Carboxytherapy in Aesthetic Medicine

43

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43.1 Introduction

Carboxytherapy – therapy by carbon dioxide (CO_2) – is a traditional medical technique used in modern times since 1932. The term carboxytherapy was used for the first time by Parassoni in 1995 [1]. Synonymous terms – carbocrénotherapié, carbondioxidetherapy (abbreviated as CDT) – are more traditional, often used in Francophone angiologic medical literature and in South American information sources. During the last 15 years, the method has had unexpected gradual revival, the peak of which is now. New therapeutic possibilities have been shown including those in aesthetic medicine. Interesting results were reached in skin rejuvenation, in the treatment of certain types of scars, especially atrophic ones, of striae atrophicae distensae (stretch marks), of so-called cellulite-fibrolipodystrophy adhesions after liposuctions, and in the treatment of hair fall and different types of alopecias. The method is "natural" which makes it attractive for many patients; however, the application itself can be a bit painful or unpleasant. In comparison with modern instrumental techniques or botulinum toxin, the results of carboxytherapy are good, but usually not so fast or so manifest. Sometimes they tend to be also rather unpredictable concerning to the intensity of reached improvement, depending probably a lot on biologic age of the subject. However, in the treatment of cellulite, adhesions after liposuctions, stretch marks, some atrophic scars, and alopecias, the effects are sometimes surprising and really valuable for both the patient and the treating physician.

Carbon dioxide (CO_2) is a trace gas of the atmosphere (cca 0.038%), it is noninflammable, nontoxic in small concentrations, nonallergenic, and 1.5 times heavier than the air. It is soluble in water depending on the pressure and the temperature. Adaptation to increased levels of CO_2 can occur (e.g., the case of workers in submarines or similar closed and small spaces). Through normal ventilation of 6 L of the air per minute, 250 mL of O_2/min is consumed and 200 mL of CO_2/min is exhaled. In hyperventilation, 4–5 L of O_2/min is consumed and 4–4.5 L of CO_2/min is exhaled. Through carboxytherapy made by gas flow of 30–50 CO_2 mL/min, slight unconscious hyperventilation resolves mild increase of CO_2 levels. In laparoscopy even 12–20 L of CO_2 can be used to expand abdominal cavity, without any toxic effect [1–3]. Moreover, the patients subjected to sigmoidoscopy performed with CO_2 insufflation of the bowel are reported in 84% with no postexamination discomfort compared to 64% with no discomfort after air insufflation [4]. Findings from angiographic procedures proved the safety of CO_2 gas. CO_2 gas is nonembolic and even a bolus injection of 100 mL of CO_2 or continuous flux of 20–30 mL/s is referred to lead to no adverse reactions [5].

Normally a balance between CO_2 and O_2 is kept as a part of homeostasis. Both CO_2 and O_2 are bound to hemoglobin, although not in the same sites. In lower pH and higher partial pressure of CO_2 (pCO_2), the affinity of hemoglobin to oxygen is decreased – Bohr effect, resulting in higher release of oxygen from

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hemoglobin. This, together with temporary vasodilatation (local increase of CO_2 and H+ in extracellular fluid cause relaxation of smooth muscles of the vessels) leads to better oxygenation and overall improvement of local metabolism – one of the main mechanisms of the effect of carboxytherapy.

CO_2 gas in the human body is transported in different ways:

1. 70–80% is converted in erythrocytes to bicarbonic ions HCO_3^- by carboanhydrase ($CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$). This reaction is very fast, in cca 1 s. H+ in erythrocytes binds to buffer systems, mainly to hemoglobin. HCO_{3-} diffuses out from the erythrocyte to plasma (and from 70% is exchanged to Cl^-). If the patient is treated by inhibitors of carboanhydrase, he should not be treated by carboxytherapy, as the main way of CO_2 transport is inhibited.
2. 5–10% of CO_2 is carried in plasma as dissolved gas (CO_2 is 20 times more dissolvable in blood than O_2).
3. 5–10% of CO_2 is bound to hemoglobin forming carboxylhemoglobin (CO_2HHb) in the reaction: $Hb–NH_2 + CO_2 \leftrightarrow Hb–NH–COO– + H^+$.
4. Less than 2% of CO_2 is bound to plasmatic proteins, also in carbamino binding. This reaction is very slow and hence not very important [6].

43.2 History of Carboxytherapy in General Medicine

In certain areas of the world natural spring CO_2 gas, often of 99% purity, rises from the ground. Such gas can mix with deep sources of water usually of meteoric origin, beside trace components. Pure gas springs of temperature under 100°C are called “mofets” [7]. Sometimes water and gas springs create interesting natural phenomena, burbling muddy lakes colored by minerals (e.g., sulfur, ferrum) are protected as the unique natural heritage. In certain sites, naturally based spas had been established during history (Spa Royat in France, Massif Central where local gas spring of power 150 m^3/h contains 99.5% of CO_2, Marianske Lazne – Marienbad in Western Bohemia, spa places in Karpats – in Hungary, Romania, in Japan).

Perhaps the best documented historical tradition is that of Spa Royat in France, where first Roman spa “Rubiacum” (because of rosy water contenting ferrum) was found in 20 BC, in the era of the emperor Augustus. Later the Celtes worshipped the place, which had a reputation of “miraculous,” however, after the invasion of Barbars in fifth century the site was forgotten. In later Middle Ages, the Benedictine abbey was found in the place, and although it was soon devastated by wars, later it was slowly rediscovered [8]. In twentieth century, new, modern times came, based not just on the tradition, but gradually more and more on scientific research. Here in 1932, Barrieu first treated his patients by CO_2 spring gas injections [9]. In the same year, the method was explored also in Argentina [3], with publications in Spanish medical literature as soon as in 1934. In 1946 in France, L’Institute de Recherches de Royat was inaugurated, managing to produce during the second half of the century nearly 400 publications about carboxytherapy (carbocrenotherapie) [8]. In 1953, Romeuf [10] published his 20 years experience with the method. Hence, basic research about carboxytherapy (carbocrenotherapie) can be found in the studies from Royat: Ambrosi et al. documented in their paper [11] that after subcutaneous injection of CO_2 gas (150–300 mL) unilaterally to the ankle, the puls curve was augmented with the peak 15 min after the injection, and additionally, that the smaller puls curve augmentation came also on the contralateral side (probably by reflex mechanism). Ambrosi [12] showed also improvement of $tcPO_2$ (transcutaneous oxygen pressure) of the patients with intermittent claudication passing the therapeutic cure (3 weeks of CO_2 gas subcutaneous injections) in Spa Royat. After the cure, the curve of the $tcPO_2$ before, during, and after the walking test was augmented and recuperation of the niveau of its base came faster. $tcPO_2$ monitoring is known in clinical praxis as a more reliable indicator of preoperative ischemia and postoperative outcome of revascularization than hemodynamic, Doppler-derived pressure tests [13].

In another work, Ambrosi and Lafaye [14] proved by thermography that after the 18 days lasting thermal cure of CO_2 injections (500–800 mL), 23 from 32 claudicative patients showed more than 20% warming of the lower extremities while 2 had smaller warming and 7 were negative, showing slight cooling. In a paper by Avril et al. [15], 143 ulcers were studied (80 of arterial origin, 13 venous, 9 capillary, 31 mixed or atonic, 10 of slow cicatrization), all not reacting for usual treatment methods. After the cure of local gas baths (dry baths) of the wounded extremity, 22.2% of the ulcers were healed, 57.3% improved, 16.1% unchanged, and only 1.4% worsened.

In 1989 and again in 1999, the consensus about the effects of CO_2 was formulated on the international conference in Fribourg-en-Brisgau (Freiburg im Breisgau) [16, 17]:

- Local increase of blood supply and opening of functionally closed capillaries
- Dilatation of precapillary segments
- Improvement of oxygenation by increased liberation of oxygen based on Bohr effect (in lower pH and higher pCO_2, the affinity of hemoglobin to oxygen is decreased)
- Improved deformability of erythrocytes
- Modification of threshold of thermoreceptors
- Antiseptic effect

Recently, the research is more detailed. Toriyama et al. [18] treated 83 critical ischemia extremities of 68 patients with peripheral arterial disease by bathing in CO_2 water (1,000 ppm, 37°C) for 10 min twice daily for more than 2 months. Sixty-nine limbs (81.2%) could be salvaged. These were 27 limbs from 28 (96.4%) having in the beginning of the treatment ulcer and gangrene on 1 toe, 13 from 16 limbs (81.2%) with ulcer/gangrene on multiple toes, and 29 from 39 (74.4%) limbs with ulcer/gangrene in all toes. The authors concluded that the effect of CO_2-enriched water on subcutaneous microcirculation might be brought by peripheral vasodilatation reflected by increased parasympathetic and decreased sympathetic activity.

The most comprehensive summary can be found in the paper of Irie et al. [19] who explored the effects of CO_2 bathing of ischemic lower limbs of mice. They demonstrated that CO_2-enriched water (1–1.2 g of free CO_2/L of water, pH 5.0) caused the enhanced induction of local VEGF synthesis associated with activation of the NO (nitric oxide)-cGMP pathway and mobilization of endothelial progenitor cells, resulting in NO-dependent neocapillary formation that led to an increase in collateral blood flow. Thus, CO_2-enriched water bathing therapy could be included in angiogenic therapies associated with neovascularization.

43.3 Carboxytherapy in General: Different Kinds of Treatment [20]

In nonspa places where natural spring CO_2 gas or water is unavailable, we use commercially provided and cheap, medical grade CO_2 gas. In spas, depending on natural conditions, local natural gases and waters are still widely used.

1. External baths in water containing free gaseous CO_2 in concentration at least 1 g of gas/L of water (whole body baths/baths of the limbs/individual or common walking in CO_2 water corridor – "couloir de marche individuelle" or "collectif" in Spa Royat, France)
2. Dry external baths – "baths" in CO_2 gas placed in bath tube (because the gas is heavier than the air) or in the sac (whole body/more than lower half or half of the body/the treated limb)
3. Variations of above – jets of CO_2 water, vapor of CO_2 water used locally on the treated limbs or their parts, hot mud prepared from local soil, and CO_2 water applied locally, e.g., on joints (Spa Royat)
4. Injectional carboxytherapy – carboxytherapy in narrow sense, more intensive, better targeted to the problem because the application is performed just to the problematic site or around it. This kind of therapy is usually meant in aesthetic medicine. Injected CO_2 immediately spreads in the tissue and "diffuses" fast in blood (the transport of CO_2 is described earlier). Most of the gas is eliminated by lungs, and a small portion is converted to carbonic acid and eliminated through kidneys [3].

43.4 General Indications

Carboxytherapy can be useful in the treatment of any disease when we need improvement of vascular supply and of the local tropics or analgesic effect. Traditionally, there are good results in the treatment of vasculopathies, ischemic diseases including diabetic periphery syndrome, Morbus Buerger, Reynaud's syndrome, chronic venous insufficiency, and chronic venous-lymphatic insufficiency. New indication is the treatment of erectile dysfunction associated with microangiopathy. In dermatology, the method is very useful in wound healing including leg ulcers, in the treatment of hair disorders, sometimes it helps to improve psoriasis, sclerodermia, paradoxically even angiectatic rosacea (although during CO_2 administration temporary local vasodilatation is present, in repetitive treatments there is a tendency to normalization of vascular circulation, so sometimes during CO_2 facial rejuvenation we observe diminishing of small vessels in the eyelids or on the cheeks). Some physicians experiment with the treatment of nail

disorders, vitiligo, or erysipelas with success, but these experiences can be dependent also on the individual patient state and not always are reproducible.

43.5 General Contraindications

General contraindications of carboxytherapy are severe respiratory insuficiency, severe renal failure, chronic congestive heart failure, patients treated by carboanhydrase inhibitors (e.g., acetazolamide, diclophenamide), severe anemia, chronic liver insufficiency with decrease of plasmatic protein levels, gaseous gangrene (Clostridial infection). However, in the treatment of concrete patient in bad general state with additional, e.g., leg ulcer or incipient gangrene, the physician should decide individually. As carboxytherapy is not a pharmacological treatment and the next alternative can be sometimes only amputation, it can be worthy to try the method, although less intensively than in the case of healthier patient. In aesthetic medicine, the most frequent contraindications are pregnancy and breastfeeding (mainly because of legal reasons).

43.6 Indications in Aesthetic Medicine

The possibilities of carboxytherapy use were gradually explored since 1993 [21], first during pioneer research of Brandi and D'Aniello in the University of Siena, Italy. Brandi et al. [22] described the effect of injectional carboxytherapy on the fatty tissue on histological level: lysis of adipocytes resulting from fracturing of fatty tissue with the release of triglycerides in the intercellular spaces, these changes however did not damage connective spaces with vascular structures and nerves. The dermis had a thicker appearance than before the treatment, with collagen fibers distributed more diffusely. It was also found that improvement of skin elasticity after carboxytherapy measured by cutometer SEM 474 Courage-Khazaka was as high as 55.5% (Brandi, workshop Warsaw, September 2007).

