

Study protocol for thermographic analysis of the nasolabial fold region in women submitted to hyaluronic acid filling

Protocolo de estudo para análise termográfica da região do sulco nasolabial em mulheres submetidas ao preenchimento com ácido hialurônico

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ABSTRACT | INTRODUCTION: Due to the increasing number of cases with immediate and late complications caused by the action of facial fillers such as hyaluronic acid (HA), there is an urgent need to better evaluate the effect of these aesthetic and functional procedures. In this sense, it is relevant to use Infrared Thermography (IRT) as an auxiliary tool for the diagnosis of local dysfunctions. This diagnostic method allows the professional who applies the injections to be certain about the condition of the microcirculation of the anatomical site being treated, enabling the possibility of early intervention in case of adverse effects, such as the development of microbubbles, vascular compression, among other conditions.

OBJECTIVE: The aim is to describe the thermal coefficient of the nasolabial sulcus (NLF) region of patients undergoing HA filling, using TRI. **METHODS AND MATERIALS:** This is a prospective study involving 25 female patients from a private clinic. Thermal imaging will be performed before, immediately after, 1 hour, 3 hours, and 1 month after filling the NLF region with AH. Study approved by CAAE: 34546620.7.0000.5544.

RESULTS: The result of this study will allow preventive follow-up and early intervention in cases of vascular alterations related to facial fillings with AH.

KEYWORDS: Infrared thermography. Hyaluronic acid fillers.

RESUMO | INTRODUÇÃO: Devido ao aumento do número de casos com complicações imediatas e tardias causadas pela ação de preenchedores faciais como o ácido hialurônico (AH), há uma necessidade urgente de avaliar melhor o efeito desses procedimentos estéticos e funcionais. Nesse sentido, torna-se relevante a utilização da Termografia Infravermelha (TIV) como ferramenta auxiliar para o diagnóstico de disfunções locais. Esse método diagnóstico permite ao profissional que aplica as injeções ter certeza sobre a condição da microcirculação do sítio anatômico em tratamento, possibilitando a intervenção precoce em caso de efeitos adversos, como desenvolvimento de microembolos, compressão vascular, entre outras condições. **OBJETIVO:** O objetivo é descrever o coeficiente térmico da região do sulco nasolabial (SNL) de pacientes submetidos ao preenchimento de AH, utilizando TRI.

MÉTODOS E MATERIAIS: Trata-se de um estudo prospectivo envolvendo 25 pacientes do sexo feminino de uma clínica privada. As capturas de imagens térmicas serão realizadas antes, imediatamente após, 1 hora, 3 horas e 1 mês após o preenchimento da região SNL com AH. Estudo aprovado pelo CAAE: 34546620.7.0000.5544. **RESULTADOS ESTIMADOS:** O resultado deste estudo permitirá o acompanhamento preventivo e a intervenção precoce nos casos de alterações vasculares relacionadas aos preenchimentos faciais com AH.

PALAVRAS-CHAVE: Termografia infravermelha. Preenchimento de ácido hialurônico.

Introduction

The use of HA for the treatment and prevention of facial aging has been growing every year. The search for aesthetic procedures to prevent and treat facial aging with the use of this material has been frequent in contemporary society. In 2011, dermal fillers were used in about 1.6 million aesthetic procedures, with an increase to 2.3 million and 5.5 million in 2013 and 2014, respectively.¹ HA is one of the most commonly temporary dermal fillers used to correct expression lines and facial furrows due to its proven safety and efficacy.

Dermal fillers composed of HA are preferred to correct wrinkles, furrows, depressions, lip contour, and volume improvement, acne scars, and facial volume replacement.² Due to the growing demand of the market, multiple dermal fillers are available, with differences in their compositions. They present different physical and chemical characteristics, which directly impacts on the duration of the effect, palpation, application technique, and potential complications.² Moreover, achieving the desired result depends critically on the knowledge of the different characteristics of each material, its application methods, risks and limitations, and a learning curve that requires practice and manual skill from the health professional who uses it.³

Due to the growth in the number of facial fillings with HA, an increase in cases with evident complications has been reported in the literature, especially those involving facial blood vessels, by compression or embolism.⁴ If not promptly diagnosed and treated, they may cause irreversible damage to their users. In fact, these complications can be reduced or even prevented through a vigilant and systematic approach.⁵ Anatomical knowledge of the face's arterial distribution is indispensable to prevent extravascular compression and direct obstruction caused by the fillers.⁶

After the injection of a HA filler, a mild inflammatory reaction occurs.⁷ Recently, it was reported that the incidence of complications is increasing.⁴ Notably, late-onset nodules⁸, and intravascular events, represented by skin necrosis and blindness, have been described in the literature.⁹

