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Injection Lipolysis – an update

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KEY WORDS: Fat reduction, Injection Lipolysis, NETWORK-Lipolysis, lipodissolve, standard protocol

SUMMARY:

The NETWORK-Lipolysis has played a major role in the development of the minimally invasive alternative therapy for reducing minor deposits of fat which is known today as Injection Lipolysis (IL). Since the introduction of the standard protocol for Injection Lipolysis in 2004, the process of collaboration between a large number of colleagues has led to continuing improvement and adjustment of the protocol. The resulting continuous improvement in the treatment outcomes and the fall in the level of sideeffects has led to strong acceptance on the part of the treating practitioners and patients.

INTRODUCTION

The NETWORK-Lipolysis has played a major role in the development of the minimally invasive alternative therapy for reducing minor deposits of fat which is known today as Injection Lipolysis (IL). The consolidation of the Network in 2003, which until then had been operating without any organizational structure, to create a new form of organization triggered a wide range of developments. For one thing, a standardized treatment protocol was developed, and has meanwhile become established throughout the world. And for another, studies were undertaken in cooperation with universities into how the therapy – which until then was only known to insiders – actually worked, and these helped the therapy to achieve its current recognition as a useful tool in the field of aesthetic treatments. The newly formed organizational structure, which today can be equated with the NETWORK-Lipolysis, also contributed to acceptance of the therapy thanks to initiatives on the part of numerous members, for example through the installation of work groups on specific topics and the further development of the standard protocol, but also and above all through the compilation of user observations by the members. This has produced a very comprehensive statistical database not only on treatment outcomes but also on the side-effects and complications, with the results being meanwhile presented in 4 Lipolysis Reports [1]. The time therefore now seems right to provide all doctors who concern themselves with aesthetic therapies, and especially the international medical community, with an overview of the current state of development of the therapy. And within this context, one name should be mentioned in particular – that of Dr. Franz Hasengschwandtner, of Bad Leonfelden, Austria. With his untiring commitment to the cause of lipolysis, Dr. Franz, as he was generally known internationally, decisively shaped the early development of the therapy. It is therefore only right and

proper that, following his retirement, he has been appointed Honorary President of the NETWORK.

INJECTION LIPOLYSIS – A NETWORK IN PROGRESS

In the early phases of organization of the NETWORK-Lipolysis, a number of highly diverse initiatives were supported by it. Working with a very small but highly committed team in the background, one of the primary activities was to respond to the many international inquiries from doctors and societies wanting to know more about the therapy. From 2004 to 2008, training courses were held on all continents and in many different countries, aimed at enabling the participants to introduce the therapy. And, we now have to add self-critically, we were at the time far from able to meet all the demands associated with the courses. To give just a few examples: We had to ensure that our Compound was legally available in the countries where we held the training courses; we had to ensure compliance with national laws, which even within the European Union differed widely; we wished to be able to supply our international members with all key aids and equipment, such as the very useful multi-injectors; we sought to inform the patients about the new therapy in the language of their own countries; and we received inquiries from many members about the possibility of protection in the shape of insurance. And our most important task, ultimately, was to support our members as broadly as possible in providing the therapy. In 2008, however, given that we were not a multinational company with subsidiaries in every country, but only a small network operating out of Germany, we realized that we had taken too much upon ourselves.

So in 2008, in view of our limitations, which we had been painfully forced to recognize and accept towards the end of our “wild youth” phase, we initiated a radical change of direction and adopted a new set of goals. We resolved to focus our efforts primarily on our German-speaking members in Austria, Switzerland and Germany and ensure that they received the professional support they needed. Taking a realistic view of

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the situation, we were convinced of our ability to develop the instruments needed for providing professional support in those countries. So while we have always maintained contact with our international members, we have been unable to offer them the services which in our view are essential for maintaining a living network.

Since 2008, therefore, we have restructured our basis in the three aforementioned countries, and through this reorientation have gained a great store of experience of the kind that is essential for embarking on a broadening of our international activities.

INJECTION LIPOLYSIS TODAY

The primary interest of readers of **Cosmetic Medicine Online** will certainly not be in how the NETWORK-Lipolysis has got to where it is today. Of much greater interest to them will be the advances that have been made in the therapy. The following section therefore focuses chiefly on this aspect.

