



ANNEX 5
PROOF OF PERFORMANCE
Extract – Clinical Studies Pre-MKT

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ANTIAGING TREATMENT OF COLLAGEN TISSUE
AN OBSERVATIONAL MULTICENTRIC CLINICAL TRIAL
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INTRODUCTION

Chronological aging of the skin is the result of a mixture of biological, biochemical and molecular events established by the genetic code of each individual (chronoaging). Other environmental chemical and physical factors contribute to aging and these are of varying importance in determining its type and severity (photoaging).

Chronoaging and photoaging have a significant impact on the alteration of some physiological cutaneous mechanisms, not only as independent events, but also as synergic factors.

Chronoaging affects all the structure of the tegumental system: at the epidermis level, one can see a reduction in mitoses, a tendency towards premature keratinisation, the dispersion of melanocytes, and a reduction in Lagerhans cells. The dermis shows a loss of thickness and thinning out of the vascular support: the collagen fibres are fragmented; the elastic fibres are disorganized; the interstitial substance (matrix) tends to become uniform, and there are lower number of fibroblasts.

The reduction in collagen type I synthesis is clearly linked to age.

The connective tissue lay down in the extracellular matrix that is not just a supportive tissue but a very specialized and organized structure, where all changes in the internal and external environment affect the cell mechanism via the interstitial substance (matrix).

When chronoaging and photoaging changes affect the fibrillar connective tissue in the dermis, skin aging is clearly visible in loss of elasticity and turgidity and appearance of wrinkles.

PATIENTS AND METHODS

This cohort clinical study evaluated the effectiveness of COLLAGEN TISSUE in the treatment of wrinkles and skin slackening via a series of subjective and objective clinical indicators.

340 patients of both sexes (289F – 51M) aged between 35 and 75 (F) and between 40 and 70 (M), were included into the study that lasted 1 year. They were divided into 5 different age ranges (F) and 3 different age ranges (M). All patients attending the clinics of the medical doctors taking part in the study were included, without exclusion criteria.

The period of the study lasted 6 months (from Sept. 2004 to Feb. 2005).

The treatment consisted of 8 sessions on a weekly basis.

3.8% of the patients dropped out of the treatment after the first few sessions, for reasons that were not dependent on the program.

The application method was done as linear infiltration 1 cm apart, which was parallel to the skin surface in the medium and medium-deep dermis layers, or wrinkles infiltrations, according to the *tunneling* technique.

RESULTS

The results were evaluated before and after the specific treatment via the subjective classification of the visual and tactile characteristics of the wrinkles and the slackening of the face and neck tissues.

Mild reactions to the treatment were observed in 8 cases (2.3%) with slight erythema in the injection site, which disappeared spontaneously after a few minutes.

The results of the treatment with COLLAGEN TISSUE are shown in FIGG. (*see later*).

Six months after the end of the treatment, all Clients had been contacted by phone. We could visit directly 200 of them for an overall evaluation of the treatment. The treatment was still performing well and some Clients decided to make one single reinforcement treatment.

The other Clients contacted by phone express their good satisfaction for the treatment.

CONCLUSIONS

This observational cohort clinical study has shown that COLLAGEN TISSUE is highly effective and has high levels of tolerability in the treatment of all types of wrinkles, especially linear periocular and perilabial wrinkles, in Group A and B, in particular, there was a considerable reduction ranging up to the disappearance of wrinkles; in Groups C, D and E (patients from 35 to over 70) there was a steady improvement, from the index “obvious” to the index “slight”.

The treatment is safe and not painful, with long-lasting results.