Development of practical skills, different styles of injectional application, and experimenting with new or rare indications of carboxytherapy proceeded in South America, especially in Brazil, quite likely because of the versatility and art of local physicians. Thanks to these experiences mixed with those from the other areas of the world (Brandi, Parmigiano, D'Aniello in Italy, Liebaschoff, Cadic, etc.), it is clear now that carboxytherapy can be very useful in many indications in aesthetic medicine: These are skin rejuvenation (face, neck, decolleté, dorsal hands, skin of the body), the treatment of stretch marks and certain types of scars (especially linear both atrophic and hypertrophic scars), the treatment of cellulite (fibrolipodystrophy), and adhesions after liposuction. As hair state is also the subject of aesthetic medicine, the treatment of the hair fall and alopecias should be also added to this part, similarly like the treatment of the wounds of different origin.

43.7 CO_2 Gas in the Tissues in Aesthetic Medicine

Traditionally, communicated effects of CO_2 gas in the tissue are vasodilatation, improvement of local blood supply, normalization of the circulation, angiogenesis, and resulting increase of local metabolism leading to improvement of the trophics. However, in aesthetic medicine, because of sometimes surprisingly impressive improvement after even just one carboxytherapy session in certain cases of scars, skin rejuvenation, or cellulite/adhesions, it was hypothesized that also other factors may play an important role in building of the effect. These are first of all mechanical undermining by the gas flow (similarly like in needle subcision, e.g., in the treatment of scars or wire scalpel technique on adhesions or severe cellulite depressions treatment). Second, there are effects of mechanical tension on the cells (especially in rejuvenation) and pressure (especially in the treatment of cellulite or adiposities) resulting from relatively strong gas flow during the CO_2 administration. Third, presumably there is also some slight influence of temporary acidosis [23, 24].

Currently, because of the liveliness of CO_2 gas and speed of local cellular reactions it is not clear how to proof the real role of these factors of hypothetically high importance in experiments either in vitro or in vivo. Human skin cell cultures are routinely cultivated in the atmosphere enriched with CO_2 (5–10% depending on the concentration of hydrogen carbonate in the medium) [25]. To simulate conditions of carboxytherapeutical treatment (ideally including the mechanical force of the gas flow) in cell culture or artificial skin model is currently not possible and we can only speculate, backed by the results of other experiments. There are numerous papers describing the effects of mechanical forces

(usually stretching, but also pressure) on dermal fibroblasts, keratinocytes, and melanocytes [26–32]. It is known that the cells, especially fibroblasts, are able to respond to mechanical signals by expression of numerous genes and influence or transform such stimuli into a series of biological events, resulting in changes, e.g., in connective tissue. Fibroblasts release cytokines and growth factors of autocrine and paracrine effects. Autocrine activity includes transforming growth factor beta (TGF-ß) induced synthesis and secretion of connective tissue growth factor (CTGF) which promotes collagen synthesis and fibroblast proliferation. Paracrine activity has influence on keratinocyte growth and differentiation through fibroblast secretion of keratinocyte growth factor (KGF), granulocyte-macrophage colony stimulating factor, interleukin IL-6, and fibroblasts growth factor (FGF). Keratinocytes synthesize IL-1 and parathyroid hormone-related peptide, which stimulates fibroblasts to produce KGF. Fibroblasts produce also vascular endothelial growth factors (VEGF-A, B, C, and D) which are important in regulation of vascular and lymphatic endothelial cell proliferation through specific receptors leading to angiogenesis and lymphangiogenesis. However, although fibroblasts from different anatomical sites have similar morphology, they are highly heterogeneous populations of cells demonstrating, depending on their origin, their own gene-expression profile and phenotypes and synthesizing extracellular matrix proteins and cytokines in a site-specific manner [26, 33].

Additionally, in experiments there can be differences depending on the type of the stretching (uniaxial, biaxial, cyclic, etc.), its lasting, and underlying substrate. In carboxytherapy, we can expect more or less uniaxial stretching in the case of skin rejuvenation, treatment of wounds and scars, and "multiaxial" stretching and pressure in the treatment of cellulite. Generally, it was postulated that mechanical stretching leads to cellular proliferation, while mechanical pressure induces the cascades leading to cellular differentiation [27].

Kessler et al. [28] demonstrated that cytoskeletal structures of dermal fibroblasts on collagen lattices changed drastically depending upon mechanical load. Such fibroblasts developed prominent actin stress fibers traversing the entire cell body, making the cells to resemble myofibroblasts. On the contrary, lack of tension led back to total reorganization of actin cytoskeleton and focal adhesion architecture, fibroblasts appeared rounded and actin stress fibers disappeared. VEGF-C was induced in fibroblasts exposed to tensile stretch. Fibroblasts showed maximal expression of TGF-ß1 after 12 h of cultivation on tensile collagen gels (with much less expression on relaxed gels). After 20 h the TGF-ß1 expression remained high only under tension and declined in the relaxed system. (Although these data could seem irrelevant to carboxytherapy because the gas is "metabolized fast," from praxis we know that the gas can stay in the tissue for quite a long time: some patients refer about heavy or swollen legs lasting for 1 or 2 days after the administration of higher volumes of the gas – like 600 mL or more per one lower extremity. Also after medium insufflation of the eyelids sometimes we observe the rest of the gas staying in the tissue for many hours. With lower volumes the situation is less pronounced, but it is clear then that we should count with mechanical force of the gas on cellular level lasting sometimes even for dozens of hours.) Expression of CTGF was during the whole course of the experiment and significantly higher in stressed cells than in relaxed cells. CTGF was independent of high TGF-ß levels and its induction appeared to be directly dependent on mechanical stress.

Both HaCaT cells (the spontaneously immortalized human keratinocyte cell line used often in skin cell culture experiments) and normal human skin keratinocytes are highly sensitive towards mechanical stretching and respond with increased DNA synthesis, which supports proliferative properties of the cells [29]. Even a single mechanical stretch applied to HaCaT keratinocytes elevated the substrate adhesion, in particular to fibronectin and collagen type IV and also rose a rapid redistribution of ß1-integrins in clusters on the basal cell membrane, although the overall amount of this integrin subset was not changed. Clustering of ß-1 integrins was described also for other cell lines (endothelial cells, fibroblasts, osteoblasts, heart muscle cells) indicating a universal response to this stimulus. It seems that dynamic reorganization of integrins regulates the binding capacity [30].

Grinnell et al. [29] stated in 1999 that release of mechanical tension triggered apoptosis of human fibroblasts on a model of regressing granulation tissue, while early passage human diploid fibroblasts under the mechanical tension showed little or no apoptosis. Kippenberger et al. [27] demonstrated on HaCat cells that mechanical stretch induced activation of epidermal growth factor receptor (EGFR) which meant functional activation of the cells. They showed in experiments that mechanical stretch protected the cells against the onset

of apoptosis and that increase in cell numbers of the culture in response to mechanical stress was, at least in part, due to a suppression of apoptosis. In the paper of Ferreira et al. [34], it was proven in the experiment on Wistar rats (10 male ones, born from the same mother and father) that intradermal or subcutaneous injection of CO_2 gas leads to increased collagen turnover in the dermis in comparison with the dermis of animals injected only with saline solution. Moreover, after intradermal gas injection the collagen was more compact and its arrangement in the dermis of the old animals was similar to that of the young ones. These findings are interesting, in concert with Kippenberger et al. [27] experiments supporting certain uniqueness of carboxytherapy as a "natural antiaging" treatment which connects the effects on angiogenesis and improvement of the trophic as well as the effects induced in the cells by mechanical powers of the gas flow and gas volume. However, for full and detailed explanation of these mechanisms, further research is highly needed.

43.8 Devices for Carboxytherapy

Some simple devices are designed for the application of adjusted fixed amount of gas (usually from 1 to 5 mL) in single punctures in uncontrolled speed. These are safe only for balneotherapy and physiotherapy. In aesthetic medicine and especially in the treatment of the face we need a more precise tool, with ability to apply very different amounts of the gas in different speeds, depending on the indication, state, and the compliance of the patient. Also "the power" – the pressure of the gas in the tube is important.

Anecdotally, different impression and incomparable results were observed in rejuvenation of facial complexion by two different machines adjusted at the same gas flow (velocity), but evidently providing different gas pressure in the tube. The one with smaller pressure, and thus "softer," with not so centered power of the gas led to visibly smaller results and experienced patients noticed not only the difference in feeling of the gas flow in the tissue during the application but also smaller effect after the "softer" device (unpublished observation, Koutna).

Some South American devices (Carbtek Advanced® by Estek) are able to work also in intermittent, pulsing regime, which can be interesting for the treatment of cellulite. The best machines provide continual, stable and adjustable flow of the gas. They contain mechanical and anti-bacterial filters assuring the sterility of the gas, and prewarm the gas (the administration of the "cold" gas of room temperature is usually more unpleasant for the patient). Such devices are, e.g., Rioblush® (Rioblush) or Evolution® (Carbossiterapia Italiana). Certain devices copy traditional mesoguns – Carboxypen® (Anti-aging Medical Systems), some offer even the combination of carboxytherapy and mesotherapy – Mesoflux® (PromoItalia).

Although some physicians state that good results can be reached with any apparatus and that the results achieved with different kinds of machines are the same, the author does not agree with this opinion. It is true that cellulite or scars can be basically treated by any carboxytherapeutic device (although with different levels of comfort for the patient), but if one wants to work liberately, in wide spectrum of indications including facial rejuvenation, to offer the best comfort to the patients and not to be afraid of one's own technical mistake, it is highly recommended to invest in a modern, sophisticated, versatile device.

The treatment session (Table 43.1) and recommendations after the treatment: Generally, for a treating person it is quite essential to know "how it is" during the treatment and what kind of sensations the patient feels. The injection of the gas one can try to apply to himself or herself, often the first self-experience with the treatment happens on the workshops. There is a difference in the treatment of different areas, by different machines, etc., but it is good at least to experience a small injection of the gas somewhere on the forearm or on the dorsum of the hand. In daily praxis, carboxytherapy on the body can be performed by a trained nurse and depends on the responsibility of the physician and legal situation in the particular country. However, at least facial and neck treatment should be performed by a physician.

After explaining the course of the treatment to the patient including possible local sensations which may occur during the application (feelings like slight or more intensive burning, strange feelings or pressure in the treated area, feelings like when cold water flows in the area, these all lasting for cca dozens of seconds), informed consent is signed. Then the parameters (gas flow – velocity, expected time, type of the treatment, etc., depending on the technical possibilities of the machine) are adjusted on the therapeutical device (Fig. 43.1). After the disinfection of the area (this can be

Table 43.1 Summary of carboxytherapeutical treatment for different indications

	Gas administration	Usual intervals between the sessions	Usual number of sessions	Usual expected effect
Skin rejuvenation	As superficially intradermally as possible	2–4 weeks	3–10	Very good (smoothness, often slight tightening)
Scars – flat atrophic	As superficially intradermally as possible	3–4 weeks	2–6	Very good, especially on narrow ones (smoother surface, often slight tightening), on wide ones variable effect
Scars – deeper atrophic	As superficially intradermally as possible + also under the scar with aim to destroy here pathological fibrotic strands	3–4 weeks	Try 2–3, then only if there is perspective for further improvement	Variable, minimal in the case that adhesions under the scar are too tough
Scars – linear hypertrophic	Into the mass of hypertrophic scar	3–4 weeks	Try 2–3, then only if there is perspective for further improvement	Good (bleaching, decrease of the surface, sometimes slight tightening)
Scars – keloids	Into the mass of the keloid	1–2 weeks	Try 2–3, then only if there is perspective for further improvement	Minimal
Acne scars – ice pick, large pores	As superficially intradermally as possible	2–4 weeks	Try 2–3, then only if there is perspective for further improvement	Limited
Acne scars – saucer shape, rolling, boxcar	Intradermally			
Stretch marks	As superficially intradermally as possible	2–4 weeks	3–20, sometimes more	Good (smoother surface and tonus)
Hair fall and alopecias	Superficially subcutaneously	1–2 weeks	From 3 to approximately 30, there should be some effect till 8–10th session	Good, depending on general state
Wounds	Superficially subcutaneously and if on the limb, apply also along the main superficial veins	2–3 days, later 1 week	From 6 to 30 or more	Good, depending on general state
Cellulite and adhesions after liposuction	Deeply subcutaneously, to the fat	4 days – 1 week, later 2 weeks, 1 month	From 4 to approx. 10, then maintaining	Very good, usually faster and better on soft cellulite than on the hard one, the same for adhesions No effect on stone hard adhesions
Facial contouring	To the subcutaneous fat	1 week	8 and more	Variable, depending on general state
Body contouring		3–4 days, 1 week		

Fig. 43.1 One of devices for carboxytherapy (Carbomed®), ready for the treatment

Fig. 43.2 Sterile single use tube and mesotherapeutical needles 30 gauge

Fig. 43.3 (**a**) Redness just after several CO_2 injections for rejuvenation by carboxytherapy – forehead, upper eyelids. (**b**) Redness just after several CO_2 injections for rejuvenation by carboxytherapy – forehead, around the left eye

done only in the injection spots just before the individual injection-because the gas is sterile and has antiseptic effect by itself, the method is very safe and possibility of folliculitis or any pyodermia as a side effect is very unprobable), the gas injection is applied. The original single use tube set leading the gas from the device to the needle (usually we use mesotherapeutical needle 30 gauge) must be sterile and always new, individual for every patient (Fig. 43.2). (Although the gas has antiseptic effect, there occurred a case of transfer of hepatitis from one patient to the other by nonchanged tube). Because after connecting the tube with the needle, the tube contains first the air, not CO_2, it is recommended to get it out. This can be achieved either by first pressing the foot switch, wait some seconds for the full gas flow (this, in case if one is not sure can be felt if the open needle or just tube is put close to the skin of the ventral wrist area of a physician for a moment) and then to inject. This is the easiest and proper solution, however, with the disadvantage for the patient because he or she feels the gas together with the pain resulting by the needle puncture, without any preparation, "at once." The other possibility, but manually more difficult and maybe easier for male physicians because of the power in fingers, is to wait for the full gas flow and then to pinch the tube near the needle by thumb and index finger, then to inject, then to release the fingers and let the gas flow into the tissue (Brandi, workshop Warsaw 2007).