One of the most characteristic signs of facial aging is evidenced in the NLF region, located to the nose wing up to 1 to 2 cm laterally to the lip commissure.¹⁰ The progressive ptosis of the malar fat and the overlying skin contribute to the deepening of this region.¹¹ The knowledge of the anatomy of the area to be treated and of the indicative signs of vascular alterations during and after the procedure is essential.¹² However, this method is subjective and observer-dependent.¹³ The NLF region is a risk area since it is closely related to the facial artery (FA), a vessel that accounts for most of the facial blood supply. The main trunk of the facial artery is juxtaposed to the NLF.¹⁴ Given the above, as this is an anatomical region of great importance, it has raised the interest of the scientific community.

IRT is a resource that has been used by a growing number of medical specialties.¹⁵ All objects, including the human body, emit a spectrum of infrared radiation. According to Wien's Law, the frequency at which maximum energy is emitted is dependent on the body temperature. Thus, by measuring the infrared radiation emitted by the skin's surface, its surface temperature can be determined through a temperature capture using an IRT camera.^{16,17}

The analysis of the thermal coefficient of an anatomical region may indicate a possible dysfunction, which may be related to the thermal pattern of a particular disease and/or condition. In particular, the inflammatory process, as a rule, will show blood hypoperfusion, manifested in the thermogram as temperature increases or as a hyper radiant area. In contrast, there are pathological changes, such as ischemic conditions, where hypoperfusion is observed, with a consequent drop in temperature and in hypo-radiant areas.^{17,18} The skin blood flow is controlled by the hypothalamus, in a uniform and symmetrical way; alterations in this thermal distribution indicate abnormality.¹⁹

In a recent literature search, it was observed that there is a scarcity of studies associating infrared thermography (IRT) with the use of dermal fillers in the daily clinical practice of health professionals, such as physicians and dental surgeons, to monitor possible disorders of vascular nature. Due to the increase in the number of cases with immediate and late complications caused by the action of facial fillers, such as hyaluronic acid (HA), there is an urgent need

to better evaluate the effect of these aesthetic and functional procedures. In this sense, the use of IRT as an auxiliary tool for the diagnosis of local dysfunctions becomes relevant. This diagnostic method allows the professional giving the injections to be sure about the condition of the microcirculation of the anatomical site in treatment, allowing the possibility of early intervention in case of adverse effects, such as the development of microemboli, vascular compression, among other conditions. The present study aims to evaluate the variation of the thermal coefficient of the NLF region after filling with HA by IRT in different periods after this procedure.

Methods

Study design

This is a prospective cohort study that will encompass female patients.

Place

Clínica de Assistência e Reabilitação Odontológica - Clarodonto, based in the city of Salvador (Bahia).

Target Population

Women who will undergo filling of the SNL region with HA.

Sample Selection

Convenience sample, from a private clinic, through free demand.

Inclusion Criteria

- a) Women aged between 45 - 55 years old;
- b) Presence of deepening or depression of the NLF;
- c) Never undergo filling of the SNL region with HA before;
- d) No comorbidities;

e) Signature of the FITC.

Exclusion Criteria

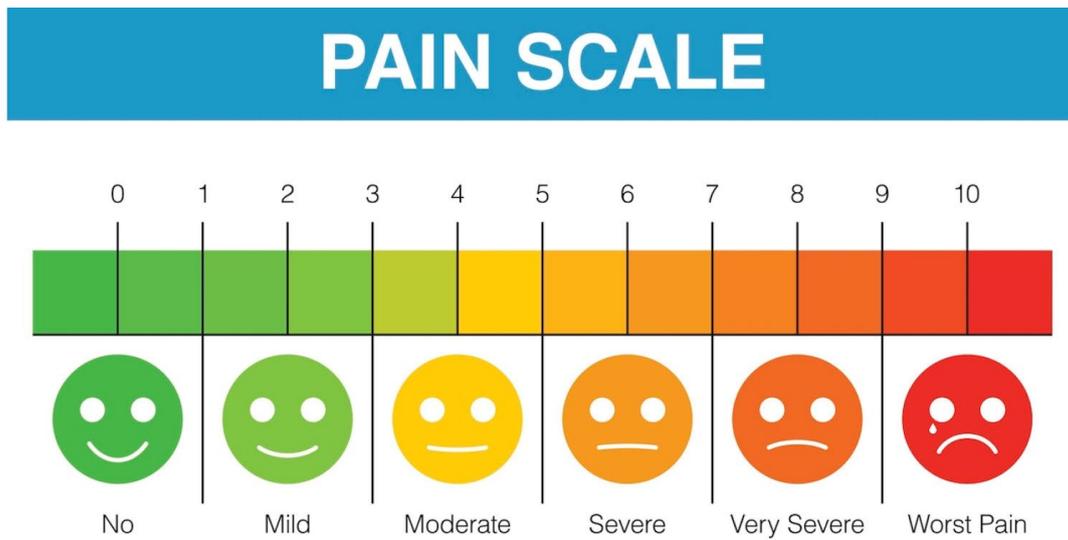
- a) Lactating women;
- b) Pregnant women;
- c) Smokers;
- d) Women with autoimmune diseases;
- e) $\Delta T > 0.3^\circ$ between the Regions of Interest (ROIs) of the hemifaces.