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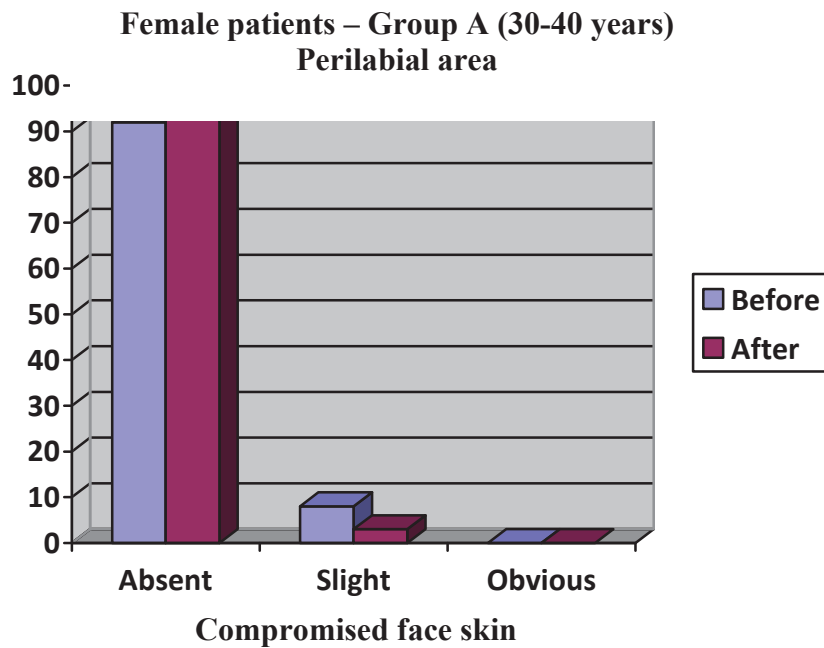
COMMENTS

The activity of MD TISSUE is surely due to the replacing of the epidermis broken or absent collagen fibers with new collagen (substitute mechanic effect) and to the supplementation of biochemical ingredients in low dose that give texture to the local extracellular matrix.

FIG. 1 – Group A (female patients – 30-40 years old), before (B) and after (A) therapy; no. = 37.

WRINKLES Compromised face skin (visual and tactile characteristics)	Cheek (Glyphic wrinkles) No. patients		Perilabial area No. patients		Periocular area No. patients		Forehead area No. patients		Eyebrow area No. patients	
	B	A	B	A	B	A	B	A	B	A
Absent	35	36	34	36	17	27	34	36	23	25
Slight	2	1	3	1	18	10	2	1	11	9
Obvious	0	0	0	0	2	0	1	0	3	3

FIG. 2





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FIG. 3

Female patients – Group A (30-40 years)
Periocular area

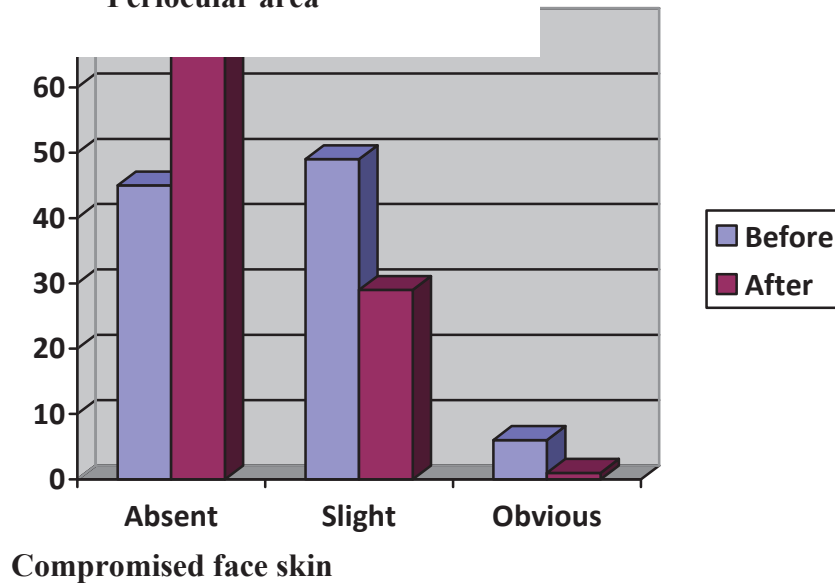


FIG. 4 – Group B (female patients – 40-50 years old), before (B) and after (A) therapy; no. = 48.

WRINKLES Compromised face skin (visual and tactile characteristics)	Cheek (Glyphic wrinkles) No. patients		Perilabial area No. patients		Periocular area No. patients		Forehead area No. patients		Eyebrow area No. patients	
	B	A	B	A	B	A	B	A	B	A
Absent	43	45	32	39	14	27	30	34	24	25
Slight	3	2	9	7	22	13	15	13	17	18
Obvious	2	1	7	2	12	8	3	1	7	5