The current Standard Protocol

The Standard Protocol as it stands today covers the following aspects:

- The injectable
- Patient selection
- The treatment protocol
- After care (pain and side effect management – PSM)

Injectable

In this area, we can indicate three different possibilities, which in themselves are already a reflection of the current discussion. These are either DOC (deoxycholate) by itself, or else a combination of PPC (polyenylphosphatdylcholine) and DOC in pure form, or the same combination but with the PPC/DOC diluted with NA_{CL} (1:1) and the addition of a vitamin B complex. This last variant has become known as the **NETWORK Compound (NC)** and is used by most colleagues [2, 3]. It should not go unmentioned that there are meanwhile many suppliers of PPC/DOC products on the market. In this area, the NETWORK, which was, after all, formed primarily to protect the patients and practitioners, has done an excellent job by arranging for all the products to be tested by an independent laboratory and so saved its members from working with what in some cases were toxic or ineffective solutions.

Patient selection

It has become clear that the statistical treatment outcomes improve significantly with increasing experience. It can therefore be assumed that good patient selection resulting from growing experience is one of the reasons for this.

A factor of crucial importance in all cases is the consistency of the fat tissue to be treated: Is it soft fat, or does it contain a high proportion of connective tissue? It stands to reason that soft fat dissolves more easily than deposits containing a lot of connective tissue. Further patient selection criteria are the size of the fat deposit and the region which it is proposed to treat.



Fig 1: Result of Dr. Thierry Marechal, France

Part of the definition of IL is that it is only suitable for treating smallish deposits of fat.

Larger deposits should normally be dealt with surgery, i.e. by liposuction, except where the patient rejects any such surgical intervention outright. In such cases, however, the patient must always be informed that in order to treat larger deposits it will probably require more than the usual average of 2–3 treatments before the final result is achieved; instead, 5–7 treatments should be reckoned with – a number which should normally only apply in such exceptional circumstances (Fig. 1).

The question as to the region to be treated has only arisen as a result of more recent discoveries in the field of fat cell



Fig 2a+b: Result of Dr. Johannes Müller-Steinmann, Germany

TABLE 1: STANDARD PROTOCOL OF THE NETWORK-LIPOLYSIS

Maximum dose per treatment	100 ml NETWORK Compound (2,500 mg PPC, 1,250 mg DOC)
Maximum dose per injection	0.5 ml Compound
Space between injection points	1.5 cm
Injection depth	Face 4–6 mm, body 10–12 mm
Treatment interval	8 weeks

research [4, 5]. It was originally assumed by most people that the region was only of secondary importance. However, the reported discovery of different types of adipocytes, each with its own specific behaviour, raises new questions for IL users which will have to be answered in future.

Other selection criteria can be stated as follows: Does the patient want a rapid body contour change (i.e. liposuction) or a slower and therefore less conspicuous one (IL)? One priority indication that has emerged is the treatment of lipomas (lipo lipomas only), especially for patients with multiple lipomatosis. In view of the resulting scar formation, the former practice of excision is no longer acceptable for this group of patients.

A contraindication applies in the case of adipositas patients (with a BMI of more than 30). The following are also contraindicated: Children and adults, pregnant and breast-feeding women, diabetics with micro- and macroangiopathies, inflammatory connective tissue disorders, certain autoimmune diseases (not including rheumatic disorders and Hashimoto's thyroiditis), severe liver conditions, known allergy to one of the ingredients used (soya allergy sufferers are allowed to be treated!) as well as allergy sufferers with MCS syndrome. Patients with kidney problems, lipodystrophy and blood clotting disorders or with acute and chronic infectious diseases

are only partially eligible for treatment and then only with extreme caution.

Treatment protocol

It should be pointed out in advance that knowledge of the protocol by itself is not sufficient for achieving good results. Therapy beginners are advised to at least undergo a one-day hands-on training course offered by the NETWORK-Lipolysis, where many details can be presented that are decisive for the success or failure of the therapy [6]. Tab. 1, which is shown left, can be viewed as the standard protocol.