In skin rejuvenation, fresh scars, flat atrophic scars, large pores, ice pick scars, and stretch marks, the gas is applied as superficially intradermally as possible. Local skin bleaching coming just in the moment when the gas is injected can be observed, changing fast into redness (Fig. 43.3). If we inject more gas (depends on the area

Fig. 43.4 CO_2 administration – visible running emphysema (the treatment of cellulite on the thigh of a thin person)

and indication, as will be discussed later) or inject less superficially, usually "running" emphysema in stripes or routes can be observed depending on the state of the skin and subcutis (Fig. 43.4). The gas, however, tends to "run" not simply in the direction of the needle as one would expect, but often also in the direction of the lowest resistance of the surrounding tissue (so also deeper). This is important especially in the treatment of the face. Emphysema is typically entirely fading in minutes, although sometimes its rests can be seen or felt for many hours and crackling sensations in the treated area can be palpated as well, especially by sensitive patients. This crackling is percepted usually as something rather interesting or exotic and patients do not tend to evaluate it as something bad. Redness and warmness of the area can be present for longer time, but usually not longer than 10 min. The gas volumes used here are usually small, from 0.5 to 3 mL per 1 injection spot.

For the treatment of hair disorders, wounds, or some superficial aches (like syndrome of carpal tunnel), the gas should be applied superficially subcutaneously. In this situation, visible emphysema is present only in areas of thin skin and usually just redness can be observed. The gas volumes per injection spot are usually from 1 to 5 mL.

In the treatment of cellulite, adhesions after the liposuction, and in body or facial contouring, the gas should be applied deeply subcutaneously into the fatty tissue. Here we see just increase of the volume of the treated location and redness. The volumes applied here per injection spot must be much higher, from 5 to even 50 mL per injection spot, depending on the state, gas flow, and tolerance of the patient.

After finishing the treatment there still can be capillary bleeding in some injection sites, requiring cleaning by disinfection solution, momentary compression, and sometimes (the legs) a small piece of sticking plaster. This can be removed approximately after 20 min or later. As the method is injectional, there can be occasional bruising (usually more often on the legs and neck than in the face). Make-up is not recommended to apply sooner than 20 min after the treatment, however not every patient respects this.

After carboxytherapy is performed on the forehead or in capillitium, some patients can feel sensitivity in the treated area (because of the pressure of discrete emphysema) or very rarely a headache. These sensations usually do not last long, but headache can disturb sensitive patients for even 24 h. Sometimes there is a feeling of heavy legs in the treatment of cellulite, lasting for 2–3 days.

It is not necessary to totally forbid exercising in the day of the treatment, but it is good to discuss it with the patient and recommend avoiding extreme body positions, exhausting exercising, or certain more exotic sports (such like piloting of the aircraft or diving, but also some kind of yoga could theoretically lead to abnormal sensations or eventually even to legal problems).

43.9 General Pitfalls

Sometimes physical (mechanically induced) urticaria can be seen during the application on the skin of disposed patients (Fig. 43.5), which fades itself usually in 20 min.

Some patients tend to faint during any injection treatment, with carboxytherapy being no exception. For the treatment of the upper half of the body, sitting or half-sitting position of the patient is usually good; for the treatment of the lower half of the body, horizontal position of the patient is comfortable. If treating the head areas of the patient in more horizontal position, one must count more than in the case of the sitting/half sitting patient that the CO_2 gas is heavier than the air and so tends to go down with the gravitation, which is not always the best for the purpose of the treatment. In the case of more sensitive patient, pauses in the therapeutic session, drinking cold water, fresh air, and relaxing environment can help a lot.

Fig. 43.5 Physically induced urticaria in disposed patient just after carboxytherapy treatment of stretch marks

If the treatment is too painful for the patient, topical anesthetics can be used, however, as, e.g., Emla® (lidocaine/prilocaine – currently the only one available worldwide) leads to vasoconstriction, it is not known if its application can significantly change the final results, e.g., of CO_2 rejuvenation or not. Therefore, in my praxis, I conclude that for the deeper treatment (cellulite) it can be used without problems, but for skin rejuvenation (including the treatment of stretch marks, scars, or wounds) it is better to avoid it, although one should always decide individually with regard to the concrete patient. This approach, as far as the author knows, is also common worldwide.

As for any method, there is a learning curve on the side of the treating physician. In the beginning, everybody follows recommended protocols and during the treatment checks applied gas volumes carefully on the monitor of the device. Later (except research), with more experience, in nearly all indications the treating person usually watches mainly the site of the treatment and concerning to the applied gas volume decides nearly exclusively according to the observed spreading of the gas, not according to some prepared plan. This is the best way how to individualize the treatment and the best way how not to harm the patient as well. The thing is that the gas can run very fast either along the limb or in the face, producing burning (on the limb) or sometimes several days lasting emphysema (e.g., around the eyes), as will be discussed in further sections (Pitfalls – skin rejuvenation, Pitfalls – the treatment of cellulite).

43.10 Current Possibilities of Use in Aesthetic Medicine

43.10.1 Skin rejuvenation

It is often demanded by patients for the facial complexion, neck and decolleté area, dorsal hands, and arms. Generally, similarly like in other therapeutical methods, the outcomes are usually more visible on thinner skin, while heavy complexion reacts just a little and such therapy not very often leads to the patients' satisfaction. Typically we see improvement of skin elasticity and smoothness also in areas treated for other indications, like for cellulite or for hair disorders (in the treatment of capillitium we can expect also certain secondary rejuvenation effect on the forehead, depending on how far in frontal area the gas gets). So, although we inject a bit deeper, the gas succeeds to improve the surface.

However, the treatment usually does not work enough in the case of incipient lower face ptosis (here other treatment modalities such as radiofrequency can appear as very useful). The best effects can be expected on the forehead, under the eyes (dark circles, tired skin), on jawlines and on the neck, even on oral commissures, however usually not much on smokers lines of the upper lip. On upper eyelids at times the results of carboxytherapy are encouraging, because if all the forehead is treated together with the upper eyelids, collagen rebuilding can lead to slight improvement based on discrete tightening (although of course, it cannot be any substitution for blepharoplasty).

Sometimes, improvement of small angiectasis is seen as a result of normalization of local circulation and as a result of neocollagenesis around and upon the vessels. The application is done in several or relatively numerous injection points, depending on the state of

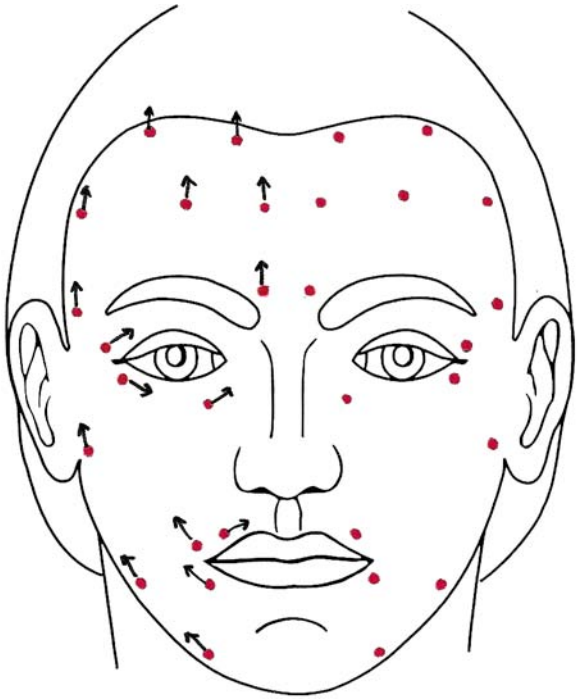

Fig. 43.6 The scheme of application for facial rejuvenation – modification after J.C. Lopez (Sao Paulo, Brazil). It is not necessary to inject in all these points and it depends on the state of the skin, observed gas spreading, and compliance of the patient

the skin, on the compliance of the patient, but also on the spreading of the gas, which must be carefully watched by the treating professional during the whole treatment session. It is safer to inject small amounts of the gas (approximately 0.5–1 mL per injection spot), in velocity 30–40 mL/min; on some devices, the gas flow can be higher and depends on the recommendations of the producer. The scheme of the treatment – modification of the application protocol of Lopez is shown in Fig. 43.6. The vectors of the injection drawn here are widely performed as proved by the best world experience, although individual physicians can inject in slightly different schemes depending on their training and opinions. Often we apply perpendicularly to the wrinkle (horizontal lines on the forehead, oral commissures) and against the direction of gravitation. Insufflation of larger amounts of the gas looks impressive at workshops or maybe on YouTube, but in ordinary practice can coincidentally easily lead to visible intradermal or subdermal emphysema (see Pitfalls) (Fig. 43.7), which, if by chance is too big, easily disappoints the patient forever.

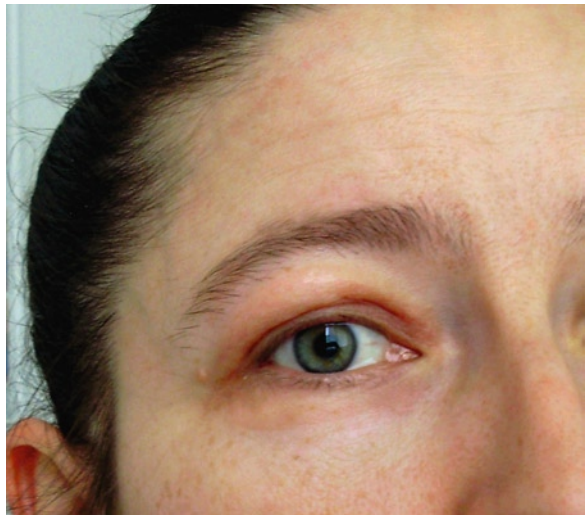

Fig. 43.7 Possible state just after the CO_2 injection into upper and lower eyelids (small temporary emphysema visible as swelling)

In the neck area we apply diffusely, more along the wrinkles if there are any. In decoletté and on dorsal hands, the application scheme is similar to mesotherapy. The author applies in relatively regularly diffusely placed injection points in the whole treated area with aim to reach more or less diffuse momentary spreading of the gas, especially in parts where aging is more expressed. It is important to apply the gas in the face as superficially as possible, in other sites superficially intradermally. Ferreira showed in his experiments on rats, that the neocollagenesis is higher after more superficial CO_2 injection [34]. As the gas is very vivid, one must be aware that some gas always gets also into subcutaneous soft tissues, where it can potentially influence primarily fatty tissue instead of intradermal collagen and so lead to unwanted lipolytic effect and, e.g., to worsen the tired image of mature face (see Pitfalls) (Fig. 43.8).

