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# Photography in surgical and cosmetic dermatology-Part II

*A fotografia na cirurgia dermatológica e na cosmiatria – Parte II*

## ABSTRACT

The evolution of the digital photography in the last decades has revolutionized the documentation of patients in dermatology. The photographic record has become much more practical and affordable, and today we can say that photography is part of the Dermatologist's routine. In cosmetic dermatology, the photographs enable the analysis of the improvement of the skin with the procedures. In dermatologic surgery, the images are used to document pre-and post-operative as well as intraoperative details (such as marking the operated area and the surgical steps). And the clinical dermatologist uses the photography to observe the evolution of lesions during treatment. However, as we become more intimate of the photographic act itself, some troubles are more easily detected, and sometimes, we need to be creative in order to solve them.

**Keywords:** photography; dermatology; surgery; surgical procedures.

## RESUMO

*A evolução da fotografia digital nas últimas décadas revolucionou a documentação dos pacientes na dermatologia. O registro fotográfico tornou-se muito mais prático e acessível, e hoje podemos dizer que a fotografia faz parte da rotina do dermatologista. Na cosmiatria, a fotografia permite avaliar o aspecto da pele, antes e depois dos procedimentos. Na cirurgia dermatológica, as imagens são utilizadas para documentar o pré e o pós-operatório, assim como detalhes intraoperatórios (como a marcação da área operada e os passos cirúrgicos). Por sua vez, o dermatologista clínico utiliza a fotografia para observar a evolução das lesões durante um tratamento. No entanto, conforme nos tornamos mais íntimos do ato de fotografar, encontramos alguns problemas, e muitas vezes, precisamos ser criativos para solucioná-los.*

**Palavras-chave:** fotografia; dermatologia; cirurgia; procedimentos cirúrgicos.

## Continuing Medical Education



### Authors:

Maria Valéria Bussamara Pinheiro<sup>1</sup>

<sup>1</sup> Collaborating Physician at the Cosmiatry Sector, Dermatology Department, Universidade Federal de São Paulo (UNIFESP)—São Paulo (SP), Brazil

### Correspondence:

Dr. Maria Valeria Pinheiro Bussamara  
Rua Afonso Brás, 864 cj 51  
Vila Nova Conceição  
Cep: 04511-001—São Paulo—SP, Brazil.  
E-mail: valeria@valeriapinheiro.com.br

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## INTRODUCTION

As dermatologists, we are interested in medical photography, as discussed in the first part of the present article, published in this journal (Volume 5, Number 2, April-June 2013). Medical photography is a medium that accurately describes what we see in the patient's skin, and is performed following basic photography techniques and a rigorous standardization of images in order to gather the necessary information for comparing photographs.<sup>1</sup>

From the moment we decide to use medical photography in a case, we should think in terms of a script to be followed, starting with the preparation of the location where the photographs will be taken through to the preparation of the patient. At each step in the process (even with knowledge of photography techniques) we can still come across a range of problems, such as issues involving physical space, lighting, image composition, and operation of equipment, among others. To generate good quality images, we should note all these details.

## STANDARDIZATION OF IMAGES

In order to compare two photographs—one taken before a procedure, the other taken after it—we must take into account that the only variable factor in the photographs should be in the patient's skin. Parameters, such as exposure (aperture + shutter speed + ISO), the focal length, the ambient lighting, the position of the patient and camera, and the background used in the images, should always be the same and be consistently applied in all photographs.

### Exposure

Ambient light can be natural (from a window) or artificial (such as ceiling or wall lighting, or flash), however the correct exposure parameters should always be the same. Recalling that exposure is the balance between the aperture, shutter speed, and ISO, each of these parameters should be adjusted according to the type of lighting present in each environment. Ideally, one should run several tests (using the “manual” mode of the camera) to arrive at the correct exposure. Once the exposure has been determined, it must be applied to all “before and after” photographs of each patient.<sup>2</sup> Depending on the photographer's preference, the “automatic” setting of the camera can be used instead, however the process will certainly not be as interesting for the photographer.

### Background

The most cited background colors in scientific papers are black and white, however some shades of blue or green can be used in cases of surgical photographs. Medium gray is considered a neutral tone in photography, and is therefore a good option (Figure 1). The background must be neutral and smooth in order not to distract the observer.<sup>3</sup> Furthermore, it must occupy the entire frame of the picture, meaning that the photographed subject should occupy the central area of the image, with the entire surrounding background being filled solely by the chosen color.

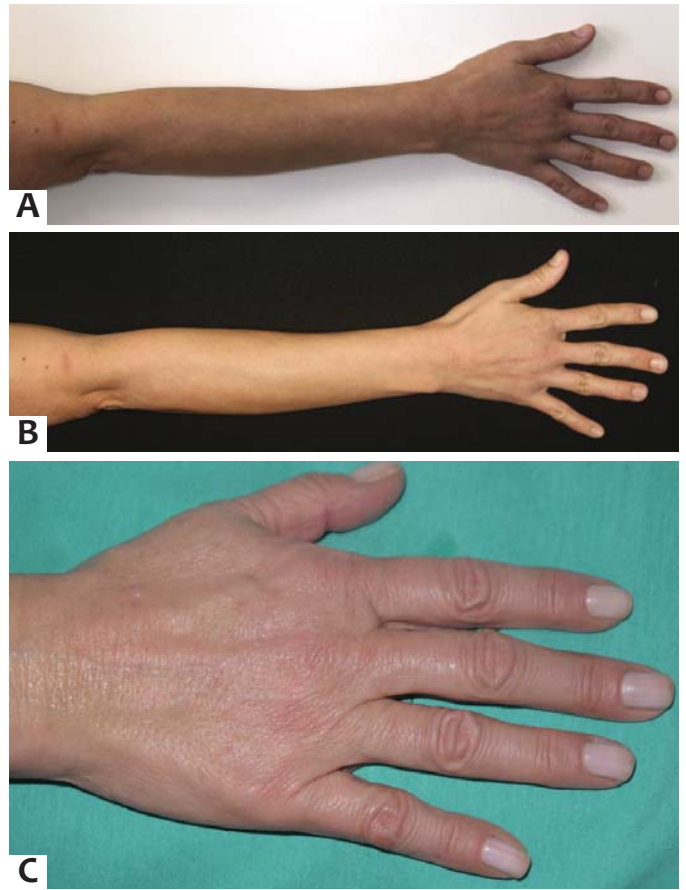


FIGURE 1: A and B - Black and white background. A slight shadow can be observed on the white background. C - Green background