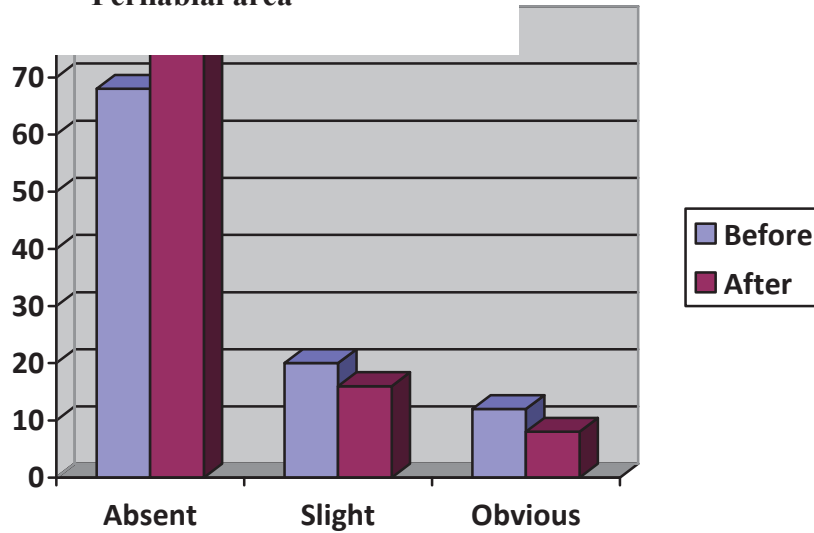


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FIG. 5

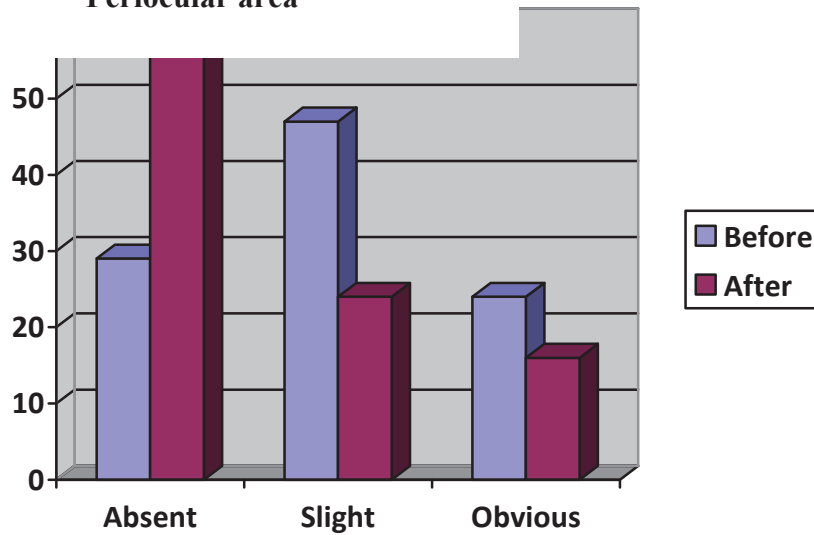
Female patients – Group B (40-50 years)
Perilabial area



Compromised face skin

FIG. 6

Female patients – Group B (40-50 years)
Periocular area



Compromised face skin



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FIG. 7 – Group C (female patients – 50-60 years old), before (B) and after (A) therapy; no. = 94.

WRINKLES Compromised face skin (visual and tactile characteristics)	Cheek (Glyphic wrinkles) No. patients		Perilabial area No. patients		Periocular area No. patients		Forehead area No. patients		Eyebrow area No. patients	
	B	A	B	A	B	A	B	A	B	A
Absent	67	73	24	37	3	5	1	0	0	1
Slight	17	13	55	47	63	67	49	54	48	51
Obvious	10	8	15	10	28	22	44	40	46	42



