediate saturation. Finally, the result is built up progressively based on pigment retention and the tissue's demonstrated tolerance between sessions.

Accumulated clinical experience suggests that this adaptive approach may be particularly relevant for patients who have previously undergone radiotherapy; literature confirms that these patients present greater challenges regarding pigmentation and a higher likelihood of requiring additional procedures.

Systematizing these observations provides the foundation for developing—and subsequently validating—a specific protocol for oncological dermopigmentation on irradiated tissue, capable

of correlating initial skin characteristics, technical parameters employed, and the outcomes achieved.

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