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A randomized, prospective study using the LPG® technique in treating radiation-induced skin fibrosis: clinical and profilometric analysis

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Background/purpose: Cutaneous fibrosis is the quite mandatory sequela after a breast cancer treated by radiotherapy and it induces more or less important functional troubles. The LPG® technique is a technique of mechanical massage that allows skin mobilization by folding/unfolding. The aim of this study was to evaluate the changes on irradiated skin before and after LPG treatment by clinical and skin replica analysis.

Methods: Twenty women, 43–55 years old, who had been treated from 6 to 16 months before, for breast cancer with a conservative surgery and radiotherapy, had been enrolled in the trial. They were divided into two groups after randomization: the first group was LPG treated three times a week for 1 month; the second group was only placed under medical supervision. The clinical criteria studied were systematically studied before (T0), at the end of treatment (T1) and 1 month after the end of treatment (T2): pain, itching, skin dryness, erythema, skin infiltration, feeling of tightness and of induration of the skin. Softening of the skin was assessed at T1 and T2. Cutaneous replica was performed on the internal upper 1/4 of each breast with silicone material before, after and 1 month later after the end of the treatment. After polymerization, the replica was stored and then blindly analyzed by image analysis software. The following parameters were systematically measured: average skin roughness, average of wrinkles' depth and residual length, wrinkle number and the space between them.

Results: Clinically, the LPG treatment induced a decrease of erythema (10% of the patients vs. 40% before treatment), a decrease of pain and pruritus (10% vs. 20% and 40%, respectively) and a decrease of the feeling of induration of the skin (10% of the patients vs. 70% before treatment). Furthermore, a skin-softening sensation was noted by seven patients vs. one in the control group. Replica shows an increase of roughness and of furrow depth without any change in the residual length and an increase in the space between the wrinkles, whose number decreases.

Conclusion: This study confirms the impact of the clinical sequelae induced on skin after radiotherapy and shows improvement of the clinical signs after treatment by the LPG® technique. The latter induces changes of micro relief, suggesting a softening effect on the skin. These preliminary results have to be confirmed on a more important group of patients.

Key words: radiodermatitis – mechanical massage – profilometric analysis

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CONSERVATIVE SURGERY for breast cancer is always followed by radiation treatment. This treatment normally begins 3 weeks after surgery, once healing is satisfactory and shoulder abduction has been improved through re-education.

The immediate tolerance of the skin to the radiation is generally satisfactory, beyond 30 grays inflammation with erythema, dry skin and breast edema may occur. Damage to the endothelial cells of the dermal blood cells may also occur (1).

During the first months, mammary radiation is responsible for inflammation and a thickening of the skin. A mammogram reveals disorganization of the 'Duret's crests' and densification of the sub-dermal trabeculation (2). These phenomena reach their maximum intensity 6 months after the end of treatment in 70% of patients.

Superficial radiation-induced fibrosis translates clinically as a change in skin texture (dry, scaly, firmness on palpation with difficulty in pinching the skin to form a fold) and skin retraction, which may sometimes cause functional discomfort. The appearance of telangiectasia, pain and itching may also occur. All levels of severity have been described, from radiated skin that is

slightly less supple, to handicapping sclerosis, more than 20 years after exposure (3, 4).

The aim of this study was to assess the impact of a mechanical massage technique with documented dermotrophic properties (5–7) on radiated skin trophicity, by comparing it with spontaneous development (i.e. without massage or application of an emollient) and, where appropriate, to validate its use alongside other anti-fibrosis therapies (8).

Materials and Methods

Population

Twenty patients aged between 43 and 55 took part in the study, randomized into two groups: 10 were treated with the LPG® technique (LPG group) and 10 did not receive any treatment (control group). The women were all included after conservative breast cancer surgery, followed by a post-operative radiation therapy (50 grays cobalt+10 grays electrons) for at least 6 months. All subjects gave their written informed consent, and the ethical committee of Nîmes approved the experiment.