After-care

A significant factor in the success of the treatment and the level of patient acceptance has proved to be the introduction of the after-care method known as PSM (Pain & Side Effect Management): This involves the use of a 1 megahertz ultrasound device to massage a soothing and cooling gel (Skin Attitude Gel) into the skin, which results in both better distribution of the injectable as well as a reduction in the treatment pain and the associated swelling. Additionally, Degozym, a preparation developed by the members and containing the enzymes bromelain and papain, is administered orally for one week so as to speed up the reduction in the swelling and the healing of haematomas and to reduce the pain occurring during the first three days. According to a more recent study [7], dual frequency ultrasound (LDM) can be used instead of, or in addition to, the 1 MHz ultrasound. As well as reducing the pain, this produces a 65% improvement in the treatment outcome if used several times following the IL treatment (Tab. 2).

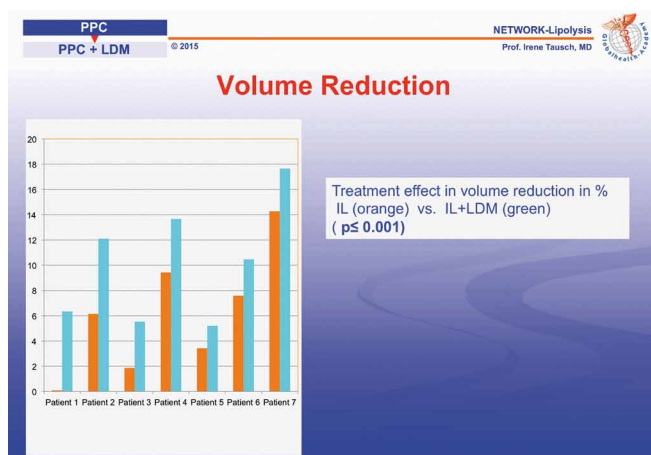
Finally, with regard to the standard protocol, it should be added that because of the use of a compound, special attention should be paid to ensuring that the patients are comprehensively informed, particularly as this is not a treatment which is medically necessary. Patient information and consent forms which have undergone legal scrutiny are freely available to NETWORK members in the most important languages.

INJECTION LIPOLYSIS TOMORROW

The question as to the direction in which IL will develop in future depends on numerous variables and also players who enter the market and then leave it again. Not least its future is also dependent on the NETWORK's activities. A role will also be played by the direction in which aesthetic medicine develops as a whole. The Network intends to play a central role in this.

Topic 1: What direction is aesthetic medicine moving in?

We can see from the changes in patient behaviour that what people increasingly want is a holistic, non-aggressive and all-embracing response to the aesthetic challenges of the aging process. This should encompass all aspects of age-related change, i.e. the build-up and reduction of volume, the treatment of mimic and non-mimic wrinkles, as well as improvements to the skin status [8, 9]. If one looks at the changes caused by aging, Injection Lipolysis is able to offer a convincing



Tab 2: Volume reduction contralateral: IL alone vs. IL + LDM Ultrasound



Tab 3: Patient satisfaction in facial treatments, source: Lipolysis Report 2015

response to the lowering of the areas of fat in the face and the increase in the proportion of smallish areas of body fat, which frequently resist attempts at reduction through lifestyle changes such as changes in diet and physical exercise. The latest statistic published by Prime [10] in 2015 on the increase in patient inquiries shows that the interest of the patients remains high and is increasing dynamically.

Topic 2: The approval of Kybella™ in the USA

The current discussion is being stimulated by the approval of Kybella™, a drug for the treatment of double chin, in the USA. This approval was also so interesting financially that Allergan has meanwhile taken over Kythera, the company that obtained the approval in 2015, for a sum of 2.1 billion US dollars. The active substance in Kybella™ is deoxycholic acid (!). Both inside and outside the Network, the question is being raised [11, 12]

as to whether, and to what extent, the second active ingredient, PPC, has any additional effect at all or whether DOC is not sufficient on its own, seeing that it has been shown to be able to destroy the cell membranes of the adipocytes by itself. The position adopted by the Network is that while it welcomes the approval of Kybella™, a number of published studies indicate that it remains preferable to continue adding PPC as a second active ingredient to the injectable. The main question in this context is what happens to the fat cells **after they have been destroyed** and to what extent PPC fosters the metabolization of the fat that has been released, thus also improving the result. The mechanism by which PPC acts can be described as follows, although it should be added that we would consider it desirable for the studies that already exist to be subjected to renewed scrutiny and assessment:

- PPC diminishes the aggressiveness of the DOC (Klein et al.)
- PPC diminishes the toxicity of the DOC (Nagasaka et. al.)
- PPC stimulates fat-reducing enzymes such as lipase (Desmereaux et.al.)
- PPC acts as an emulsifier for the fat that is released
- PPC increases the absorption capacity and fosters transport of the cholesterol ester to the liver (Zierenberg et.al., Navder et.al.)
- As well as destruction of the cell membrane (necrosis), PPC also causes apoptosis (Peckitt, Lee et.al.) and thus further contributes to improving the long-term results [13]

Topic 3: What possibilities are there for still treating non-responders successfully?

Statistically speaking, 10% of facial treatments and 15% of body treatments do not produce satisfactory results. We summarize these unsatisfactory treatments under the heading

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Fig 3: Result of Dr. Johannes Müller-Steinmann, Germany

“Non-responders”, although from a chemical point of view no fat cells actually exist that cannot be destroyed by DOC. The NETWORK has devised a set of convincing instructions for the treatment of this group of patients, who can be defined as patients who, after the first treatment, show no or only very slight improvement in the size of their fat deposit. As a new treatment strategy for this group of patients, we now propose that the standard protocol should be adjusted for the second treatment. Depending on the concrete findings, this would involve either increasing the dose, increasing the concentration, or injecting at two different depths.



Fig 4: Double chin treatment of Dr. Kai Rezai, Germany, with higher concentration

Topic 4: Refinement of facial treatment

Since the beginning of 2015, a discussion has been taking place on the extent to which the standard protocol should be varied in the case of facial treatments. The background to this is that descended fat deposits are in many cases only very small and the complete elimination of them may be undesirable. This does not apply to an extensive double chin, for example, but rather to the regions around the nasolabial fold or the jowls. A reduced dose per injection, paired with a reduction in the injection spacing, can allow better focussing of the intended result and at the same time reduce the level of swelling, which, being in the face, is more than welcome to many patients, even though it can mean that they may have to undergo one or even two additional treatments. This procedure could be described as being a move away from **treatment** and towards **modelling** (Fig. 2 + 3).

In the case of very large accumulations of fat – a voluminous double chin, for example – an increase in the dose or the concentration may sometimes be called for (Fig. 4).

Topic 5: New active substances

The use of an aggressive, toxic substance such as deoxycholic acid can indeed be viewed critically. While the current risk profile of the PPC/DOC combination – provided treatment is performed in compliance with the standard protocol – can be rated as very good [14], there is nevertheless every justification for looking for alternative active substances. Besides Kythera, two other firms in the USA are working on such alternatives, though currently only at a very early stage. Somewhat more advanced is a new combination of nanotechnologically modified PPC and glycyrrhizinic acid (without DOC!) that has been developed by the Network in cooperation with the Institute of Biomedical Chemistry, Moscow, and has already been patented. However, due to lack of the necessary Phase 1–3 studies for lipolysis, approval for this new product cannot be reckoned with in the near future.

DISCUSSION

Since the introduction of the standard protocol for Injection Lipolysis in 2004, the process of collaboration between a large number of colleagues has led to continuing improvement and adjustment of the protocol. The resulting continuous improvement in the treatment outcomes and the fall in the level of side-effects has led to strong acceptance on the part of the treating practitioners and patients. During this time, the patient demand has risen constantly [15]. Since being integrated into a holistic treatment concept which, under the name “New Compositional Aesthetics”, involves both a philosophical and ethical reorientation as well as a clear definition of the meaning of minimally invasive therapies, Injection Lipolysis is being increasingly adopted as an important module in age-related facial treatment (Fig 5).

Does this mean that we have reached the end of an elaborated protocol, or do further development possibilities present themselves for the future? Chemical-based Injection Lipolysis

unquestionably possesses further development potential, and the urge for creative further development in this area among medical colleagues both inside and outside the Network appears unbroken, so that we can reasonably expect to see further innovations in the future. These are likely to manifest themselves both in the continuous refinement of the standard protocol as well as in combination with other fat-reducing procedures (sculptsure, cryolipolysis, ultrasound), and in the development of new active substances.