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FIG. 8

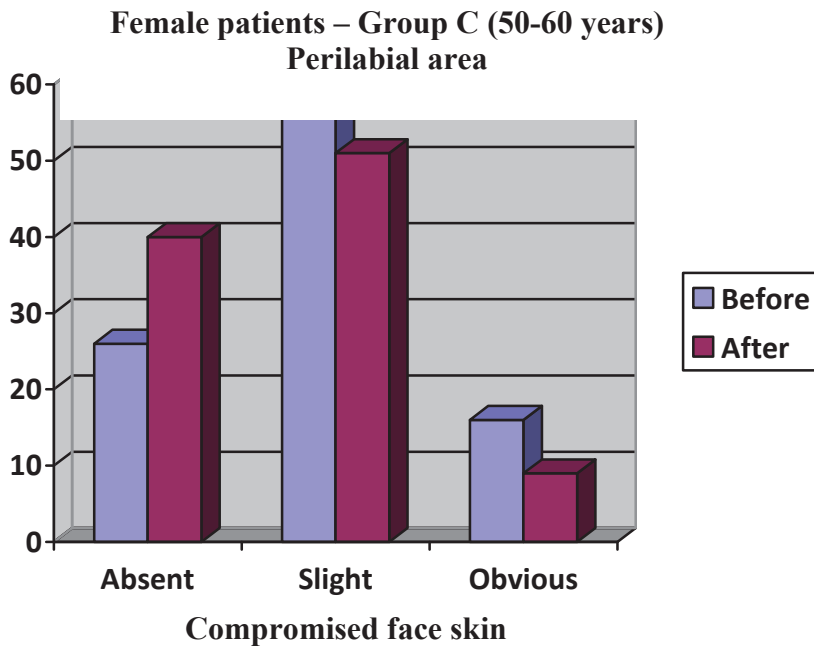
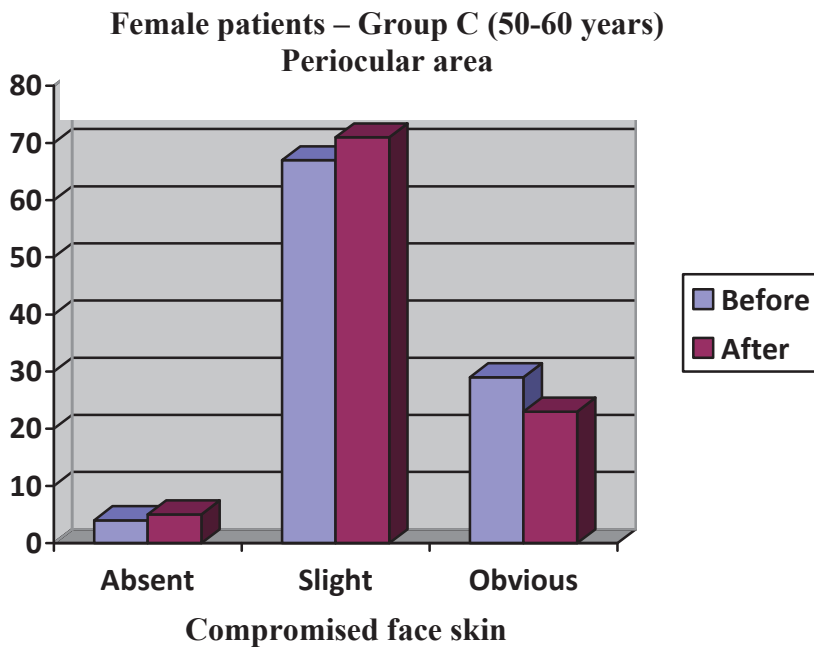


FIG. 9





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FIG. 10 – Group D (female patients – 60-70 years old), before (B) and after (A) therapy; no. = 58.

WRINKLES Compromised face skin (visual and tactile characteristics)	Cheek (Glyphic wrinkles) No. patients		Perilabial area No. patients		Periocular area No. patients		Forehead area No. patients		Eyebrow area No. patients	
	B	A	B	A	B	A	B	A	B	A
Absent	9	14	0	0	0	0	1	1	0	0
Slight	26	22	27	33	26	33	29	30	28	31
Obvious	23	22	31	25	32	25	29	28	30	27