The intervals between sessions should be 2–4 weeks (because collagen rebuilding takes some time, approx. 3–4 weeks to develop). More frequent treatments can temporarily lead to more impressive or faster results, but mean more time and more frequent pain for the patient. It seems that in longer run more frequent sessions do not mean any real advantage. Carboxytherapy can be combined with other treatment options like mesotherapy (by vitamins or hyaluronic acid or both, or by organic silicon solution – in Europe the product Conjonctyl®). This approach can increase the effect,

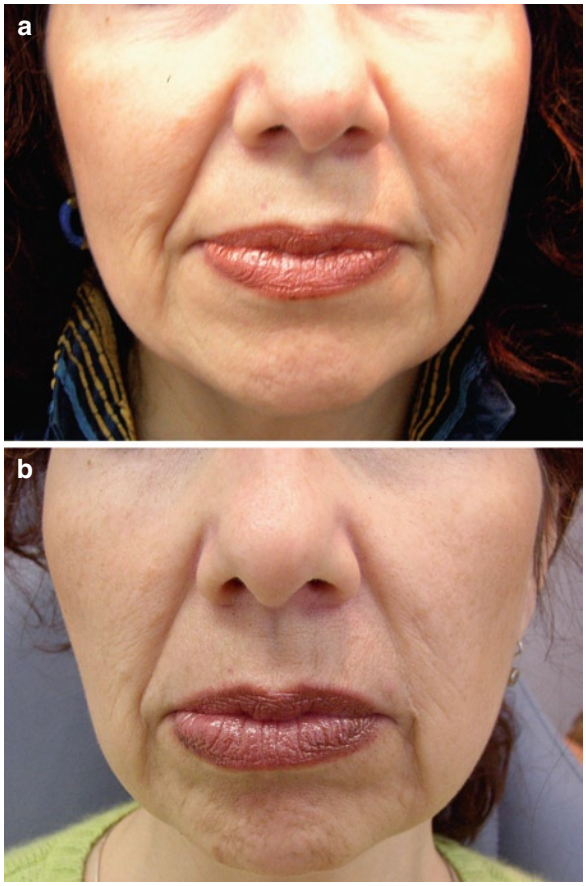

Fig. 43.8 (**a**) Unwanted side effect: 48-year-old patient before the skin rejuvenation. (**b**) Unwanted side effect: 48-year-old patient after five treatments – slight unwanted lipolysis and ptosis

Fig. 43.9 (**a**) Forehead of 46-year-old patient before rejuvenation by carboxytherapy. (**b**) Forehead of the same patient after seven treatments (no BTX was used)

but requires more patient visits in the office, as it is not common to combine such treatments in single session.

Usually from 3 to 10 carboxytherapeutical sessions are performed. The results can vary a lot, many patients reach really nice results in the course of just four treatments, their complexion is refreshed, smoother, more compact, often we observe slight tightening effect, mainly on the forehead (Fig. 43.9). Depending on the compliance of young or middle-aged patient, if there is no sure positive result in four sessions, it is better to recommend to switch to other kind of therapy.

Patients older than 55–60 years usually react more slowly. Overall effect is, similarly like in other rejuvenation methods, dependent not only on number of the sessions or simply the volume of injected gas, but rather on the patient's genetics, general state, and biologic age. At this point it can be interesting to mention the paper of Varani et al. [35] where the authors conclude that depressed collagen synthesis in photoaged skin is presumably the result of reduced fibroblasts interactions with intact collagen (the collagen in photoaged skin is fragmented). In chronologically aged skin, we can expect reduced surface contact between the epidermis and dermis as a result of skin atrophy, with the outcome of reduced exchange of nutrients and metabolites on this level. There are fewer fibroblasts and mast cells and collagen fibers become loose, with increase and thickening of elastic fibers and resorption of most subepidermal fibers, there is also decreased number of dermal blood vessels [36]. In both states (extrinsic/intrinsic aging) carboxytherapy can help (Fig. 43.10). The stability of the effect depends on the style of living

Fig. 43.10 (**a**) Neck of 62-year-old patient before rejuvenation by carboxytherapy. (**b**) After two treatments of carboxytherapy

and further care, and lasts usually from 2 to 6 months (Fig. 43.11), sometimes more. It is important to avoid unrealistic expectations of the patients and to prefer plastic surgery or other approaches especially if the patient demands fast, sure and impressive result, preferably in not many sessions. Satisfied patients later often like to come for carboxytherapeutic treatment regularly, once in 2 or 3 months for years, some prefer once a year a course of several treatments.

Application of botulinum toxin (BTX) can be done before beginning of carboxytherapy course (more logical – on completion with relaxed wrinkles the neocollagenesis should be more uniform, leading to better result), between the sessions or after finishing the course. It is highly advisable not to apply the gas and toxin into the same area in one session – this would lead to the spreading of the toxin. Very rarely it was observed (Lopez, Koutna) that sometimes, if carboxytherapy was performed in the same area soon after BTX application (approximately 3 days to 2 weeks after), the patient announced that the effect of BTX visibly decreased after carboxytherapy. This "anecdotal" reaction remains to be not sufficiently explained.

The combination of carboxytherapy and fillers is the subject of discussions. The majority of physicians do not hesitate to use carboxytherapy carefully superficially in the sites where resorbable fillers were applied, and also in the sites where certain unresorbable fillers are present (polyacrylamide). However, it is wise to avoid the CO_2 application near polyacrylimid, liquid silicon, or in the site where polylactic acid was used. Here CO_2 could lead to incidental implant damage or to unwanted fibroplasia. Granulomas or other side affects after the fillers are not good indication for carboxytherapy, in the case of attempt to treat granulomas after Dermalive® these were tougher and slightly bigger after a single session of carboxytherapy (Koutna).

43.10.1.1 Pitfalls Skin Rejuvenation

In certain types of mature face, one must be very careful with carboxytherapy, because even with best aimed superficial treatment some small amount of the gas can get secondarily deeper, leading after repetitive sessions to slight lipolytic effect producing tired, unwanted appearance (Fig. 43.8). In one isolated case, I found unique side effect – totally unexpected visible fibroplasia of the skin on the treated neck, generated gradually during three treatments (Fig. 43.12). The only unusual coincidence here was that the patient simultaneously had a respiratory infection and was treated with antibiotics.

A relatively frequent side effect can be unwanted longer lasting insufflation in facial areas, especially around the eyes. Normally the gas fades quickly, during minutes, but sometimes it tends to stay for 2–3 days,

Fig. 43.11 (**a**) The effect of carboxytherapy in time: 49-year-old patient before facial rejuvenation. (**b**) Patient after three treatments. (**c**) 4 months after the end of carboxytherapy (she had four sessions altogether, no other treatment was used)

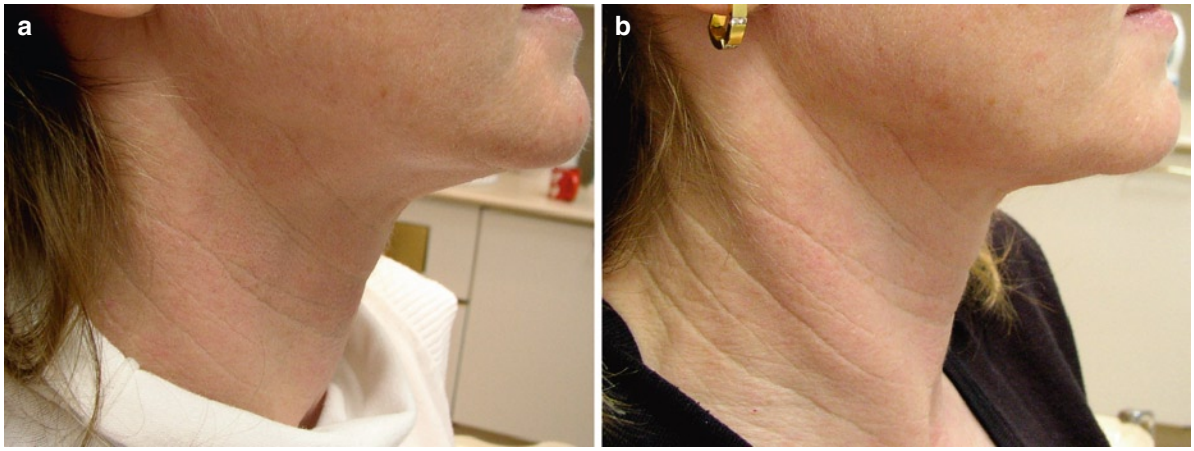

Fig. 43.12 (**a**) Before rejuvenation by carboxytherapy. (**b**) Unexpected and unique side effect: unwanted visible fibroblasts after three carboxytherapeutic sessions (the patient had respiratory infection treated by systemic antibiotics in the middle of the course of the treatments). The state improved back to the starting point very slowly over time

being visible and hence leading to a social problem of the patient. This situation can occur even in careful approach, because facial areas communicate one with the other and so sometimes we can be surprised to find accumulated gas around the eye as a result of injections not only on the forehead or in frontal capillitium but also in nasolabial or cheek area. The accumulated gas must fade away itself and be metabolized, sometimes it helps to use mimic (to blink), but things like mechanical pressure, needle puncture with aim to get the gas out, or cold compresses do not lead to any improvement. It is important to insure the patient that this state improves itself and to advise not to sleep on the side with emphysema, because CO_2 tends to settle down with gravitation. Especially in faces of older persons more stable emphysema occurs easily, evidently because of loose tissues and more "space" between the tissue layers.

43.10.2 Scars

In the carboxytherapeutical treatment of scars we can obtain varying, slightly unpredictable results, because every scar is original and can react in individual way depending on the toughness of both the scar itself and of the tissue underneath, deepness and oldness of the scar, the site of the body, and individual reaction of the patient. It is known that any scar maturates for as long time as 2 years after the trauma and so we must keep in mind also a tendency to self-improvement in this horizon. However, even with emphasizing this fact, the effects of carboxytherapy on scars are clear and valuable and reached improvement is usually permanent (it could change perhaps, e.g., as a result of enormous weight changes, which is not very common).

The intervals between the sessions are usually from 3 to 5 weeks as it is necessary to wait for collagen rebuilding (although in certain cases the reaction is seen very fast) (Fig. 43.13).

For red, fresh, just healed scars it can be good to use pulsed dye laser (PDL), however here is the disadvantage of UV light sensitivity after the treatment. It has sense to perform some treatments by PDL and continue by carboxytherapy aproximately one month after the PDL treatment (Fig. 43.14).

43.10.3 Linear Atrophic Scars

These react usually very well, often we see visible improvement after only one session of carboxytherapy (Fig. 43.15), especially if they are not too deep or too wide (Fig. 43.16) (a bit wider scar). In the treatment, the injection is superficial intradermally with the vector of the needle in the direction of the scar, either directly into it or in the distance of 2–10 mm (this in the case that the scar is fresh (Fig. 43.17) and hence maybe not firm enough and could be potentially

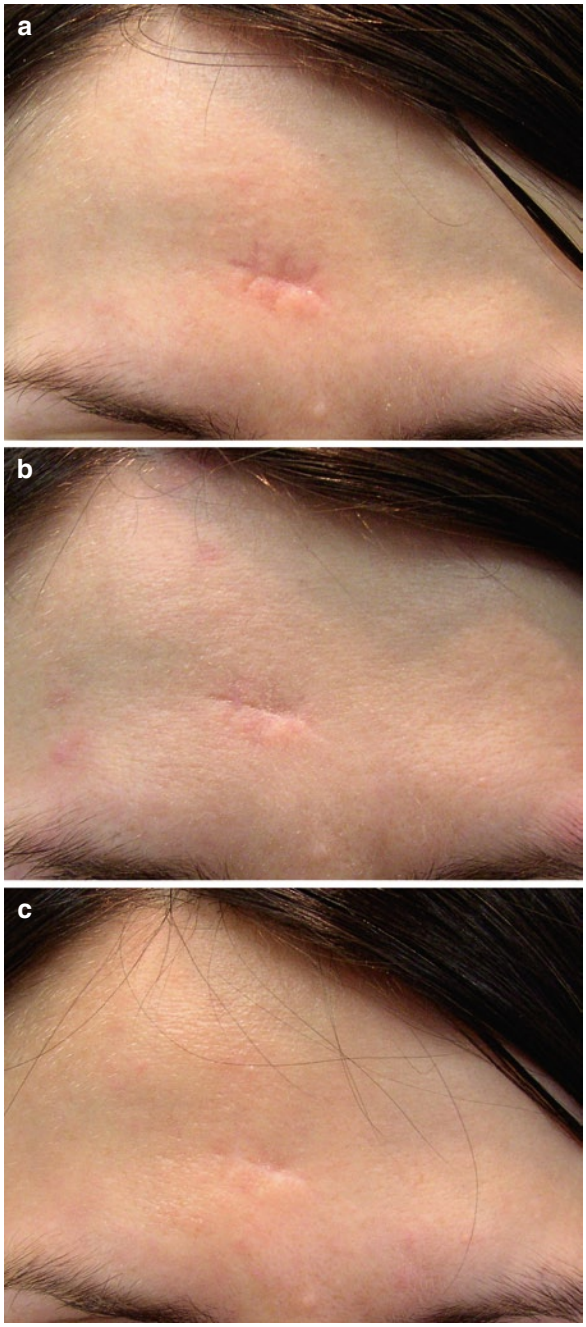

Fig. 43.13 (**a**) 2.5-month-old atrophic scar on the forehead before carboxytherapy. (**b**) 3 days after the first treatment (before BTX 12U to the forehead and glabella, which the patient wished besides scar treatment). (**c**) 4.5 months after the first treatment of carboxytherapy