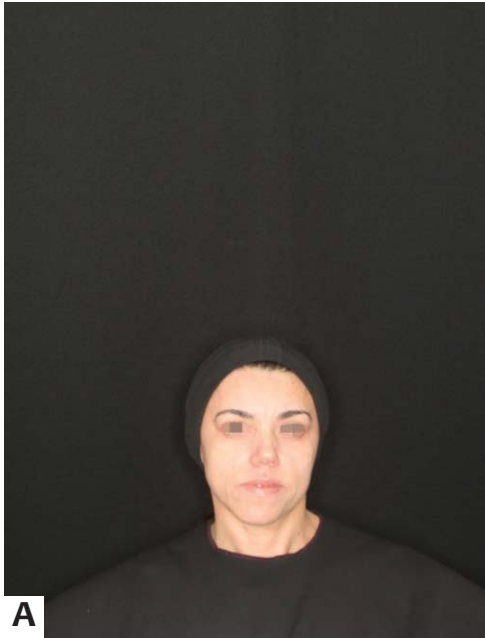
The presence of elements that have no relation to the photographed subject can distract the observer. For example, in a full-body photograph an angle lens (wider scope of view) is used, resulting in a significant part of the room also being photographed with all its components (chairs, cabinets, door, etc.). A background that spans the entire length of a wall in the room, as well as removing all furniture at the time of the shooting, solves this problem.

### Patient Identification

All patients must be clearly identified on the picture. This information will be extremely important when retrieving the images from the photographic archive. Provided that they are small and neutral in color (white, preferably), and do not interfere with the picture, self-adhesive labels can be used. Another alternative is to write all of the patient's data on a blank sheet of paper, photographing it before the first image of the patient is taken.

### Preparation of the patient

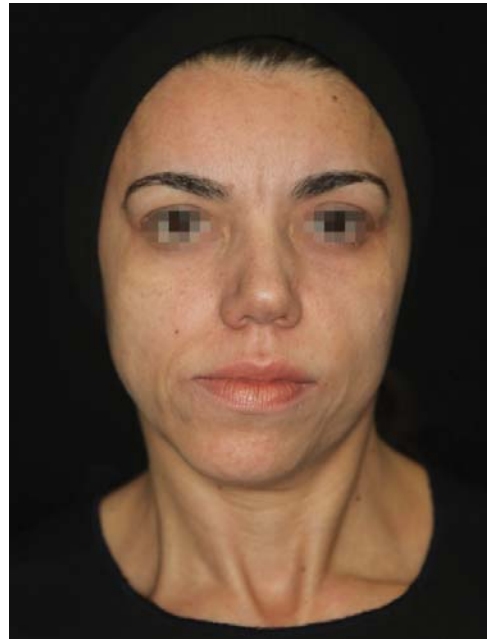
In regards to framing a shot, the more of the patient (or the body part that is being photographed) that occupies the photograph, the better its quality will be. It is important to bear



**FIGURE 2: A and B** - The framing of the photograph (a) is wrong, for the majority of the image is made up of the background. To use this image in an enlarged photograph, it will have to be cropped, a process that will entail wasting pixels or lowering the resolution



**FIGURE 3:** The clothes “pollute” the image, drawing attention away from the subject.



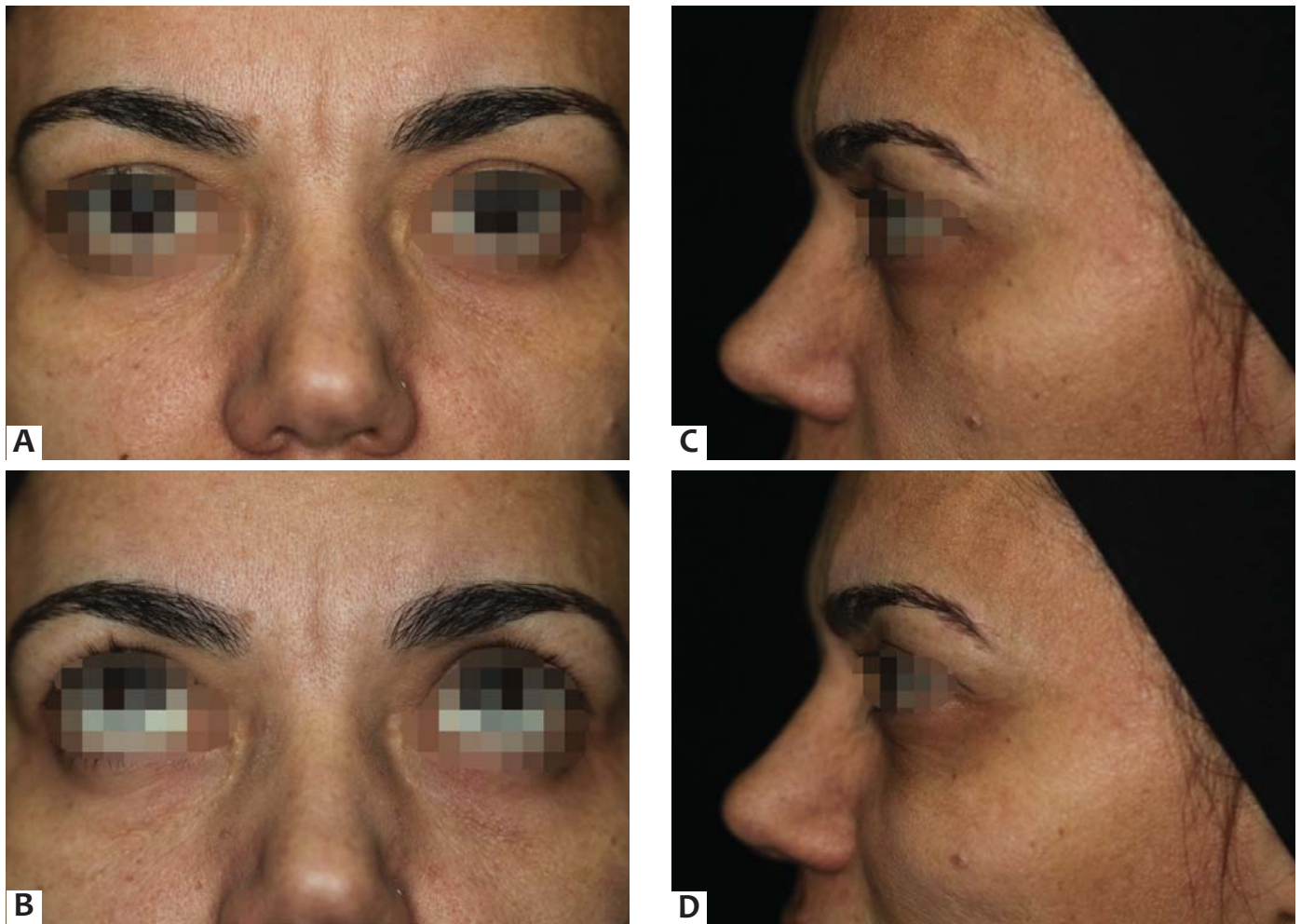
**FIGURE 4:** Patient gazing forward, neutral expression