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FIG. 11

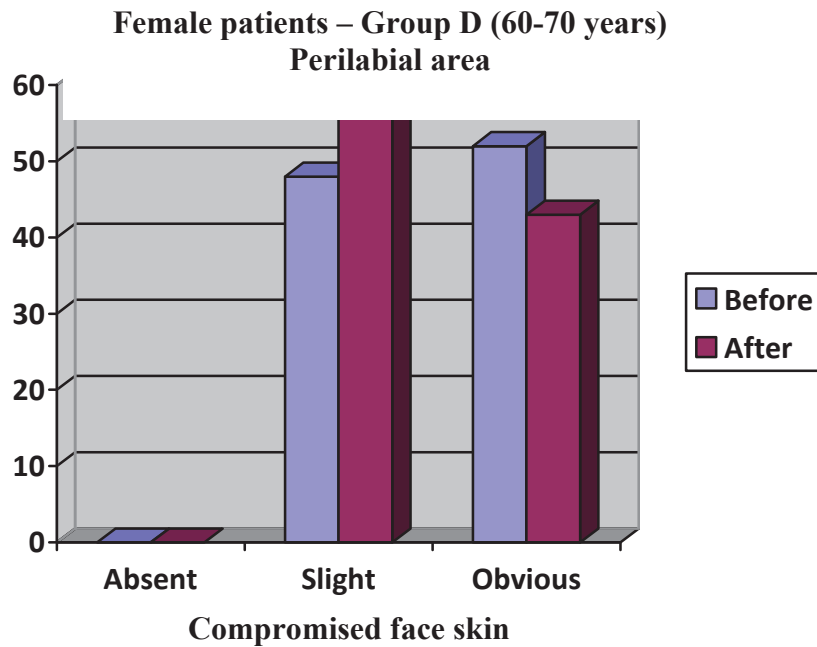
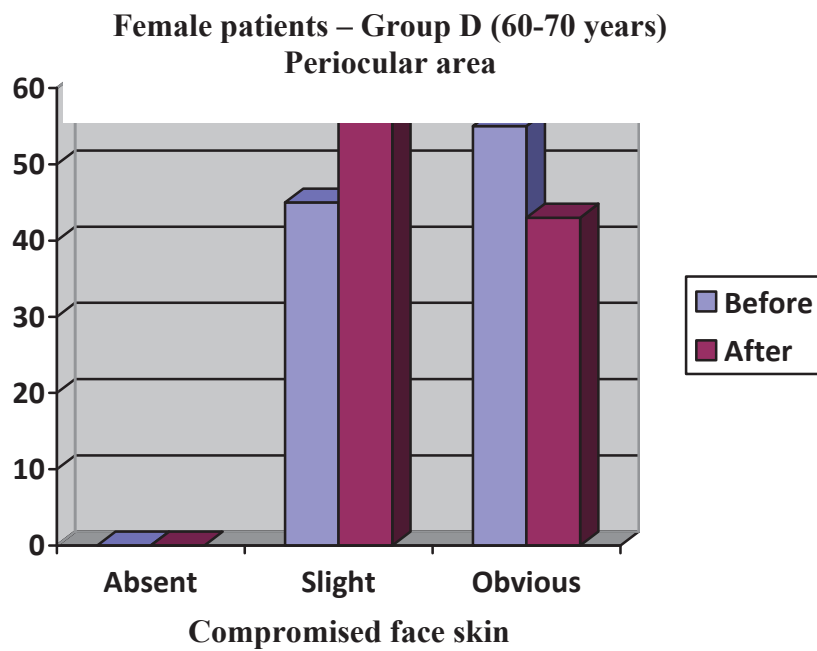


FIG. 12





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FIG. 13 – Group E (female patients – >70 years old), before (B) and after (A) therapy; no. = 52.

WRINKLES Compromised face skin (visual and tactile characteristics)	Cheek (Glyphic wrinkles) No. patients		Perilabial area No. patients		Periocular area No. patients		Forehead area No. patients		Eyebrow area No. patients	
	B	A	B	A	B	A	B	A	B	A
Absent	2	2	1	0	0	0	0	0	0	0
Slight	25	28	23	27	24	26	24	24	22	22
Obvious	25	22	28	25	28	26	28	28	30	30