Fig. 43.14 (**a**) 4-month-old hypertrophic scars after a car crash, before PDL treatment (author of this photo – Gabrysova, T., GHC Clinic Prague). (**b**) The worst of these scars 1 week after the first PDL treatment, before the first carboxytherapy. (**c**) The same scar after four treatments of carboxytherapy and 4 weeks after the second PDL treatment (2nd PDL treatment was done between third and fourth carboxytherapy). Carboxytherapy seemed to help more on the smoothing and decrease of the tough hypertrophic surface, PDL seemed to make more effective bleaching

widened by the flow of the gas, which we do not want of course) from one of its pole (usually from lower pole up, if the patient is sitting, because CO_2 gas is heavier than the air) and moves linearly in several

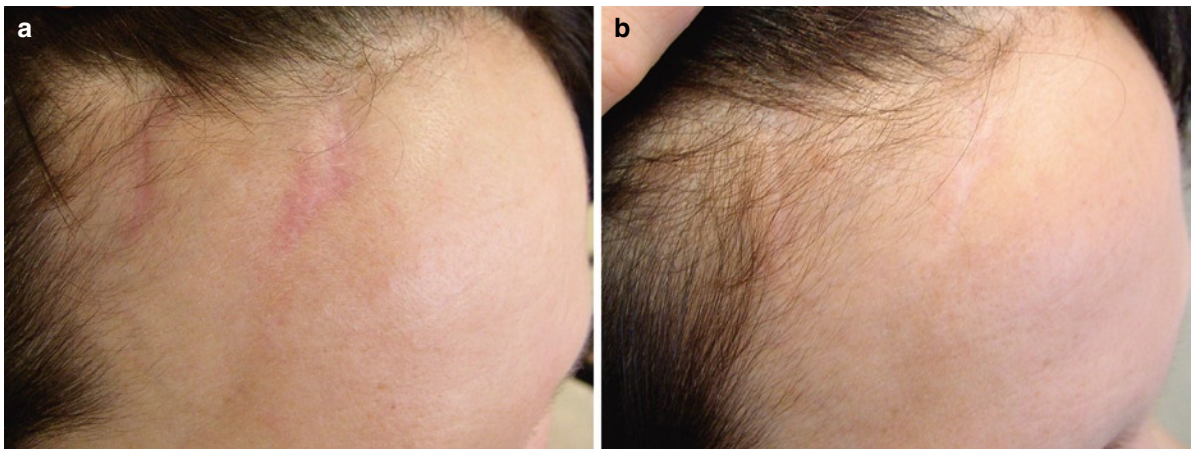

Fig. 43.15 (**a**) Atrophic scar of the forehead before carboxytherapy. (**b**) Atrophic scar on the forehead 2 months after one treatment with carboxytherapy

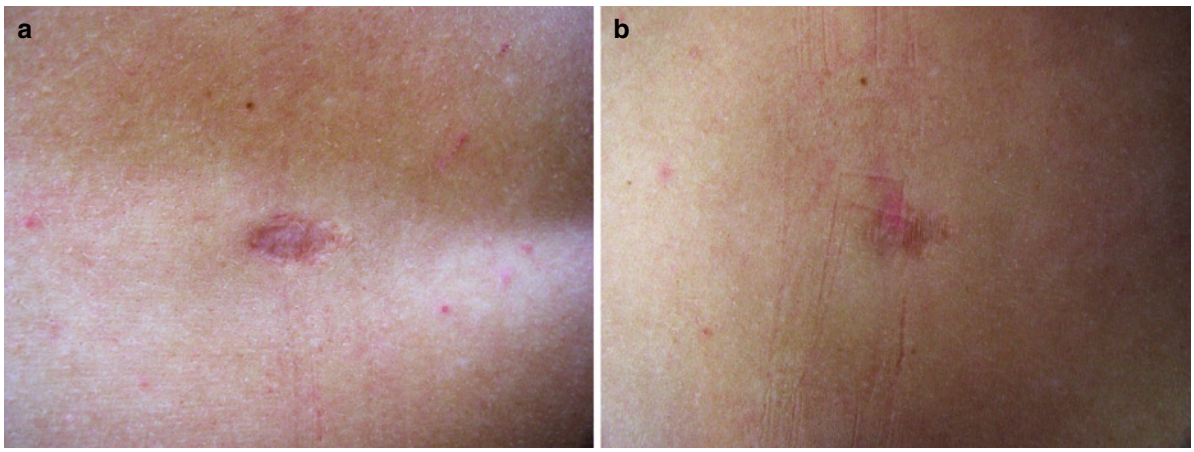

Fig. 43.16 (**a**) Atrophic scar on the back before carboxytherapy. (**b**) Atrophic scar on the back after one treatment with carboxytherapy

injections up along the scar (again either just into the scar or 2–5 mm on its side) as necessary, expecting the gas to infiltrate the whole scar and close surrounding tissues (at least 5 mm around) which we can observe first as whitening and discrete increase of the volume, then as redness lasting for several minutes. In superficial scars we can inject superficially, but if there are adhesions under the scar, it is advisable to infiltrate by the gas also the tissue underneath, i.e., to use the gas flow instead of the needle just as in needle subcision.

The gas velocity should be 30–40 mL/min, depending on the toughness, for tougher scars to adjust 40 mL/min or on some devices even more is better. The amounts of the gas injected are not big, just enough to infiltrate the scar and surroundings as described earlier, and depend on the scar size.

Usually the effects (smoothing of the surface, paling of redness) are visible already after 1–2 sessions, we perform approximately 3–10 sessions altogether. If there is no improvement in four sessions, it is better to switch to other therapy.

43.10.4 Atrophic Scars

Especially in the treatment of certain deep scars (e.g., scars after metal pieces of fixators used sometimes in the treatment of limb fractures or postsurgery scars which

Fig. 43.17 (**a**) Fresh (7 weeks after the trauma) atrophic scars in the face before carboxytherapy. (**b**) Scars after three treatments of carboxytherapy. (**c**) Scars 6 months after the fourth treatment of carboxytherapy

healed per secundam (Figs. 43.18 and 43.19) the gas insufflation can be sometimes very unpleasant for the patient. Such scars also do not tend to improve much. Therefore, in such cases, surgical intervention (if it is suitable) can be a much better solution than carboxytherapy.

Fig. 43.18 Deep postfracture atrophic scars on the lower limb – bad indication for carboxytherapy

43.10.5 Linear Hypertrophic Scars

Also for this kind of scars, carboxytherapy can be very useful. Such surgical scars tend to pale and their surface lowers after the treatment (Fig. 43.20), however we rarely see total normalizing of the surface, some slight hypertrophy usually stays permanently. Often the patient refers relief of the feelings of pull in the scar.

In the treatment, the injection is linear into the mass of the scar and continue forward in further punctures along its whole length, depending on how we observe the spreading of the gas. We should see whitening of the scar tissue during every injection, through the session the whole scar is insufflated by the gas. Soon the color changes to red. The velocity used is 30–40 mL/min. The patient can feel burning in the scar, but the therapy takes typically only 1 min or less depending on the size of the scar. As these scars are usually tougher, there is no danger to do a mistake in style of the application. According to the author's experience for this kind of scars, carboxytherapy can reach better results than PDL,

Fig. 43.19 Deep atrophic scar after trauma by a shrapnel in the time of the World War II – tough adhesions under the scar appeared to be an effective barrier for the CO_2 gas and so no clear improvement occurred – not very good indication for carboxytherapy

in certain cases also modern radiofrequency devices (Accent® bipolar handpiece) can appear as very useful.

43.10.6 Hypertrophic Scars

However, sometimes we must be careful, as in the treatment of hypertrophic scars on the chest of a teenager (Fig. 43.21). Carboxytherapy led to no improvement of these scars and the author even had the impression that flow of the gas had a power to slightly widen them. Such experience is very rare.

43.10.7 Keloids

For keloids unfortunately carboxytherapy does not seem to be effective enough, definitely not as a single technique. For individual patient however it can have sense to try this therapy, there can be slight improvement in the structure of the surface, slight decrease of the height (Fig. 43.22), and especially in the feeling in the scar (patients suffering from increased sensitivity of the scar often refer tendency to normalization).

In the treatment we inject simply into the keloid, the gas velocity must be higher, from 50 to 130 mL/min., depending on the device. The treatment here should be performed once a week or in 2 weeks, sometimes the patient announces relief or subjective improvement of appearance as soon as after one treatment, but usually at least six treatments should be done. Combinations with other methods like silica gel or other topical products are useful.

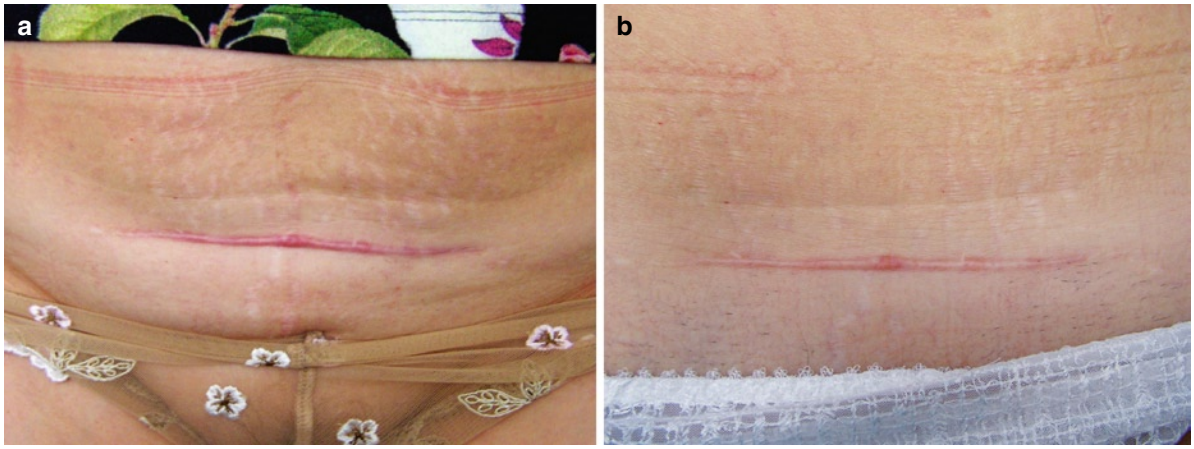

Fig. 43.20 (**a**) Hypertrophic scar before carboxytherapy. (**b**) Scar after four treatments of carboxytherapy

Fig. 43.21 The treatment of these hypertrophic scars by carboxytherapy led to no effect

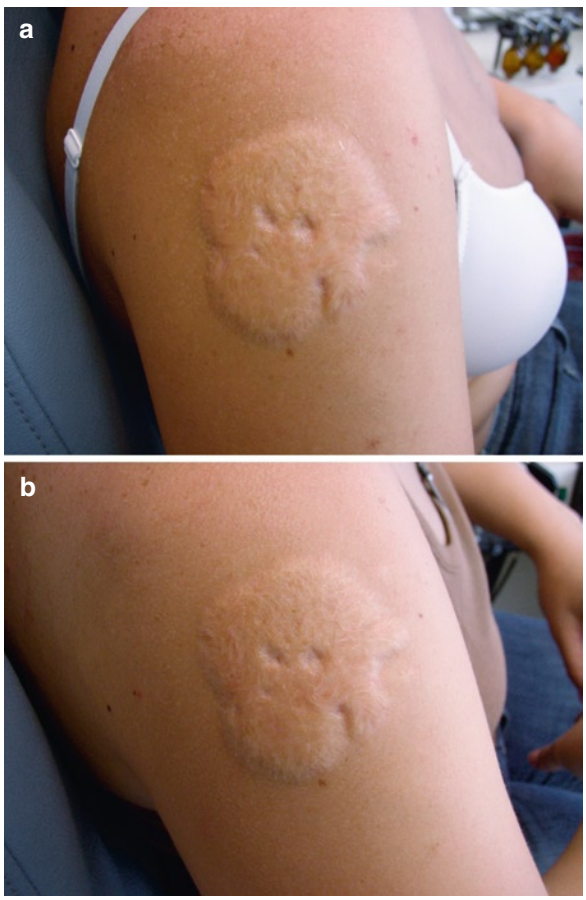

Fig. 43.22 (**a**) Keloid scar before treatment. (**b**) Scar after four treatments with carboxytherapy

43.10.7.1 Pitfalls Keloids

Sometimes, for sensitive patient, the application of any injection into the keloid (e.g., in sternal area) is nearly unbearable. Here of course, we have to switch to other method.

43.10.8 Acne Scars

Generally, for acne scars carboxytherapy is rarely really a successful technique. The method can help in the case of not very deep acne scars on not too heavy or tough skin, especially if the scars are fresh. For well-developed scars sometimes carboxytherapy functions well, specifically for not too deep and isolated ice pick scars (and large pores) with not too tough edges (Figs. 43.23 and 43.24) and for more superficial saucer shape or rolling scars. Boxcars usually don't react at all. Tough skin with numerous scars (Fig. 43.25) is definitely a bad indication for carboxytherapy, as well as scars with tougher fibrotic strands underneath. Anecdotally, it was observed (Koutna) that the results are better if the treated person does not use make-up regularly. This can be explained by the fact that collagen rebuilding takes usually several weeks and if make-up is applied, it tends to fill the pores or scars like a plug, hence effectively working against their shrinkage.