in mind that the camera’s sensor will record the image, and the greater the amount of patient “information” recorded by the sensor, the better the quality of the photograph.

The photographer should frame the photograph in a way that the patient’s image almost completely occupies the viewfinder (up to the maximum possible without “cutting” an important part of the body out of the frame) (Figure 2). The remaining areas of the viewfinder must be occupied only by the background—and not by other objects and/or people.

The preparation of the patient comprises eliminating all elements that may distract attention from the subject, such as

accessories, makeup, and apparel.<sup>4</sup> (Figure 3) Disposable underwear can be used during the shoot and discarded afterwards, and is commercially available. Aprons must be neutral in color, as strong colors may be reflected in the patient’s skin. As for the hair, ideally bathing caps should be worn or hair tied back with bands, so that it does not appear in the image. Oil on the patient’s skin must be removed in order to avoid any reflection of light.<sup>5-11</sup> The patient should be positioned comfortably, preferably sitting with his or her back supported, whenever possible. In this way, any possible body movements resulting from a patient’s fatigue at the time of exposure are avoided. The



**FIGURE 5:** **A)** Looking straight ahead, fine wrinkles can be seen in the lower eyelids, **B)** Looking up, the wrinkles disappear, **C)** Looking straight ahead, relaxed malar and periorbital region without wrinkles, **D)** Smiling slightly, the malar region shows discrete projection due to contraction, and periorbital fine wrinkles appear (note: the patient was instructed to exert slight movements to show how subtle differences can alter the photograph)

patient's facial expression must be neutral (Figure 4), with the eyes directed forward, as any muscle movement can alter the expression, increasing or reducing wrinkles and palpebral bags, for instance (Figure 5). The head and neck must be in a natural and fixed position (it can be helpful to put a focal point on the opposite wall to help fix the gaze). Flexing and extending the neck may give misleading impressions of the absence or presence of wrinkles and sagging (Figure 6). In the case of full-body photographs, it is important to obtain at least three photographs: one of the entire body, one taken at a medium distance, and one a close-up of the lesions. The more common facial photographic technique uses a Frankfort horizontal plane as a reference<sup>4</sup> (an imaginary line running from the external auditory canal to the infraorbital rim), which is parallel to the floor, preventing the chin from being directed upward or downward (Figure 7). In this case, the face is not totally turned to the side, and is rather at a "diagonal" angle.

When the patient needs to be photographed in the supine position, as many as possible "extra" elements, such as pillows and linens, must be eliminated from the frame. In many cases, a number of shots will be needed to form the complete picture of the patient lying down.

In macro or close-up photography, some means of showing the size of a lesion, such as a ruler next to it, must be used and should always include an identifiable body part. Hands can be photographed together (horizontally) or separated (vertically), with fingers always separated. Feet and legs are more difficult to photograph due to the angle of the ankle, and as a result, the patient's feet should ideally be resting on the background of the image (on the floor), following the same recommendations for the hands, meaning they can be photographed together or apart. A superior diagonal view and a lateral view are also useful. Legs and thighs can be photographed in different positions according to the need and possible options, however they should always rest against the background, with the same



FIGURE 6: A) Neck relaxed in normal position, B) Extension, C) Flexing



FIGURE 7:  
Frankfort plane

position being adopted in subsequent photographs. Photographs of nails should contain an overview of the foot or hand, and the affected nail (Figure 8). Eyelids should be photographed open and closed, and, whenever possible, one of the photographs should be taken very close up in order to allow the measurement of the ocular opening and the distance between the border of the upper eyelid and the beginning of the eyebrow hairs' implantation. This measurement is useful in cases of photographs documenting the post-application period in botulinum toxin administration cases, in order to verify the presence—even if mild—of ptosis prior to the procedure.

The nose should be photographed frontally, laterally (silhouettes), and seen from below. The ears must be photographed in their natural position and then under traction for the visualization of the posterior portion.

The patient's position relative to the doctor is also relevant.<sup>7</sup> All photographs must respect the distance between the camera and the patient that was used in the first picture. A useful idea is to mark on the floor the original position of the physician, the patient, and the camera. Another important detail is the physician's perspective: he or she must position himself or herself with the camera in such a way that his or her eyes are level with the patient's, at an angle relative to the floor that does not leave the patient with a "flattened" appearance (photograph taken from the top down) nor "stretched" (taken from the bottom-up). In case the physician is shorter than the patient, the first must sit on a stool; if the opposite occurs (including with children), the patient can sit upon a supporting base. Babies must be lying down and photographs taken from above.