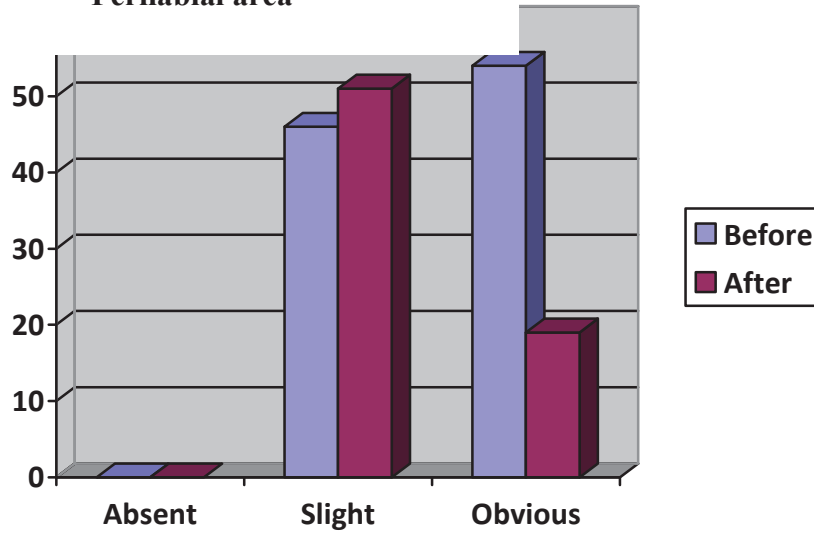


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FIG. 14

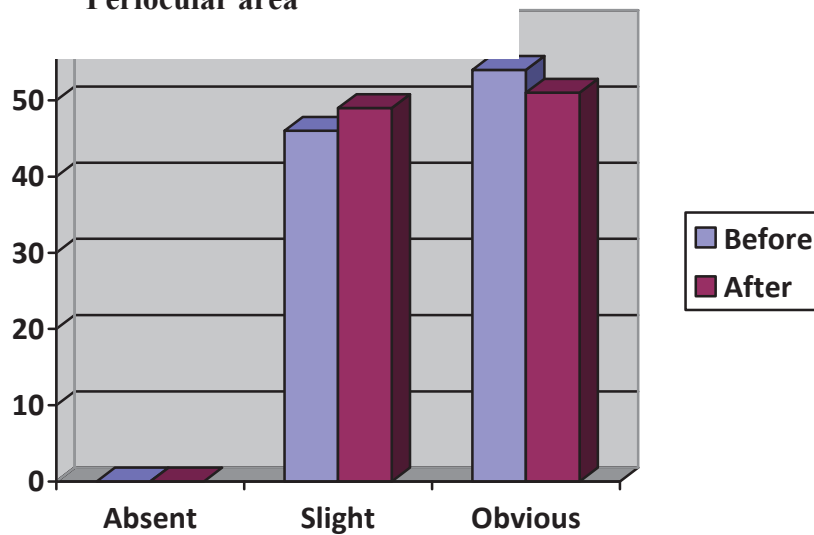
Female patients – Group E (>70 years)
Perilabial area



Compromised face skin

FIG. 15

Female patients – Group E (>70 years)
Periocular area



Compromised face skin



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FIG. 16 – Group B (male patients – 40-50 years old), before (B) and after (A) therapy; no. = 25.

WRINKLES Compromised face skin (visual and tactile characteristics)	Cheek (Glyphic wrinkles) No. patients		Perilabial area No. patients		Periocular area No. patients		Forehead area No. patients		Eyebrow area No. patients	
	B	A	B	A	B	A	B	A	B	A
Absent	21	22	19	21	9	11	19	20	18	20
Slight	3	2	3	3	11	10	5	5	6	5
Obvious	1	1	3	1	5	4	1	0	1	0

FIG. 17 – Group C (male patients – 50-60 years old), before (B) and after (A) therapy; no. = 22.

WRINKLES Compromised face skin (visual and tactile characteristics)	Cheek (Glyphic wrinkles) No. patients		Perilabial area No. patients		Periocular area No. patients		Forehead area No. patients		Eyebrow area No. patients	
	B	A	B	A	B	A	B	A	B	A
Absent	12	13	11	13	8	8	12	13	12	12
Slight	7	8	7	6	10	11	8	7	8	9
Obvious	3	1	4	3	4	3	2	2	2	1

FIG. 18 – Group D (male patients – 60-70 years old), before (B) and after (A) therapy; no. = 5.

WRINKLES Compromised face skin (visual and tactile characteristics)	Cheek (Glyphic wrinkles) No. patients		Perilabial area No. patients		Periocular area No. patients		Forehead area No. patients		Eyebrow area No. patients	
	B	A	B	A	B	A	B	A	B	A
Absent	1	1	1	2	1	1	1	1	1	1
Slight	2	3	2	3	3	3	2	3	3	4
Obvious	2	1	2	0	1	1	2	1	1	0

FIG. 19 – Global evaluation on the treatment: results.

Evaluation	Very poor No. (%)	Poor No. (%)	Acceptable No. (%)	Good No. (%)	Excellent No. (%)
Doctor's evaluation	0 (0)	0 (0)	0 (0)	105 (31)	235 (69)
Patient's evaluation	0 (0)	0 (0)	0 (0)	95 (28)	245 (72)

FIG. 20 – Global evaluation on tolerability.

Evaluation	Very poor No. (%)	Poor No. (%)	Acceptable No. (%)	Good No. (%)	Excellent No. (%)
Doctor's evaluation	0 (0)	0 (0)	0 (0)	3 (1)	337 (99)
Patient's evaluation	0 (0)	0 (0)	0 (0)	10 (3)	330 (97)