Experimental design

The LPG® technique is a mechanical massage technique delivered by a medical device. We have used the Cellu-M50 LPG Systems device (LPG Systems, Valence, France). The procedure consists of a tissue mobilization process between two rollers, creating a skin fold and stretching the underlying tissue. The treatment (10 min) was applied every other day, three times per week for 1 month (15 sessions) to the irradiated breast of the randomized LPG group patients, and followed the charts and maneuvers pre-defined in a practical protocol.

Evaluations including clinical assessment, 3D profilometric analysis and elasticity test were performed on enrolment (T0), after 15 sessions of LPG treatment or 35 days with no treatment (T1), one month after the end of the LPG treatment or after 65 days with no treatment (T2) for all patients.

Clinical evaluation

At each consultation, inspection and palpation of the skin assessed the following parameters by the practitioner:

- Skin dryness;
- Erythema;
- Skin infiltration; and
- Pain at palpation.

and a qualitative assessment by the patient on:

- a feeling of tightness;
- itching;
- feeling of induration of the skin; and
- from T1: global assessment of skin softening

The qualitative assessment measured the existence or not of each phenomenon (yes/no) and the quantitative phenomenon was given a grade on a visual analogic scale graduated from 0 'not at all' to 10 'enormously'. When a value was missing or the phenomenon was absent, it was given a 0.

Profilometric analysis

The patients were asked to relax for 15 min and then, in a sitting position, 3 mm thick silicon prints were taken of the treated breast and the non-treated breast in symmetrical areas using a silicon-print technique and a protocol described previously (9). Measurements were taken for all patients of the upper interior breast quadrant so that the location would be the same for all and so that the differing breast sizes would not affect the results of the profilometric study. After polymerization, the resin print was removed from the skin, numbered and archived, and then sent to Laboratoires Pierre Fabre at the end of the study for a blind analysis using image analysis software to provide a quantitative analysis of the skin contours. Five skin 'roughness' criteria were chosen by the bio-statistics unit to evaluate this study. RA measured average roughness, RZ measured the average depth of the 'furrows', RS measured the residual length, RN measured the number of wrinkles, and AR measured the space between the wrinkles. This 3D study is a quantitative study of the skin contours used to report on the distribution and density of the skin folds in the various surface directions and also to provide a perceptible quantification of the distributions of the highest points of the contours from a statistical and morphological point of view.

Elasticity tests

Skin elasticity measurements and skin prints were taken for the upper interior quadrants of

both breasts. Each subject therefore had her own control. The elasticity measurement was performed using the LPG tester, connected to the flexible coupling and linked to the aspiration system. Aspiration was set to strength number 1. According to the elasticity of the skin, the cursor rose and fell; results were read from a scale graduated in millimeters.

Statistical analysis

Comparison of quantitative values was performed using variance analysis of cross-over type (test of Hills and Armitage). Comparison of qualitative values was performed using a χ^2-test.

Results

Patient characteristics

As the patients were randomized, age, weight and height did not differ between treatment groups (average age: 49, average weight: 61 kg, average height: 164 cm). The average inclusion after the end of radiation therapy was 16 months for LPG-treated patients (LPG group) and 15 months for the control group; the minimum was 6 months, which fulfills the inclusion criteria. The period between surgery and radiotherapy was slightly shorter for the control group than for the LPG group but this did not affect the study. There was also a difference as regards the irradiated breasts in that there were more irradiated left breasts in the LPG group and more irradiated right breasts in the control group.

Clinical evaluation at T0

Inspection of the skin of the irradiated breast reveals that 25% of patients have dry skin, and 40% have erythema. When examined by palpation, 40% of patients were found to have infiltrated skin and 25% complained of pain.

Concerning the patient's subjective evaluation criteria, 15% of patients complained of a feeling of tightness and 45% of patients experienced a feeling of induration in the irradiated breast.

Despite randomization, patients in the LPG group have more radiation-induced cutaneous changes than have control group patients.

Clinical evaluation at T1 and T2

Although there were no statistically significant differences between the two groups, inspection of the irradiated skin showed a reduction in the percentage of dry skin, in the LPG group between T0 and T1 as well as a reduction in the percentage of erythema. At T2, dry skin had disappeared in the LPG group, and two patients have erythema.