Disclosure

Margrit Lettko is a teacher at the Globalhealth Academy for Aesthetic Medicine and Medical Director of the NETWORK-Lipolysis. No financial interests involved.

Dirk Brandl is Speaker of the NETWORK-Globalhealth and NETWORK-Lipolysis. No financial interests involved.

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Literature and notes:

1. The Lipolyse Report 2015 was presented by Margrit Lettko on 12 September 2015 at the NETWORK's MASTER Conference in Berlin; publication is currently in preparation. The statistic represents the biggest survey ever conducted, with altogether 29,889 patients and 74,000 treatments.
2. Hoffmann K (2010) Injektionslipolyse. *Hautarzt* 61: 847-55.
3. Hasengschwandtner F: Injektions-Lipolyse, in: *Selbstzahlerleistungen in der Dermatologie und der ästhetischen Medizin*, edited by Bernd Kardorff, Springer Verlag, 2nd edition
4. Kruglikov I: Kontroversen in der ästhetischen Medizin, 5. Body Contouring – eine einheitliche Vielfalt. *Kosmet Med* 34: 114-120.
5. Kruglikov I: Kontroversen in der ästhetischen Medizin, 7. Kryolipolyse-Apoptose vs. Thermogenese. *Kosmet Med* 34: 202-207.
6. For international participants, the Globalhealth Academy for Aesthetic Medicine offers the MASTER Class Injection-Lipolysis as a hands-on training course. In case of interest, please contact the NETWORK, Anna Keller, Phone +49 2508 2159-200, keller@network-lipolysis.com
7. Tausch I, Kruglikov I (2015) The benefit of dual-frequency ultrasound in patients treated by injection lipolysis. *J Clin Aesth Dermatol* 8: 42-46.
8. Brandl D, Steinert M, Lettko M, Weidmann M, Grübmeier H, Meyer-Rogge D, Rezai K, Müller-Steinmann J, Giesse S, Herzog M, Ellwanger J (2015) Überlegungen zur Standardisierung der Kompositorischen Ästhetik des Gesichts: Teil 1. *Kosmet Med* 36: 158-162.



Fig 5: Compositional Aesthetics treatment of Margrit Lettko: Injection-Lipolysis, BTX, Fillers and Mesotherapy

9. Brandl D, Steinert M, Lettko M, Weidmann M, Grübmeier H, Meyer-Rogge D, Rezai K, Müller-Steinmann J, Giesse S, Herzog M, Ellwanger J (2015) Überlegungen zur Standardisierung der Kompositorischen Ästhetik des Gesichts: Teil 2. *Kosmet Med* 36: 196-202.

10. A statistic was published in April 2015 in the online edition of the magazine Prime showing which therapies experienced a rise in demand in 2014. Injection Lipolysis appears twice in the top 10, with an increase of altogether 712% over 2013.

<https://www.prime-journal.com/new-statistics-reveal-the-top-cosmetic-treatments-of-2014/>

11. Duncan DI (2013) Commentary on: Metabolic and structural effects of phosphatidylcholine and deoxycholate injections on subcutaneous fat: a randomized, controlled trial. *Aesthet Surg J* 33: 411-3.

12. Hasengschwandtner F, Gundermann K (2013) Injection lipolysis with phosphatidylcholine and deoxycholate. *Aesthet Surg J* 33: 1071-2.

13. All the publications named were cited by Hasengschwandtner and Gundermann in Literature No. 12 and can be found there.

14. Presentation by Margrit Lettko at the MASTER Conference Berlin, 12 September 2015: The Lipolysis Report 2015 showed a risk profile of 0.01% for complications that are not completely reversible (necroses), i.e. 1:10,000 patients or 1:25,000 treatments. Investigation of these necroses revealed that they are not inherent in the system but were caused either by inappropriate action on the part of the patients or treatment error on the part of the practitioners.

15. The Lipolysis Report 2015 was completed by 4% of the members. It can therefore be assumed that around 750,000 patients were treated within the Network alone. The actual number of lipolysis treatments is likely to be very much higher.

The next international training for Injection-Lipolysis
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