In the case of intraoperative photographs, the entire scene must be cleaned: surgical instruments, blood-soaked gauzes, very soiled gloves, and surgical fields can "pollute" the image and divert attention from the main subject (Figures 9 and 10). When possible, the surgical field can be used as the background, with the surgeon or other parts of the operating room arranged so that they do not appear in the photograph. In order to avoid contamination of the scene by getting too close to the operative field, zoom lenses are preferred. Ideally, the photographer should take all of the photographs from the same observation point.<sup>7</sup>

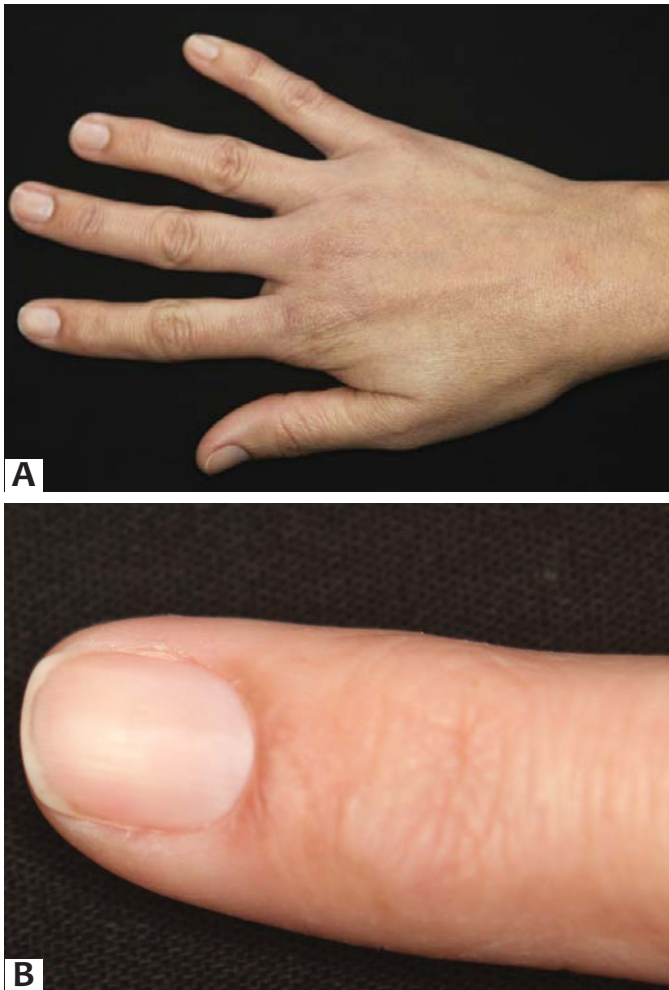


FIGURE 8: A) Overview of fingernails, B) Image of the nail.

**LIGHTING**

Ambient lighting is generally irregular, and may be natural (from a window) or artificial (such as ceiling or wall lighting, or flash). When photographing a patient under ceiling lighting, for example, the formation of well-marked shadows under the eyes, nose, and chin can be observed, lending a bizarre appearance to the patient. Flashes are used to correct ambient light. The light emitted by a flash has a very short duration (in the range of 1/1,000 to 1/50,000 of a second). All flashes come with a guide number (GN), which indicates their power: the greater the GN, the more powerful the emitted light. If the distance from the patient is doubled, the illuminated area is quadrupled and the light that reaches the patient becomes less intense—meaning that the farther the flash, the less the patient is illuminated. Flashes operate in manual, automatic (a sensor measures the light reflected from the object and controls the duration and intensity of the emitted light) or dedicated (the sensor measures the light from the flash that is entering through the lens—TTL, *through the lens*) modes.

Compact and semi-professional DSLR (digital single-lens reflex) cameras have built-in flashes, which have low power