The gas (usually of velocity from 30 to 50 mL/min) should be applied intradermally around (and under, if we predict fibrotic strands under the scar) every individual scar or a small area with several scars. This leads to insufflation and undermining, sometimes it is also possible mechanically evacuate tough comedones released by the gas flow. Red scars tend to whiten and the surface gradually slightly improves (Figs. 43.26 and 43.27). However, more sessions are necessary (from 3 to 10 or more) and with numerous scars the application can be very unpleasant for the patient. Therefore currently, when there are other, more effective techniques like fractional photothermolysis, fractional radiofrequency or some older, albeit more risky therapeutical approaches (CO_2 lasers, deep peels, etc.), not to talk about softer techniques like noninvasive radiofrequency, derma rollers or autologous products for skin rejuvenation and scars treatment (e.g., Ticeba, Germany), car-

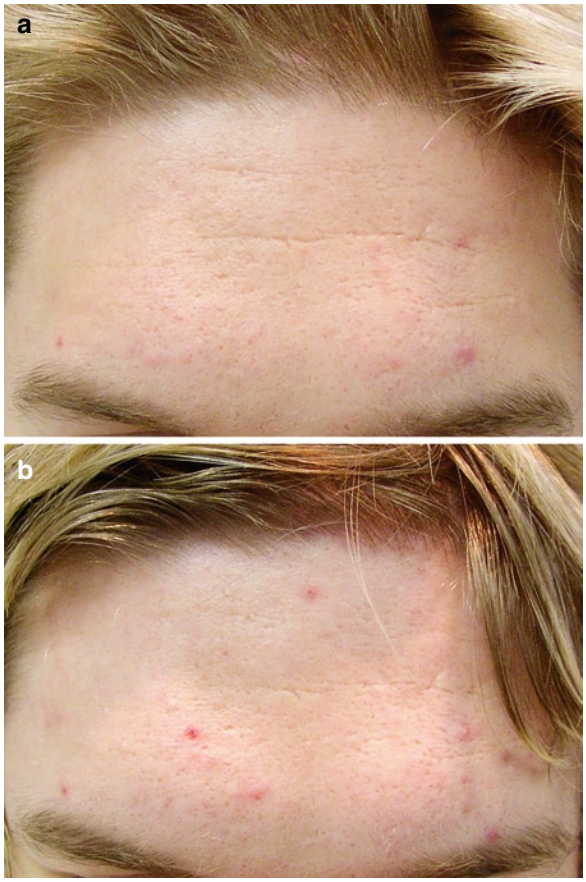

Fig. 43.23 (**a**) Not very deep ice-pick scars and large pores before treatment. (**b**) Scars and pores 1.5 months following one carboxytherapeutical treatment and BTX 6U to *M. frontalis*

Fig. 43.24 (**a**) Large pores before carboxytherapy. (**b**) After one treatment

boxytherapy for acne scars should be used very consciously, e.g., maybe for treatment of isolated ice pick scars on not too heavy skin. For other types of acne scars ablative techniques (e.g., Fraxel Repair®) or radiofrequency (e.g., Accent XL® bipolar mode) rejuvenation are usually much more effective.

43.10.9 Stretch Marks

Small amounts of the gas are applied in superficial intradermal injections directly into the stretch mark (Fig. 43.28). It is recommended to "inflate" them a bit, which can be done quite comfortably on wide, not numerous stretch marks, e.g., on the abdomen (Fig. 43.28). In treating numerous stretch marks on the buttocks or on thighs, we should work quickly with the aim not to make the unpleasant treatment too long for the patient. One fast injection is applied after the other in the whole area, preferably superficially into the stretch marks, but according to the state we can apply also deeper, with intention to make the treatment more complex and improve also cellulite. The gas velocity should be from 50 to 80 mL/min., on devices prewarming the gas even more. The treatment should be repeated once in 2–3 weeks, later in 4 weeks, the number of sessions can vary from 6 to 10, sometimes more. The method can be used for red stretch marks as well as on the matured white ones.

Fig. 43.25 Such multiple large pores and scars are not a good indication for carboxytherapy

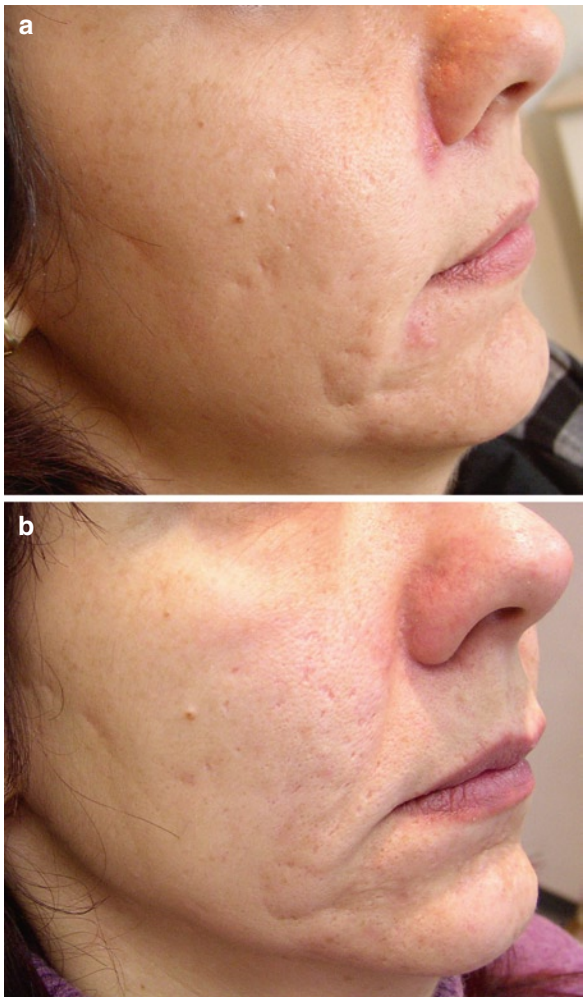

Fig. 43.26 (**a**) Acne scars before carboxytherapy. (**b**) Scars after 11 treatments of carboxytherapy with very discrete improvement

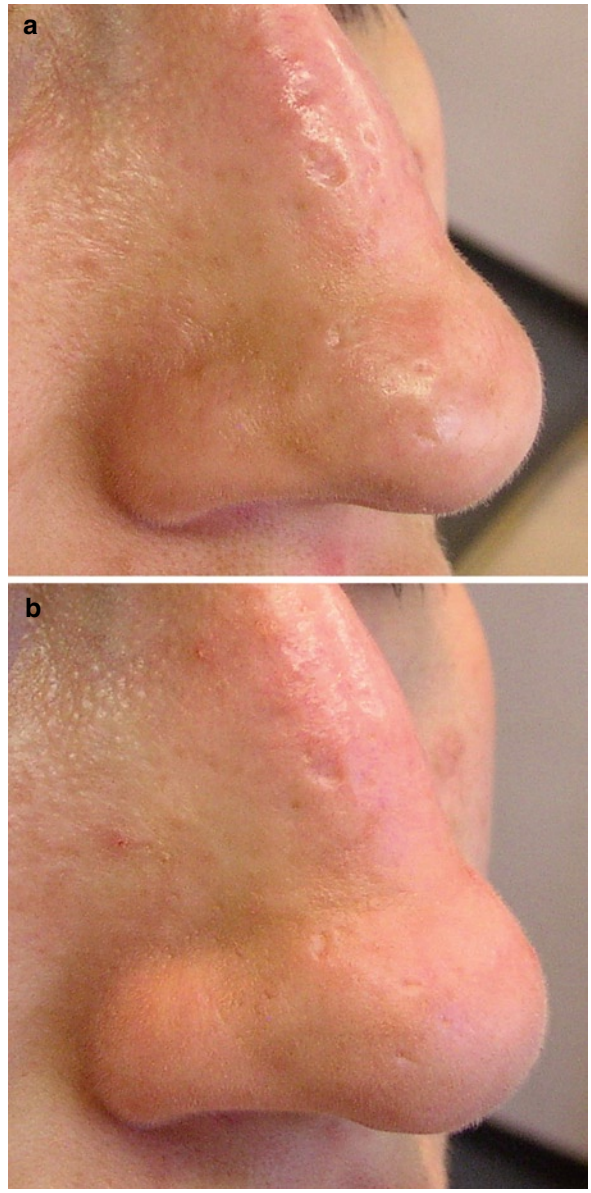

Fig. 43.27 (**a**) Saucer shape scars on the nose before carboxytherapy (the patient had treatment of lymphoma with episodes of pyodermia). (**b**) Scars after two treatments of carboxytherapy

Improvement can be observed usually after the 3rd to 4th treatment. The stretch marks are gradually slightly narrower and the whole skin surface is smoother and more compact (Fig. 43.29). Hence, although the stretch marks remain visible, the whole area looks healthier and better and often slightly tighten, which is highly appreciated by the patients, despite discomfort during the gas administration.

Fig. 43.28 (**a**, **b**) The state just after the application of CO_2 gas into stretch marks. (**c**) Possible state after the application of CO_2 gas into wide stretch marks

43.10.9.1 Pitfalls Stretch Marks

Sometimes wide striae on the ptotic skin of the abdomen can be a problem, not reacting enough to carboxytherapy. Here other methods, like radiofrequency or mesotherapy can help more. In certain cases, abdominoplasty is advisable.

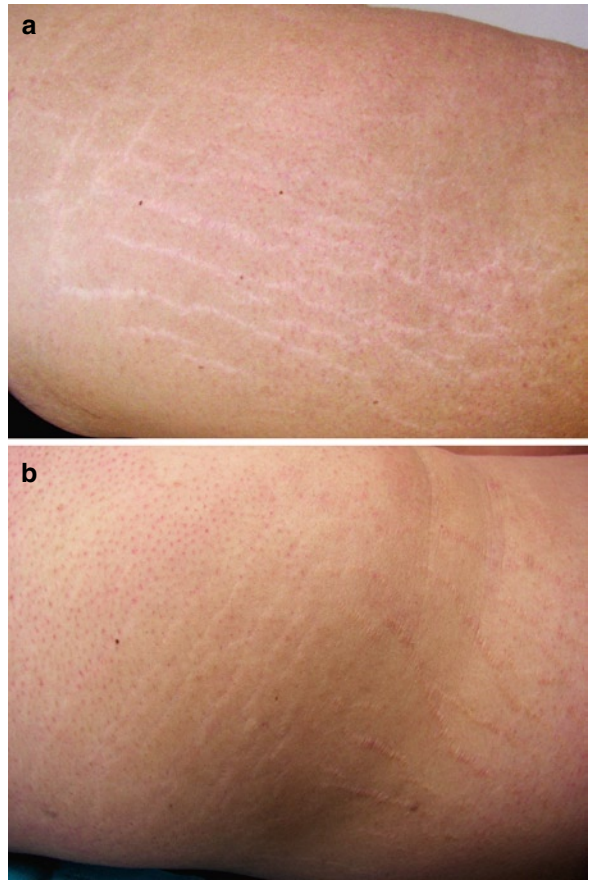

Fig. 43.29 (**a**) Stretch marks on the leg before treatment. (**b**) The leg (unfortunately not exactly the same angle of glance, but the character of improvement is visible) after nine carboxytherapeutic treatments

43.10.10 Hair Loss and Alopecias

In the case of diffuse hair loss or female androgenetic alopecia, the gas should be applied in such a manner that finally the gas diffuses nearly to the whole capillitium. This is done typically in seven injection spots (Fig. 43.30) as recommended by d'Arc Diniz, Brazil. The author applies subcutaneously (the skin can be slightly risen by the needle or later by injected volume of the gas), because we need to improve the nourishment of hair follicles, not to build collagen. For alopecia areata, the author applies into injection point somewhere in the center of small alopetic patches (Fig. 43.30), for larger ones we use several injection points, so the gas insufflates the space under the skin of the treated area. Slight redness signaling temporary vasodilatation should be observed after the finished injections. The application must be done slowly,