Palpation revealed reduced skin infiltration in the LPG group between T0, T1 and T2, but a greater reduction in percentage of pain on palpation between T0 and T1. This effect remains stable at T2.

Although there were no statistically significant differences between the two groups, a reduction in the number of patients complaining of itching was observed between T0 and T1.

Among these patients who saw their itching decrease, some associated a better tolerance of their skin to certain materials (nylon and lycra) with this reduction in itching. It was the same for other patients who noted no reduction in itching but who, by T1, no longer felt the need to place a flannel cloth inside their arm. In T2, the percentage of patients still experiencing itching at T1 remained stable.

The number of patients complaining of tightness of the irradiated skin was stable between T0 and T1 in the LPG group but at T2 no patients had feelings of tightness. Conversely, the number of patients complaining of tightness increased with time in the control group.

Regarding the patient's subjective evaluation criteria of skin induration and skin suppleness, in the LPG group a reduction in skin induration ($P = 0.003$) and increased skin suppleness was noted between T0, T1 and T2, whereas it was stable in the control group. Since T1, we measured the softening of the skin between T0 and T1. We noted a very significant difference between the patients of the LPG group and the control group ($P = 0.0062$). The softening of the skin increased by 70% in the LPG group, whereas only one patient in the control group felt a softening of the skin.

These results are summarized in Table 1.

Elasticity of the skin

Evaluation at T0

As regards the elasticity of the skin and an assessment of the radiation therapy, a pairing comparison between irradiated breasts (RT+) and non-irradiated breasts (RT –) was performed using the difference in the measurements between the RT+ and the RT – in each patient. It

was observed that the mean elasticity measures in the RT+ were lower than for the RT− ($P = 0.04$).

Evaluation at T1 and T2

Regarding elasticity of the skin of RT+, a statistically significant increase ($P = 0.04$) was observed in the LPG group between T0 and T1. A slight decrease was observed in the elasticity measurements in the skin of irradiated breasts between T1 and T2, suggesting a transient effect of the treatment on this parameter.

Profilometric analysis

Radiation changes the roughness of the skin's micro-contours. It appears that there are fewer wrinkles with radiation but that they are deeper. It was also noted that the spacing between the wrinkles across all the skin was greater (Fig. 1).

A major difference was observed in the changes between the irradiated group treated with the LPG® technique and the untreated irradiated group, between T0 and T1.

A comparison between T0 and T1 of the prints taken of irradiated breasts treated with the LPG® technique with those of the non-irradiated ones not treated with the LPG® technique highlights statistically significant changes in the roughness parameters. In the irradiated/LPG-treated group, we observed an increase in the average roughness of the skin (RA), an increase in the depth of the furrows (RZ) and an increase in residual length (RS), while in the irradiated/non-treated group these values were stable (Table 2). The increase in the micro-contour roughness parameters through the LPG® technique corresponds to a softening of the skin. This softening of the skin translates as a tightening of the micro-contours (i.e. increase in the parameters) and an increase in the skin's ability to stretch and retract (Fig. 2).

It can also be observed on the 3D images of the treated irradiated breast that the contours appear more uniform at T1 than at T0. There is less difference between the visible wrinkles in terms of 'altitude'. This increase in the roughness para-

TABLE 1. Evolution of clinical parameters in both groups from T0 to T2

	LPG group ($n = 10$)			Control group ($n = 10$)		
	T0	T1	T2	T0	T1	T2
Inspection						
Dry skin	4	2	0	1	0	0
Erythema	5	1	2	3	1	0
Palpation						
Infiltration	5	3	1	3	3	3
Pain	4	1	1	1	2	1
Itching	5	1	1	3	1	3
Feeling of tightness	2	2	0	1	2	2
Feeling of induration	7	2	1	2	4	3
Softening of the skin	–	7	7	–	1	1