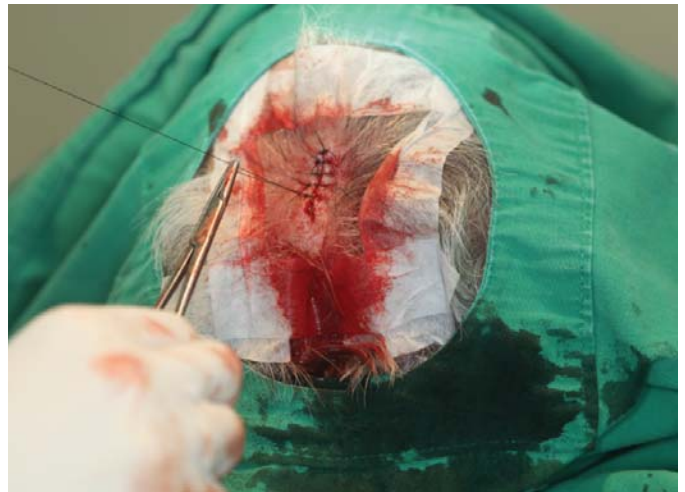


FIGURE 9: "Polluted" surgical field

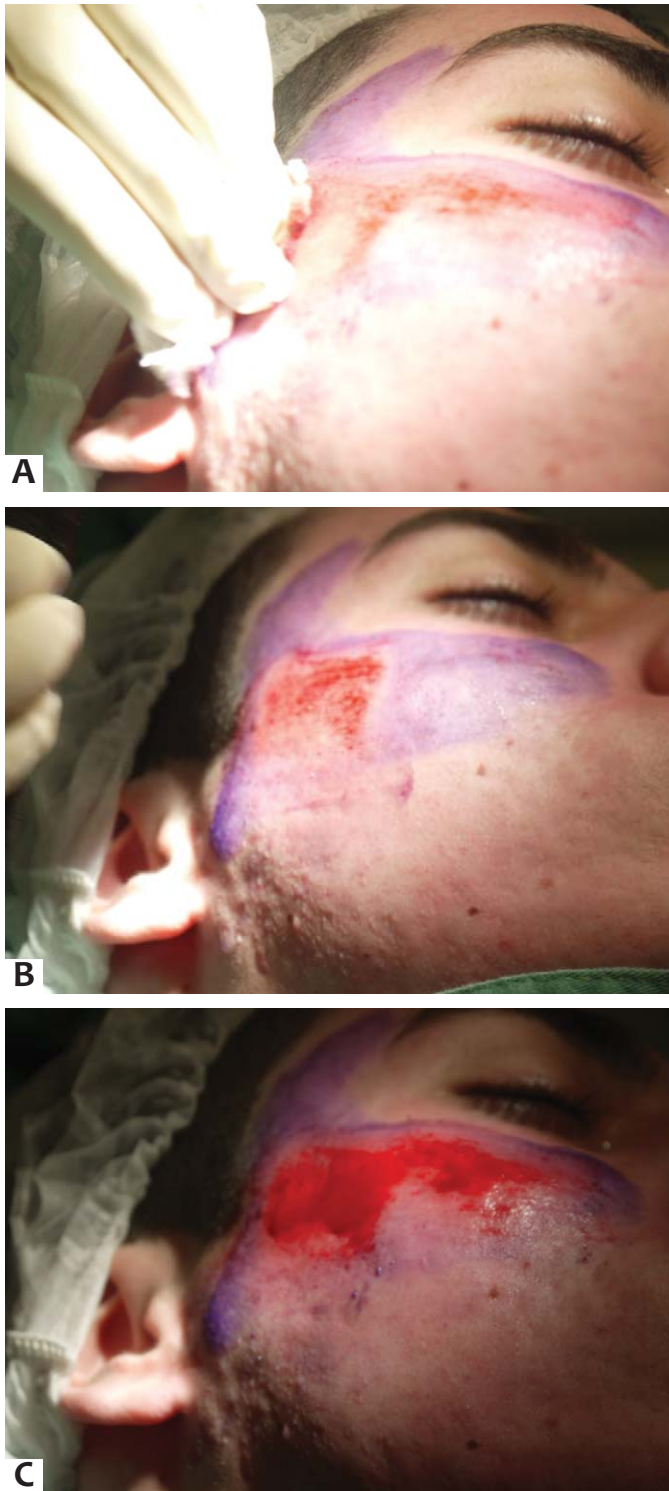


FIGURE 10: A and B - During the procedure, the field is more preserved

and are difficult control.<sup>8</sup> Some semi-professional cameras and professional DSLR cameras have fittings for external flashes that work in sync with the camera, like studio flashes.

Some details must be taken into account when using flashes:





**FIGURE 11:** A flash was not used and the operating lamp failed to illuminate the photograph correctly. The light is glaring in this photograph (a); in photograph (b); the treated area is illuminated, however the lighting is poorly distributed in the remainder of the image; in photograph (c); the entire image is underexposed, or too dark

The ISO should preferably be set at 100. If it is greater than 100, sensitivities to light will be increased. In such a case, the power of the flash must be decreased.

In environments with white walls and ceiling, the light of the flash will be reflected and bounced, making the image brighter. In order to prevent this, the aperture must be adjusted (decreased)—i.e. its number must be increased.

Here is a tip to help soften the light of a flash: place a piece of white bond paper or tracing paper over the front of the light, fixed with an elastic band or adhesive tape. Also, accessories such as diffusers and reflectors built for external flashes are available in specialty stores.

In low-light environments, the patient's pupils will be dilated, reflecting the light of the flash, and turning the eyes red. One way to avoid this red-eye effect is to ask the patient to keep his or her eyes closed, opening them only at the physician's direction, just in time for the picture to be taken.

In order to avoid excessively harsh shadows (well-defined), diffusers and reflectors can be used to redirect the light to darker areas.

The removal of skin oils is crucial to avoid the reflection of the flash on the patient's face.

During surgery, the light of the operating lamp can reflect off of metallic surgical instruments, creating a glare effect (excessive brightness in the photograph that prevents the perception of details in the lesion/surgery) (Figure 11). Turning off the operating lamp and taking the photograph with a flash enhances the image.

When using an external flash, it is important not to get too close to the patient, so that the image is not overexposed (too bright).

It is important to avoid having one side of the photographed area appear brighter than the other. This can happen when the light source is positioned only on one side of the patient.

It is always recommended that you take more than one photograph of each area, as one might come out blurry.

While there are an almost infinite number of details to consider in medical photography, with some combination of training, planning and organization, it is possible to save time and reach the ultimate goal of getting a high quality photograph.

**EQUIPMENT**

The choice of the photographic equipment is of paramount importance. Up until a few years ago, analog photography was predominant, however in recent decades there has been a revolution in the photographic market, with the emergence of digital photography. The variety of cameras that can be found today is amazing, with an availability of all sorts of equipment, from the cheapest and simplest, to the most expensive and sophisticated. Technologies continue to advance rapidly, with the development of cameras and lenses that allow increasingly better reproduction of images.



FIGURE 12: Compact Camera—dimensions: (length x depth x height): 9 x 2 x 5.5 cm. Property of the author



FIGURE 14: Micro four-thirds camera—11 x 3 x 6.5 cm. Property of the author



A



B

FIGURE 13: A) DSLR camera—14.5 x 6.5 (in the grip) x 8.5 cm; B) Macro lens, Focal Length 100mm, fixed aperture of 2.8. External flash fitted to the camera, sold separately. Property of the author

The least a dermatologist will need if he or she is to enter the world of photography is: a camera, an external flash, a memory card, a card reader, a computer with a good definition screen, good photo editing software, and a back-up system for storing images.<sup>9</sup>

The choice of the camera depends on individual needs and how much one is willing to spend. If the predominant factor is cost, a compact camera is the best choice. If image quality is more important and the budget allows, a DSLR camera is preferable: with these cameras, sensors are larger than those in compact models, and therefore the quality of images is superior. Once the camera is chosen, other items, such as the type of lenses available, the presence of a built-in flash, an optical zoom option, the ability to preview images on the LCD (liquid crystal display)—which is important, despite its high battery consumption rate—should be taken into account.<sup>10</sup>

Compact cameras have very small sensors, are cheaper and lighter, and thus are easy to carry in any situation (Figure 12). They do not allow a change of lenses, however most have optical zoom and a navigation menu with manual adjustments so they are still worth opting for. These cameras are generally subject to shutter lag, which is a delay between the instant the button (shutter release) is pressed and the moment when the photograph is shot.<sup>11</sup> In order to prevent this from happening (and missing the desired moment for the photograph), the photographer should press the shutter release half way so that the camera focuses on the subject, and only then engage the shutter release all the way. The built-in flash makes it harder to control the shooting action. The macro function of this camera type (usually the “little flower” icon) does not allow true macro photography for it distorts the borders of the image.

DSLR cameras—or simply *reflex cameras*—are more expensive and heavy bodied, however they offer advantages like the ability to change lenses, including the use of a macro lens

(Figure 13). They are faster and more complex, with more variable parameters. They also allow the connection of an external flash, which offers better lighting, due to its power being greater than that of a built-in flash. There are often accessories, such as mini-diffusers and reflectors that help to soften the light from flashes.

A new technology has arisen in recent years that combines the practicality of compact cameras with a larger sensor size (an intermediate level between the compact and the DSLR cameras): these cameras are called micro four thirds (micro 4/3) and do not have a set of mirrors (mirrorless). Moreover, they allow for the changing of lenses; offering more options and better image quality than compact cameras (Figure 14). Their price is also mid-range.