Study protocol

The patients will arrive at the Clarodonto clinic, Salvador (Bahia), where the treatment will be performed. Initially, the patients will go through an anamnesis, to confirm and ensure that they all adhere to the study's criteria of inclusion. To calculate the sample size, the GPower (Universitat Kiel, Germany) was used, with $\alpha=5\%$, power of 80%, and effect size of 0.25, increased by 20% in case of eventual dropouts, totaling $n=25$.

After evaluation, the patients will be individually taken to a reserved room, where their faces will be sanitized with 70% alcohol and their hair will be tied up for better facial exposure and image acquisition. After a period of 20 minutes, necessary for the body's thermoregulation, the patient will sit in the dental chair, and an image will be captured with the infrared camera, respecting the established parameters. Next, the filling procedure of the NLF region will be performed with AH Princess® VOLUME (Croma - Pharma GmbH, Leobendorf, Austria), finishing with the image capture, after the procedure. New thermographic recordings will also be performed both 1 and 3 hours after filling, as well as at 1 month. The area submitted to the procedure will be physically examined during the image captures. The volunteers will also answer a form with the Visual Analogue Scale (VAS) to measure pain during these 5 moments (Figure 1).

Figure 1. Visual Analog Scale

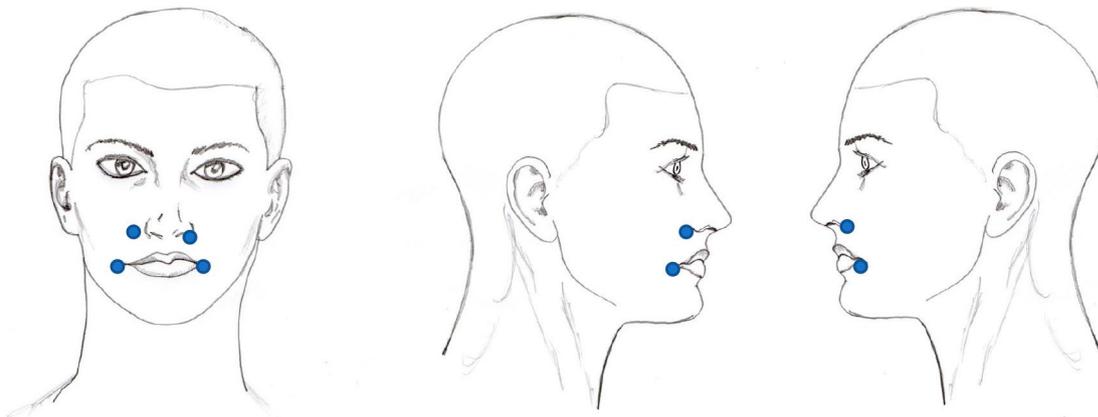


Source: The Customer Pain Scale – Jen van der Meer.

All procedures will be performed in the morning shift, standardizing the influence of the circadian cycle on body temperature throughout the day.

The HA application technique will be through a retroinjection with a 22G Pro Deep cannula (Alur Medical, China), with a single puncture, performed with a 22G needle, at the equidistant point from the four ROIs that will be evaluated (Figure 2). The HA will be placed subcutaneously, in the predetermined region, bilaterally, with a total dose of 1 ml of the product.

Figure 2. Front view (a) and side views (b,c)



Source: Own authorship.

After the care of all patients is finalized, they will receive all post-procedure care instructions to avoid any adverse effects. The data and images collected will be further analyzed.