TABLE 2. Results of profilometric parameters in patients treated (N = 10) with LPG and non-treated patients (N = 10) at T0 and T2

Variable	T0	T2	*P*
LPG group			
RA, mean ± SD	30.45 ± 14.24	34.56 ± 11.72	0.0042
RS, mean ± SD	684.44 ± 316.63	762.47 ± 248.76	0.0110
RZ, mean ± SD	138.53 ± 56.49	154.66 ± 44.65	0.0059
RN, mean ± SD	13.90 ± 4.61	12.40 ± 2.32	0.0897
AR, mean ± SD	22.08 ± 3.46	24.13 ± 3.14	0.0035
Control group			
RA, mean ± SD	22.32 ± 6.52	20.52 ± 4.91	0.1230
RS, mean ± SD	476.76 ± 175.56	440.61 ± 154.26	0.4744
RZ, mean ± SD	104.78 ± 28.26	96.61 ± 20.81	0.1129
RN, mean ± SD	14.10 ± 2.02	15.70 ± 2.45	0.1801
AR, mean ± SD	19.61 ± 3.15	18.71 ± 2.60	0.0617

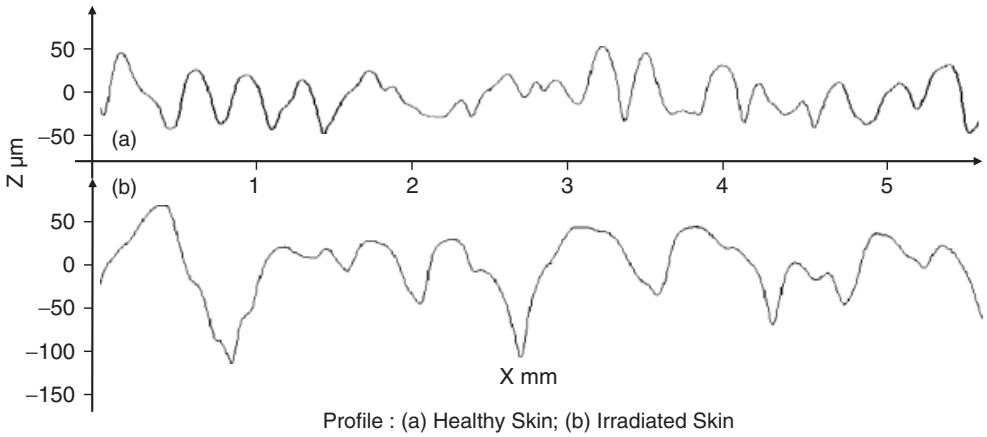

Fig. 1. Profiles of healthy skin and irradiated skin.

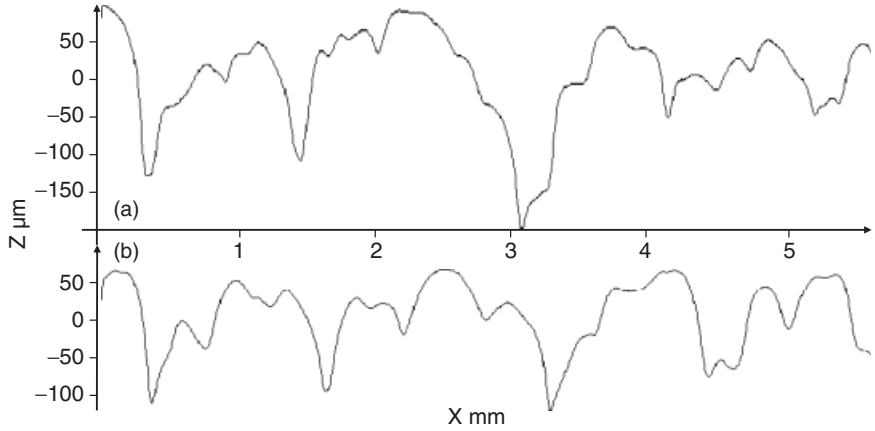

Fig. 2. Profile of LPG-treated irradiated skin at T0 and T1.