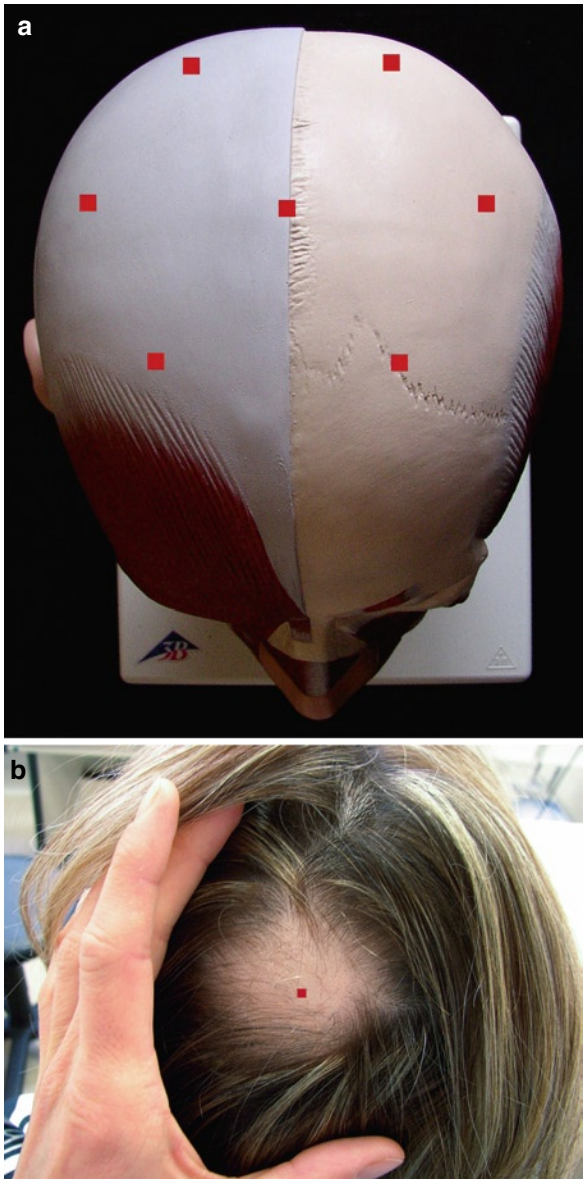

Fig. 43.30 (**a**) Scheme of CO_2 application in hair loss and diffuse alopecia. (**b**) Scheme of CO_2 application in alopecia areata patch

because there is no soft tissue allowing the gas to spread and hence the feelings of pressure in treated area can be strong and unpleasant for the patient. The gas velocity used can be from 30 to 50 mL/min for cold gas machines, 80–100 mL/min for prewarmed gas devices, depending on tolerance of the patient and recommendations of the producer, 1–5 mL per injection point. The intervals between the treatments are depending on the state, in the beginning 1–2 weeks, with successful therapy they can be prolonged to 3–6 weeks. Total number of the treatments is usually from 3 to 20.

Carboxytherapy in hair loss and alopecia is usually very effective (Fig. 43.31); however in difficult cases – patients with not ideally compensated thyroid gland diseases, autoimmune disorders, psychic problems or androgenic alopecia – the therapy is likely to be much less successful, in the best case with just temporary effects. Therefore, it is important to explain to the patient expectations realistically and in these cases concentrate also to other therapeutic possibilities.

43.10.10.1 Pitfalls Alopecia

During the gas administration, the vector of the injection should lead to the center of the capillitium area, however despite the best care and skill the gas often tends to get somewhere to the forehead, around the eye or ear, or to the back of the neck. This can be momentarily very strange and unpleasant for the patient. The feelings normalize in 1–2 min, so it is always good to wait a bit between separate injections with the aim not to make the treatment too bad for the patient. Potential longer lasting emphysema is described in the section Pitfalls – skin rejuvenation, as well as how to instruct the patient in such case.

43.10.11 Wounds

Beside traditional treatment of wounds like leg ulcers or diabetic foot, even in aesthetic medicine after different surgical interventions this treatment can be useful and rewarding. Here carboxytherapy should be applied gently, with gas velocity 30 mL/min, around the wound even still with the stitches or after their removal. The injection points should be in a distance of 1.5 cm, better 2 cm from the wound edges. Especially if the application is done in the same day as the stitches removal, one must be very gentle and take the needle out in time, because otherwise the wound or incomplete fresh scar could accidentally open more by mechanical force of the gas. The physician should observe the gas spreading into the wound borders, then redness, but the gas amount should be appropriate, 1 mL per injection spot, a bit less or more – just not too much. In larger or deeper wounds, however, applied gas volume can be bigger, depends on the mass of the tissue, the edges of the wound, and ideally also its base simply should be infiltrated by the gas.

In small wounds after excisions, etc., often just 1–3 sessions can be sufficient, however, in more problematic wounds the number of the sessions is much higher. If the wound is placed on the foot or on lower leg and

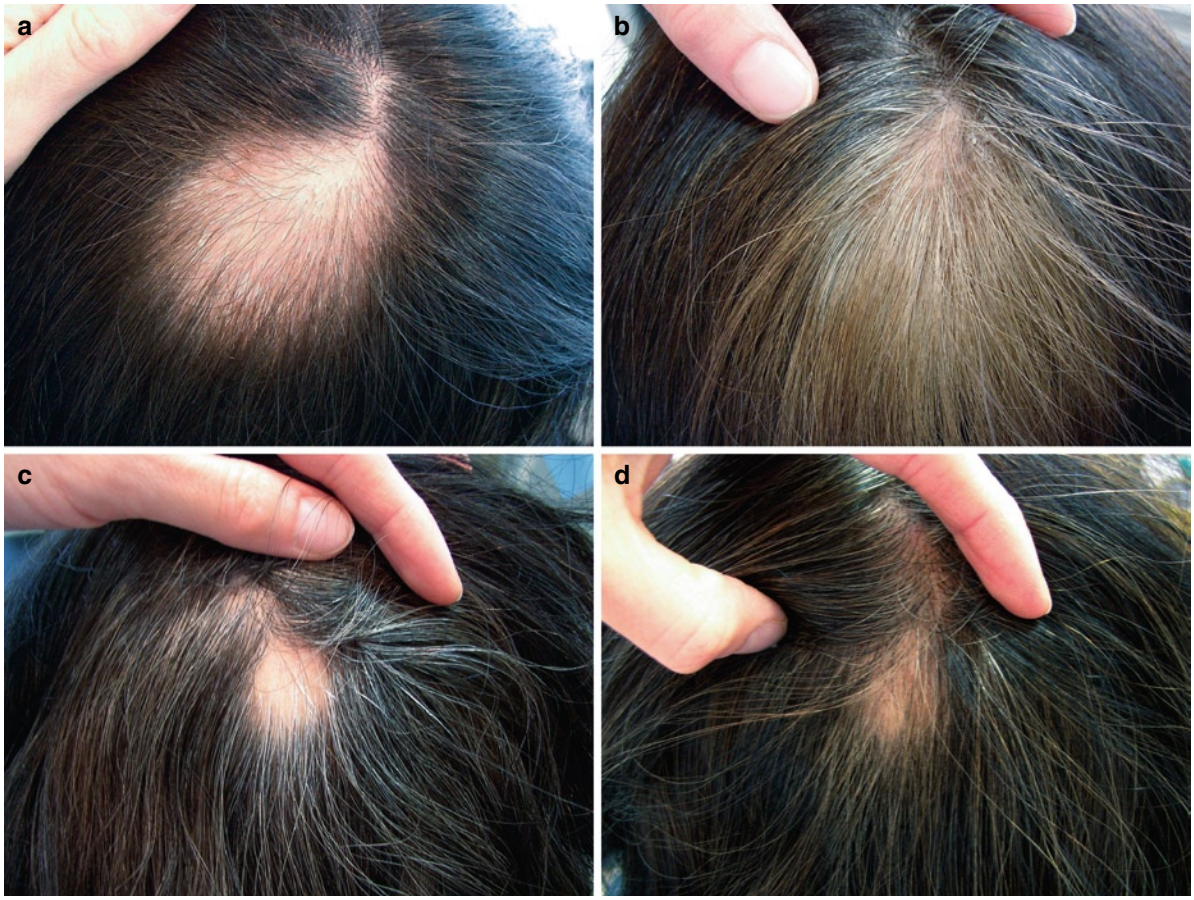

Fig. 43.31 (**a**) Alopecia areata – isolated alopecic patch in capillitium of 37-year-old patient before carboxytherapy. (**b**) After eight treatments (the patient is dying her hair, so the color is not identical). (**c**) A new small alopecia patch coming at the time of the seventh treatment. (**d**) Fast improvement of this patch after two treatments

heals only slowly, it is recommended to apply the gas also in injection spots along vena saphena magna, with the aim to improve the blood flow of the whole lower extremity. Intervals between the sessions are first short, with application even three times per week or in critical cases even every day, with improvement the sessions can be less frequent, 1–2 times per week. In the case of elderly patients in not good general state, external carboxytherapy in the form of regular dry CO_2 bath of the limb can be a much better approach, appreciated by the patient.

Usual reaction of the treated wound is slight serous or seromucous secretion temporarily (lasting for approximately 1 day), then calming down, whitening of red borders, diminishing of the secretion, cleaning of the wound, gradual healing. Carefully performed method is also a good prevention of abnormal scarring.

43.10.12 Cellulite and Adhesions After Liposuction

The use of carboxytherapy in these indications including histopathological correlations was described in detail especially in papers by Brandi et al. [22, 37], Leibaschoff [3], and Lee [38]. This treatment is also often demonstrated on workshops and is widely used in the whole world, because the administration is not complicated and is often provided by nurses as a part of medical care in aesthetic centers.

The gas is applied into the area of cellulite in several injection points, individually, depending on the state and the patient compliance. In soft cellulite or if the patient has problems to tolerate sensations during the treatment, it is useful to adjust lower velocity – 10–30 mL/min and apply slowly, only in four injection points altogether, each of them in the center

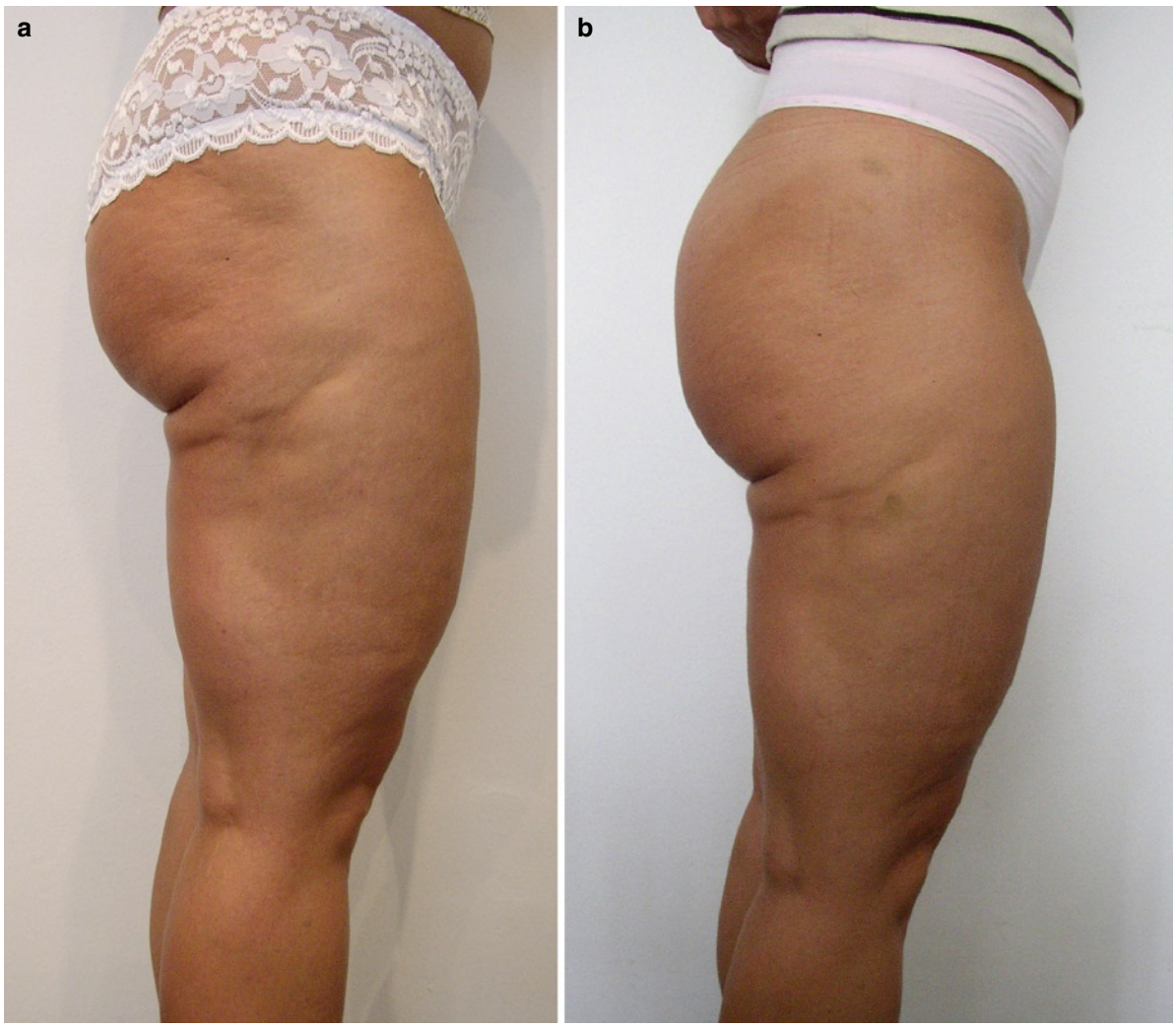

Fig. .43.32 (**a**) Cellulite in 37-year-old patient before the treatment. (**b**) After four treatments with carboxytherapy

of the outer and inner side of the upper thigh. Leibaschoff recommends "to play piano" on the treated area by fingers of the other hand with aim to ease for the patient the local feelings of burning. This maneuver can often help a lot. The volume injected should be from 100 to 200 mL per limb, usually 10 or more sessions in total are required, in the beginning twice a week, with improvement it can be once a week or less.