There are numerous websites on the Internet that assist consumers with useful tips and comparisons of different cameras. In any case, it is always good to bear in mind that the camera is only a tool, and that it is possible to obtain good photographs—even with simpler cameras—once the photographer masters the technique. A little creativity to solve problems that arise, and reading the camera's instruction manual can also be of help. ●

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## Questions for continuing medical education—CME

- 1) **A medical photograph:**
  - a) Is taken in the practice or hospital
  - b) Is taken by only one physician
  - c) Follows the rules of image standardization
  - d) Always obtains the patient's frontal and lateral images
  - e) Is that in which a physician is portrayed
  
- 2) **Which of the following are important factors in the standardization of an image:**
  - a) Exposure
  - b) Focal length
  - c) Position of the patient
  - d) Photographic background
  - e) Clothing of the physician
  
- 3) **Choose the correct statement:**
  - a) Ambient light can be natural or artificial
  - b) Exposure is achieved by the balance between ISO, focal length, and aperture
  - c) Each photo should have a different exposure
  - d) The background used in photographs must be of a bright color
  - e) Patients should occupy the lower left quadrant of the framework
  
- 4) **Choose the correct statement:**
  - a) Ideally, the patient must be photographed wearing neutral gowns or with clothing that does not appear in the photographs
  - b) The neck should always be flexed
  - c) In macro photographs (close-ups), there is no need to identify the body part
  - d) Hands cannot be photographed together, in order to avoid confusion
  - e) Bedridden patients cannot be photographed
  
- 5) **Select the false statement:**
  - a) There is no way to correctly photograph the nose
  - b) The position of the patient must be recorded in order to repeat it in subsequent photographs
  - c) The physician-photographer's eyes must always be at the same height as the patient's
  - d) Intraoperative photography should be performed with a zoom lens in order to avoid contamination of the field
  - e) The feet can be photographed resting against the floor, over the background
  
- 6) **Choose the true statement:**
  - a) Window lighting is always sufficient to illuminate the patient
  - b) The flash is used to correct the ambient light
  - c) When using the flash, the higher the ISO, the better
  - d) The walls of the room should not be white, in order to reflect the light
  - e) The farther away the flash, the more illuminated the person being photographed will be
  
- 7) **Choose the false statement:**
  - a) Oils on the skin should be removed in order to avoid reflecting the light
  - b) It is always recommended to take more than one photograph of each area aiming at avoiding loss
  - c) The light from the flash can be softened by putting bond or transfer paper in front of the bulb
  - d) In low-light environments, pupils dilate and reflect the light, resulting in the red-eye effect
  - e) All cameras, amateur and professional, have built-in flashes
  
- 8) **Which of the following is not part of the basic equipment necessary to take a photograph:**
  - a) Camera
  - b) Computer
  - c) Card reader
  - d) Editing software
  - e) Tripod
  
- 9) **Regarding compact cameras, choose the false statement:**
  - a) They have a built-in flash
  - b) They are smaller than DSLR cameras
  - c) They are cheaper
  - d) They allow for the changing of lenses
  - e) They have LCDs
  
- 10) **Regarding DSLR cameras, choose the false statement:**
  - a) They are heavier than compact cameras
  - b) They allow the use of an external flash
  - c) They are more complex to operate
  - d) They have smaller sensors
  - e) They produce better quality photographs

### Key:

**Photography in dermatologic surgery and cosmia-**  
**try—Part I. 2013;5(2):101-8.**

1 b 2 e 3 a 4 a 5 b 6 e 7 c 8 c 9 d 10 e

Answers must be submitted online using the website [www.surgicocosmetic.org.br](http://www.surgicocosmetic.org.br).

The deadline for submitting answers will be provided by e-mail with a direct link for accessing the journal.

# Evaluation of hyperpigmentation in melanomas and melanocytic nevi scars through confocal microscopy

*Avaliação de hiperpigmentação em cicatrizes de melanomas e nevos melanocíticos através da microscopia confocal*

## Authors:

Luciane Francisca Fernandes Botelho<sup>1</sup>  
Raquel P.R. Castro<sup>2</sup>  
Juliana Casagrande Tavoloni Braga<sup>3</sup>  
Sergio Henrique Hirata<sup>4</sup>  
João Pedreira Duprat Neto<sup>5</sup>  
Gisele Gargantini Rezze<sup>6</sup>

<sup>1</sup> MSc Dermatology Candidate at the Universidade Federal de São Paulo (UNIFESP)—São Paulo (SP), Brazil

<sup>2</sup> MSc Oncology Candidate at the Fundação Antonio Prudente (FAP)—São Paulo (SP), Brazil

<sup>3</sup> Assistant Dermatologist Physician, Department of Cutaneous Oncology, A.C. Camargo Cancer Center—São Paulo (SP), Brazil

<sup>4</sup> Associate Professor, Department of Dermatology, UNIFESP—São Paulo (SP), Brazil

<sup>5</sup> Head of the Department of Cutaneous Oncology, A.C. Camargo Cancer Center

<sup>6</sup> Assistant Dermatologist Physician, Department of Cutaneous Oncology, A.C. Camargo Cancer Center

## Correspondence:

Dr. Luciane Francisca Fernandes Botelho  
Av. Ramalho Ortigão, 269—apt. 92  
Cep: 04130-010 - São Paulo—SP, Brazil  
E-mail: lucianebotelho@hotmail.com

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## ABSTRACT

**Introduction:** In vivo confocal microscopy is an auxiliary non-invasive diagnostic method used in the diagnosis of hyperpigmented lesions in scars.

**Objectives:** To evaluate hyperpigmentation in the scars of benign and malignant melanocytic lesions through confocal microscopy examination.

**Methods:** Clinical, dermoscopic, and confocal microscopy images of fourteen patients with hyperpigmentation in adequately treated melanoma scars and in excised melanocytic nevi, were evaluated.

**Results:** Among the eight patients with hyperpigmentation in melanoma scars, four showed no suspicious structures after confocal microscopy examination and four showed suspicious structures. Among the six patients with hyperpigmentation in areas where melanocytic nevi had been excised, three had atypical structures, such as dendritic cells and non demarcated papillae. Patients with suspicious structures underwent histological examination, with one case of hyperpigmentation in a lentigo maligna scar evidencing recurrence.