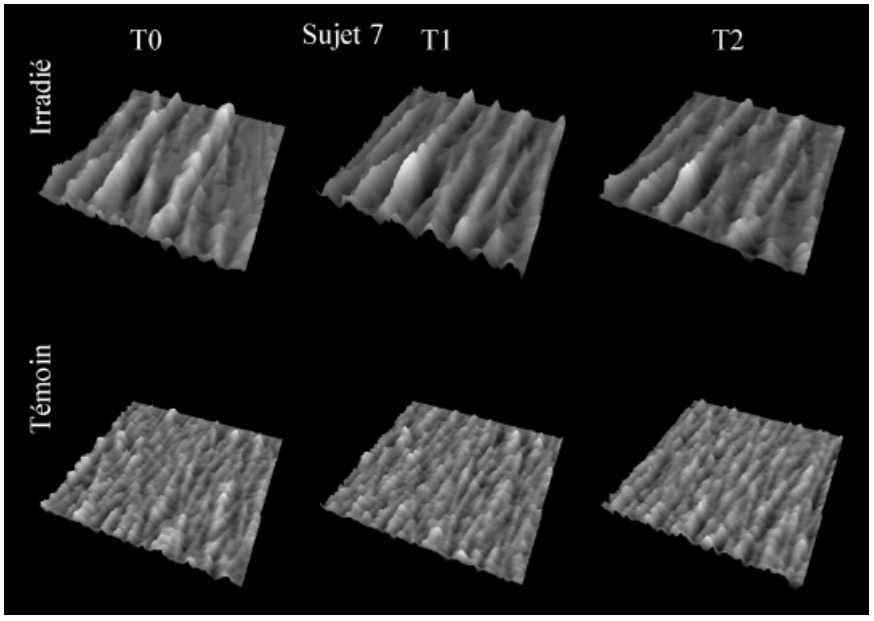

Fig. 3. 3D-image, profiles of healthy skin and irradiated skin at T0, T1 and T2.

meters is also due to the fact that the contours have become more uniform and have been strongly restructured (Fig. 3).

At T2, a comparison of the prints highlights significant changes over time for the irradiated breast treated with the LPG® technique compared with the control group. The micro-contours appear more uniform at T1 and T2 than T0. After the massage treatment stops, the contours tend to return slightly towards their initial value.

Discussion

A comparison of skin prints taken of the 20 irradiated breasts with those of the 20 non-irradiated ones highlights major changes on the skin's micro-contours after radiation.

On the 3D images, it could be seen that the wrinkles were all aligned in a specific direction compared with the non-irradiated control breasts. Together, all these observations support the fact that radiation treatment has a restructuring effect on the skin micro-contours, related to the radiation-induced fibrosis (10).

The LPG® technique seems to improve the suppleness of the irradiated breast and also reduce induration after 35 and 65 days. The test was significant in 20 patients (10 LPG and 10 control), which would appear to show that the technique has a major effect on the two side effects of skin radiotherapy. The results observed

at T2 would tend to suggest that the treatment protocol for radiation-induced fibrosis should include two phases: an 'attack' phase with about 15 sessions (three per week) and a maintenance phase of at least one session per month.

Despite the problems caused by the small size of the patient sample, this original, preliminary study highlighted the following:

- Radiotherapy causes a significant increase in the roughness of irradiated skin compared with the healthy skin of the other breast, an increase caused by the restructuring of the skin's micro-contours, with the persistence of furrows in a single direction and an increase in the depth of the furrows.
- That the LPG mechanical massage technique is effective as part of a defibrosis treatment of irradiated skin both as regards a quantitative study (study of the skin's micro-contours) or a qualitative study (clinical), leading to better comfort for the patients.

Conclusion

Therefore, use of the LPG® technique would appear to have its place alongside other treatments for skin complications of radiation-induced fibrosis that represents a non-negligible handicap for numerous patients being treated for skin cancer. Finally, the LPG® technique can be used to prepare the skin before mammary reconstruction, as the softening and reduction of skin infiltration that it causes facilitates the surgical act of mammary reconstruction.

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