To evaluate the local circulatory pattern, a FLIR ONE Pro infrared camera (Victoria, Australia) with resolution of 160×120 pixels and 8.7 Hz image frequency that captures images in real-time will be used. The equipment performs studies in the temperature range of -20°C to 400°C and has a thermal sensitivity (MRDT) of 150mK. It operates in the spectral range of electromagnetic waves from 8 to 14µm, corresponding to the far-infrared range. To obtain a pattern of images the following protocol will be adopted: the patients will be positioned in the dental chair, with the Frankfort plane parallel to the floor. The camera will be placed on a tripod, with a height and distance of 1 m from the face of the volunteer. Facial captures will be taken in frontal, right lateral, and left lateral views. All image acquisitions will be within the 24-37° C thermal window. The environment will have its temperature and humidity controlled, by a thermo-hygrometer, around 22°C ± 1°C and maximum of 60% respectively. To prevent thermal changes, sources of air convection directly at the volunteer will be avoided.

Variables

The volunteers will be analyzed according to the variables: age, profession, monthly income, level of education, and place of residence. The variations of the thermal and pain coefficients recorded during the study will also be analyzed.

Statistical Analysis

For collecting and analyzing data, the Microsoft Excel software will be used to develop a spreadsheet, built specifically for the study. As for the qualitative variables (education and monthly income), the data will be obtained from a one-dimensional frequency table, in which their respective percentages will be identified. Individual spreadsheets will be built to analyze the variation of the thermal coefficients,

obtained both through thermographic records and analysis of pain coefficients. The ANOVA test (normal distribution) or the Kruskal-Wallis Exact Test (non-normal distribution) will be used to compare the different evaluation periods. The level of statistical significance adopted was $p < 0.05$.

Feasibility

All the material needed for the study is already with the responsible researcher.

Risks

Hyaluronic acid fillers, when properly used, are associated with a low rate of adverse events. This type of filler has an advantage over other materials, as it can be degraded through the use of the hyaluronidase enzyme, which adds safety to its use.

Here are the main adverse events associated with the hyaluronic acid filler and their resolution:

Ecchymosis: to minimize this event, the application will be performed with a cannula;

Erythema: tends to be spontaneously resolved within 24 hours;

Persistent edema or hypersensitivity: prescription of corticoid (Prednisolone 40 mg/day for 3 to 5 days) and/or local application of hyaluronidase by a qualified health professional (CROBA 5755);

Palpable product or product displacement: the appropriate product cross-linking for the region to be treated will be chosen. The applied quantity will be compatible with the area to be treated (0.5 ml on each side). If necessary, the product will be removed by locally applying hyaluronidase;

Asymmetry: rigor in the amount of product applied on both sides. If necessary, the product will be complemented or removed by locally applying hyaluronidase;

Nodules: local application of hyaluronidase;

Local infection: prescription of antibiotics (Cephalexin 500 mg every 12 hours for 7 days) by a qualified health professional (CROBA 5755);

Vascular embolization: anatomical knowledge, aspiration before injection, slow injection, and with minimum pressure. If necessary, hyaluronidase will be locally applied.

The thermographic evaluation does not offer risks to the physical health of the patients being evaluated, but since it is a digital image recording it may cause embarrassment to the patient. To minimize this risk, the qualified health professional will record such images in a private environment and omit the patient's identification. All the data collected will be kept in complete confidentiality, stored only in the responsible researcher's computer for the time of the research. At the end of the study, all thermograms will be erased from the computer's memory.

If any of the patients suffer any kind of damage or injury due to their participation in the research, they will be entitled to compensation, according to CNS Resolution No. 466 of 2012 (item IV.3), which will be the responsibility of the researcher. In case of any doubt, the researchers will be available for clarification at any time, so that the patients feel safe during the entire data collection, procedure and thermographic analysis.

Benefits

The results of this study will be published as a scientific paper, contributing to the early diagnosis of possible dysfunctions in the anatomical region with hyaluronic acid filling, through thermographic records.

The volunteers will be directly benefited by the total or partial reduction of their nasolabial fold line.

Ethical aspects

This research protocol was submitted to and approved by the CEP of the Escola Bahiana de Medicina e Saúde Pública, CAAE: 34546620.7.0000.5544. All volunteers will sign the Free and Informed Term of Consent.

Expected outcomes/results

Due to the scarcity of publications, this study will provide new knowledge, enabling immediate intervention in case of embolism or vascular compression, adding safety to the procedure, and avoiding sequels.

Authors' contribution

Faria ISD participated in the literature survey and discussion of the research project. Carvalho FC and Medrado AP developed the initial design of the project and participated in its methodological construction. Medrado AP performed the critical review of the project.

Conflicts of interest

No financial, legal or political conflicts involving third parties (government, corporations and private foundations, etc.) have been declared for any aspect of the submitted work (including, but not limited to grants and funding, advisory board participation, study design, preparation of the manuscript, statistical analysis, etc.).

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