**Conclusions:** The examination method allowed for the avoiding of biopsy in confirming the diagnosis in six of the fourteen patients. The finding of cells with dendritic or pagetoid pattern in the confocal microscopy examination means a diagnostic challenge, for it can indicate melanocytes or Langerhans cells in the spinous layer. Therefore, lesions that have such structures must be removed for histology and differential diagnosis.

**Keywords:** melanoma; nevus; dermoscopy; confocal microscopy.

## RESUMO

**Introdução:** A microscopia confocal in vivo é método diagnóstico não invasivo auxiliar no diagnóstico de lesões hiperpigmentadas em cicatrizes.

**Objetivos:** Avaliar através do exame de microscopia confocal a hiperpigmentação em cicatrizes de lesões melanocíticas benignas e malignas.

**Métodos:** Avaliamos imagens clínicas, dermatoscópicas e de microscopia confocal de 14 pacientes com hiperpigmentação em cicatrizes de melanomas adequadamente tratados e nevos melanocíticos excisados.

**Resultados:** Dos oito pacientes com hiperpigmentação em cicatrizes de melanomas, quatro não apresentaram estruturas suspeitas ao exame de microscopia confocal, e quatro apresentaram estruturas suspeitas. Entre os seis pacientes com hiperpigmentação em área de cicatriz de nevo melanocítico excisado, três apresentavam estruturas atípicas, como células dendríticas e papilas não demarcadas. Os pacientes com estruturas suspeitas realizaram exame histológico, e em um caso de hiperpigmentação em cicatriz de lentigo maligno foi evidenciado recidiva.

**Conclusões:** O exame permitiu evitar a biópsia para confirmação diagnóstica em seis dos 14 pacientes avaliados. O achado de células com padrão dendrítico ou pagetoide no exame de microscopia confocal é um desafio diagnóstico, pois pode representar melanócitos ou células de Langerhans na camada espinhosa. Portanto, lesões que apresentam tais estruturas devem ser removidas para exame histológico e diagnóstico diferencial.

**Palavras-chave:** melanoma; nevo; dermatoscopia; microscopia confocal.

## INTRODUÇÃO

Hyperpigmentation in scars from melanocytic lesions constitutes a diagnostic challenge for the dermatologist, as it often presents nonspecific clinical and dermoscopic features.<sup>1</sup> It can be classified clinically and histologically into the following categories: reactional cicatricial pigmentation, recurrent nevus, incompletely excised melanoma, or metastatic melanoma (locoregional cutaneous metastasis).<sup>2</sup> More recently, different technologies have been developed in order to provide additional dynamic microscopic cutaneous information, without increasing morbidity.<sup>1-10</sup> They allow both the *in vivo* diagnosis and real time assessment of disease progression.<sup>1-10</sup>

Confocal microscopy (CM) stands out as a new noninvasive diagnostic tool that allows for the acquisition of microscopic images and real-time *in vivo* visualization of cell and nuclear morphology.<sup>1-10</sup> As a result, this technique has gained prominence as a tool in the differential diagnosis of melanocytic and non-melanocytic cutaneous tumors, and can be used in cases of hyperpigmentation in scars.<sup>1,3,9,10</sup> CM correlates both with dermoscopy and histology.<sup>1,7</sup> The fact that CM evaluates the tissue in the horizontal plane (like dermoscopy) and has high magnification with cellular level definition (like histology) implies that the first technique can be used as a bridge between the two latter methods and represents an important area for clinical research.<sup>1,9,10</sup> For trained physicians, CM technology arises as a sensitive and specific tool in the early detection of melanoma and other cutaneous tumors.<sup>1,9,10</sup> When conducted methodically and using diagnostic algorithms already described in the literature, CM allows a global architectural assessment of the epidermis, dermal-epidermal junction and upper dermis, as well as cytoarchitectural evaluation.<sup>9</sup> Cellular atypia and pleomorphism, including certain nuclear morphologies, can be visualized *in vivo*, assisting in the diagnosis.<sup>1,2,9</sup>

The present study was aimed at evaluating clinical cases of hyperpigmentation scars in benign, malignant, and non-malignant melanocytic lesions, using a non-invasive CM technique.

## METHODS

A retrospective, descriptive study, conducted at A.C. Camargo Cancer Center, in São Paulo, Brazil, included 14 patients: 8 with hyperpigmentation scars resulting from melanomas that were treated properly; and 6 with hyperpigmentation scars resulting from melanocytic nevi that had been previously excised. Dermoscopic and confocal microscopy images were evaluated by two experienced dermatologists (identified in the study as G.G.R. and J.C.T.B.).

The dermoscopic images were obtained using a Sony® Cyber Shot DSC-W290 12.1 MP digital camera, coupled to a DermLite II Pro HR (DermLite®) dermatoscope using the adapter (DermLite® II/III adapters). The confocal microscopy examination was carried out with the microscope VivaScope® 1500 and 3000 (Lucid-Tech, Rochester, New York, USA), depending on the location of the lesion to be analyzed. The confocal microscope and image acquisition methods have been

described previously in the literature. 6-8 For each lesion analyzed with VivaScope® 1500, three mosaics were obtained at different skin levels (superficial epidermis, dermal-epidermal junction, and papillary dermis) based on the use of a protocol for pigmented lesions.<sup>9</sup> In lesions examined through VivaScope® 3000, individual images (0.5 x 0.5 mm) were captured in sequence (Z stacks) from the surface (stratum corneum) to deeper levels (superficial reticular dermis), in the areas of interest.

The patients who showed suspicious structures through confocal microscopy (pagetoid cells, dendritic cells, nucleated rounded cells, not clearly demarcated papillae, and atypical nests in the dermal-epidermal junction) underwent a cutaneous biopsy of the pigmented area. After surgical exeresis, the tissue was sent to pathology, undergoing the standard routine of the Pathology Department of the A.C. Camargo Cancer Center. Patients who did not show suspicious structures remained under periodic dermatologic followup.

## RESULTS

The present study evaluated 14 cases of hyperpigmentation scars in benign and malignant melanocytic lesions. Of the 8 patients with hyperpigmentation in melanoma scars, 4 had suspicious structures under confocal microscopy and underwent cutaneous biopsy with histological results of solar lentigo, junctional melanocytic nevus, actinic keratosis, and lentigo maligna (Table 1). Patients who did not show suspicious structures remained under periodic followup.