If the cellulite is harder, with tougher fibrous septae, we should use more injectional points, depending on how we observe the gas infiltrating the area (sometimes this is clearly seen in a form of emphysema, sometimes we observe only redness and increasing of the volume). We should use also higher gas velocity – from 30 to 80 or 100 mL/min and larger total gas volume, from 300 to 700 or even more per limb (Fig. 43.32).

Varlaro et al. [1] reported the gas volumes used in the successful treatment of severe lymphedema as big as 1,000 mL per limb. South American colleagues backed by their wide and long lasting praxis with the method insist (d'Arc Diniz and Lopez, personal communications) that the total volume injected is not the main thing important for the effect, having numerous patients reacting very well even after using low volumes, like 100–200 mL per limb. However, here maybe also the quality of local food (obviously less industrial and healthier than in some European or North American countries) and life style can have positive influence.

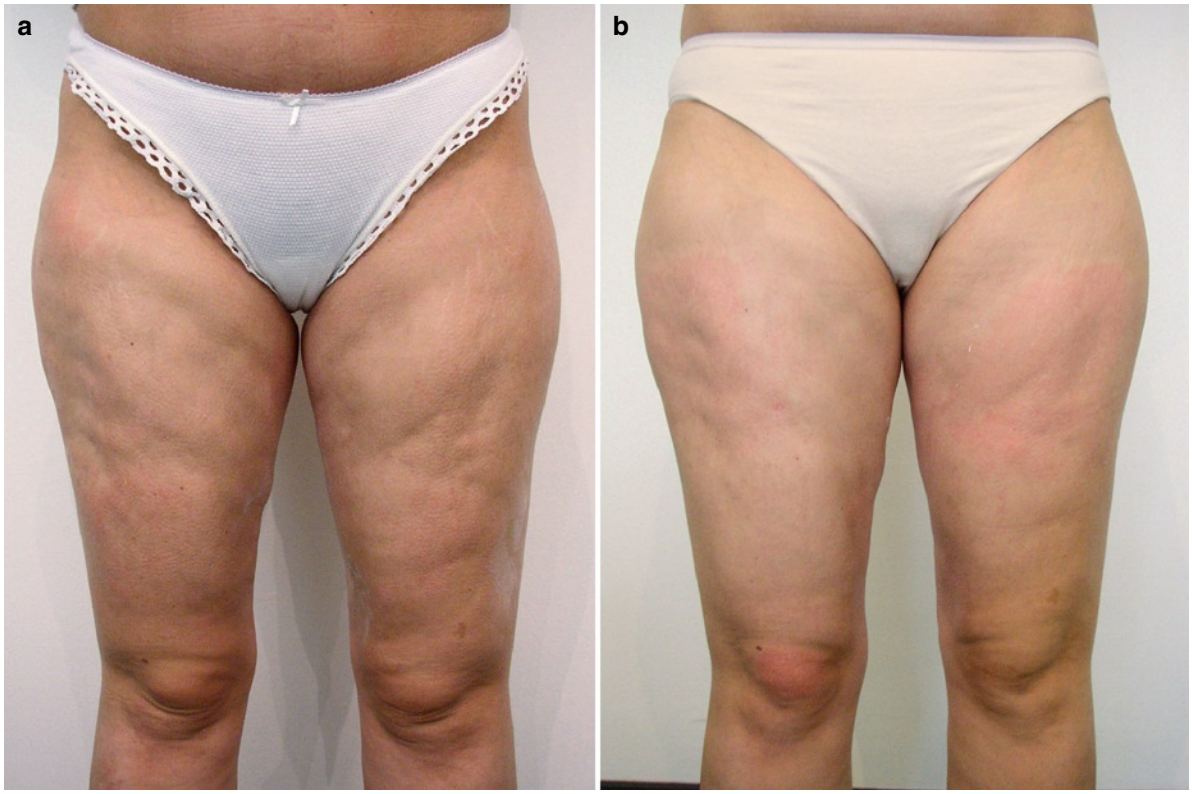

Fig. 43.33 (**a**) Adhesions after repetitive liposuctions before treatment. (**b**) After repetitive liposuctions and after 11 carboxytherapeutic sessions. However, although the patient appreciates the results very much, continues with the treatment and lately passed her 36th session. The therapy now is more about maintaining the results as well as possible, not about clearly visible further improvement

Cellulite is a modern disease, but from other point of view it is also just a kind of secondary sexual characteristic. Therefore, it tends to recur again in approximately 6 months. In the meantime, the patient can pass other methods or come for maintenance carboxytherapeutical treatments once in a month.

43.10.12.1 Pitfalls Cellulite

During the application, sometimes the patient can feel burning on unexpected places. The gas likes to run quickly along v. saphena magna or other vessels, leading to surprising fast burning impressions, e.g., in the ankle area while the gas is injected much higher, in inner thigh area or around the knee.

Adhesions after liposuctions, carboxytherapy can be used to reach more regular surface of the area. The therapy can begin 3 weeks after the liposuction [37], twice weekly, with similar treatment parameters as for hard cellulite.

Sometimes patients passing liposuction months or years ago ask for improvement of surface irregularities. Here, especially if adhesions are softer, carboxytherapy can be very rewarding, with patient seeing the results clearly sometimes even after only 1–2 sessions. We should inject the gas perpendicularly to the adhesions. As these stretch, it can be unpleasant or painful for the patient, especially if adhesions are harder and tough. Therefore, it is advisable to apply once in 1 or 2 weeks to make the treatment bearable, because altogether this indication requires numerous sessions – 10 and more (although tough septae get softer and the surface more regular, the tissue tends to reorganize partially and some septae especially in the beginning can regenerate). Later the intervals can be 1 or 2 months to keep the results, similarly like in the cellulite treatment; however, total straightening of the surface is rarely possible (Fig. 43.33).

Fig. 43.34 Very hard adhesions after liposuction – bad indication for carboxytherapy

43.10.13 Pitfalls-Adhesions

In cases of numerous hard adhesions resulting in hardness of the whole postliposuction area, carboxytherapy is too painful and not effective, therefore this is not a good indication (Fig. 43.34).

43.10.14 Facial and Body Contouring

In contouring the gas is simply applied directly into the fatty tissue of targeted area (double chin, jawlines, cheeks, hips, etc.). The angle of the needle should be approx. 45° or more, depends on the mass of the fat and on the length of the needle (sometimes longer needle can be useful). The gas velocity can be adjusted on levels from 30 to 100 mL/min, depending on the device, patients' impressions during the treatment, and the toughness of the fat (soft fatty tissue usually reacts better and faster than "tough" fat), gas volume can vary from 3 to 50 mL or more per injection spot according to the size of the treated area. We observe the increase of the volume of the area and, especially in the face, it is advisable to be careful not to let the gas spread too much around. Sometimes it is possible to protect the surrounding area by mechanical pressure of the hand, but as the CO_2 gas is very vivid and spreads lively, it is never for long. Unwanted fat reduction in the face could be easily a disaster for a person, although usually in time in healthy persons there is a tendency to normalize again local adipose amount (new mature adipocytes originate from preadipocytes even in adulthood as needed for the body, depending on hormonal influences). The intervals between the sessions can vary from several days to 1 week, in more delicate areas (face) we should be more conservative and inject once in a fortnight.

Concerning the final results, there are big differences among the patients, some respond very well even in large body areas and together with a reasonable improvement of the life style this method can be satisfying for them (Fig. 43.35). On the other hand, a physician can meet a person coming again and again (even 40 times), asking for improvement of some very discrete, presumably genetically based facial cheek fullness asymmetry, visibly reacting only partially, gradually and very slowly, in spite of the number of sessions and the volume of gas injected. Certainly, even slight endocrinologic disorders can have great influence on the results.

Altogether, this application is the easiest one, suitable for any beginner who needs to gain practice with the method, although the results are not always so rewarding like in the treatment of cellulite. Brandi et al. ([22, 33], personal communication) reported histologically approved lipolytic and lipoclastic effect of carboxytherapy; however, the method is not the one of the first choice for any demanding obese patient wishing big volume reduction. In this case, diet and liposuction can be more useful.

43.11 Conclusions

Carboxytherapy in aesthetic medicine can be attractive especially for patients wishing natural and still effective treatment. Although the results tend to be slightly unpredictable depending not only on the indication, state, and style of the application, but very probably and a lot also on the biologic age of the subject, the

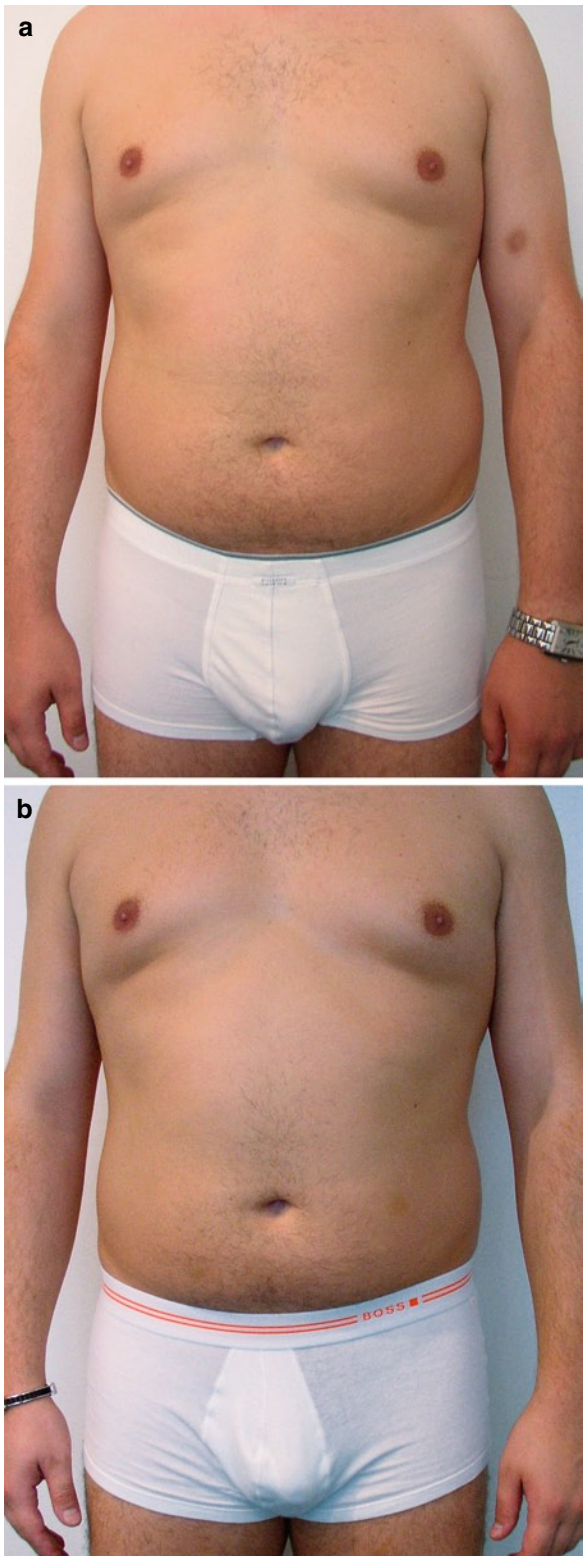

Fig. 43.35 (**a**) Body contouring – before the treatment. (**b**) After eight CDT treatments

method is able to offer fast improvement in many difficult cases when other treatment options either fail or lead to small effect (adhesions after liposuctions, cellulite, striae, healing wounds, certain scars). For a physician, it can be very interesting and versatile technique, especially for a dermatologist active both in aesthetics and in classic dermatology field.

43.12 Future

With the current speed of medical devices development and in new treatment options based on growth factors, stem cells or genetic methods, the future of carboxytherapy is hard to foretell. It is predictable that in aesthetics it could change to a method exclusively for the patients seeking "natural" treatment, especially if ideally some new atraumatic and in the same time potent way of CO_2 gas application device was invented. On the contrary, carboxytherapy in internal medicine (possibly even, e.g., improvement of the metabolism of the heart – Brandi (Brandi C, personal communication), in balneotherapy and physiotherapy probably has very good perspective in any future time.

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