Of the 6 patients with hyperpigmentation scars in excised melanocytic nevus, 3 presented suspicious structures under confocal microscopy: intraepidermal dendritic cells and poorly demarcated papillae. These three patients underwent cutaneous biopsy, with the histology evidencing dermal fibrosis associated with exogenous pigment deposit in the superficial and deep dermis in one patient, and compound melanocytic nevus in two patients (Table 2). Despite not presenting suspicious structures in the confocal microscopy, patient number 13 requested that the recurrent nevus be excised.

Figure 1 illustrates a case of hyperpigmentation in an area where a melanocytic nevus (recurrent nevus) had been previously excised. The dermoscopic examination revealed the presence of radiated striae limiting the scar. Under confocal microscopy, the presence of great amounts of dendritic cells in the superficial epidermis could be observed. Although those suspicious structures could be visualized under confocal microscopy, the histological examination confirmed the diagnosis of compound melanocytic nevus.

Figure 2 illustrates a case of recurrent lentigo maligna in the upper lip, previously treated with adequate surgical margins. Under dermoscopy, the presence of homogeneous focal hyperpigmentation in pericicatricial area can be observed. Under confocal microscopy examination, epidermis with atypical honeycomb pattern and some dendritic cells could be observed, with the presence of nucleated rounded dendritic cells, suspicious of atypical melanocytes, in the dermal-epidermal junction.

TABLE 1: Patients with hyperpigmentation in scars resulting from melanomas treated adequately

case	gender	age	location	dermoscopy	CME*	recommendation	histology
1	Female	48	Hallux	Homogeneous hyperpigmentation	Absence of significant alterations	Observation	Not carried out
2	Male	65	Nasal dorsum	Perifollicular hyperpigmentation	Suspicious	Biopsy	Solar lentigo
3	Male	52	Anterior thorax	Homogeneous hyperpigmentation	Absence of significant alterations	Observation	Not carried out
4	Male	59	Abdomen	Atypical pigment network and homogeneous hyperpigmentation	Absence of significant alterations	Observation	Not carried out
5	Male	33	Interscapular network	Atypical Pigment network	Suspicious	Biopsy junctional	Junctional melanocytic nevus
6	Male	34	Interscapular	Typical peripheral pigment network	Absence of significant alterations	Observation	Not carried out
7	Female	63	Left malar	Perifollicular brown granules	Suspicious	Biopsy	Actinic keratosis
8	Female	61	Left Supralabial	Homogeneous hyperpigmentation	Suspicious	Biopsy	Lentigo maligna

\*CME: Confocal microscopy examination

TABLE 2: Patients with hyperpigmentation in scars resulting from melanomas treated adequately

case	gender	age	location	dermoscopy	CME*	recommendation	histology
9	Female	53	Right leg	Homogeneous blue pigmentation	Suspicious	Biopsy	Dermal fibrosis associated with exogenous pigment deposit in the dermis
10	Female	42	Left leg	Radiated striae in the scar's limits	Suspicious	Biopsy	Compound melanocytic nevus
11	Female	30	Dorsum	Brown globules and pigment network located focally	Absence of significant alterations	Observation	Not carried out
12	Male	35	Abdomen	Atypical pigmentary network	Absence of significant alterations	Observation	Não realizado
13	Female	54	Right leg	Atypical pigment network and asymmetric dots	Absence of significant alterations	Biopsy	Residual congenital compound melanocytic nevus
14	Female	60	Right arm	Atypical pigment network and linear striae	Suspicious	Biopsy	Compound melanocytic nevus

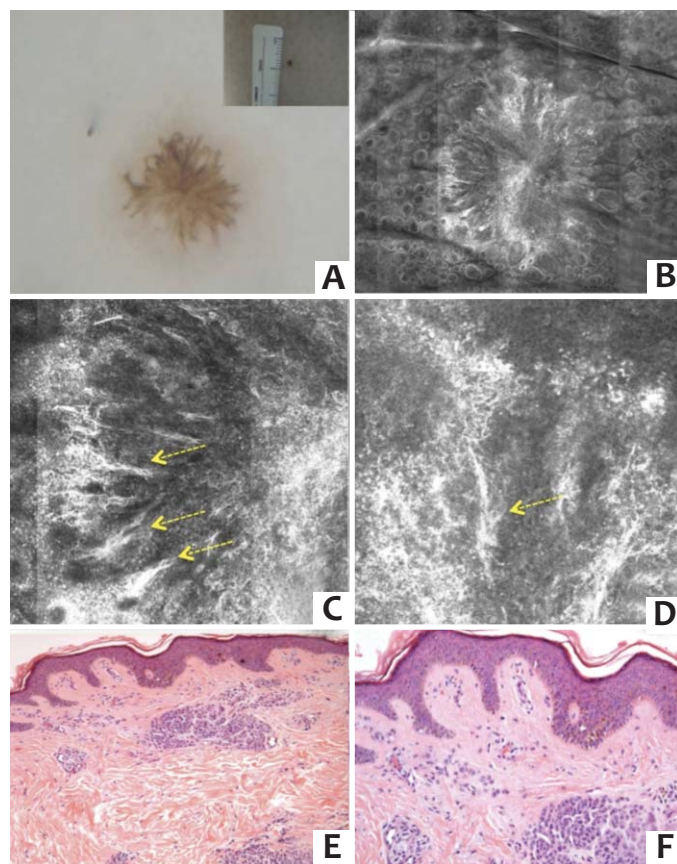
\*CME: Confocal microscopy examination.

tion. The histological examination confirmed the diagnosis of recurrent lentigo maligna.

**DISCUSSION AND CONCLUSION**

Pigmentation in scars of melanocytic lesions can be secondary to reactive phenomena linked to the healing process or can result from a recurrence of an excised melanocytic lesion.<sup>1,2</sup> Recurrent nevi are benign, however they can present morphological characteristics that simulate melanoma.<sup>1,2</sup> The appearance of pigmentation in melanoma scars is not uncommon and may raise doubts about the persistence of the tumor.<sup>1,2</sup> CM is a noninvasive and reliable method that can assist in that differentiation.<sup>2,4</sup>

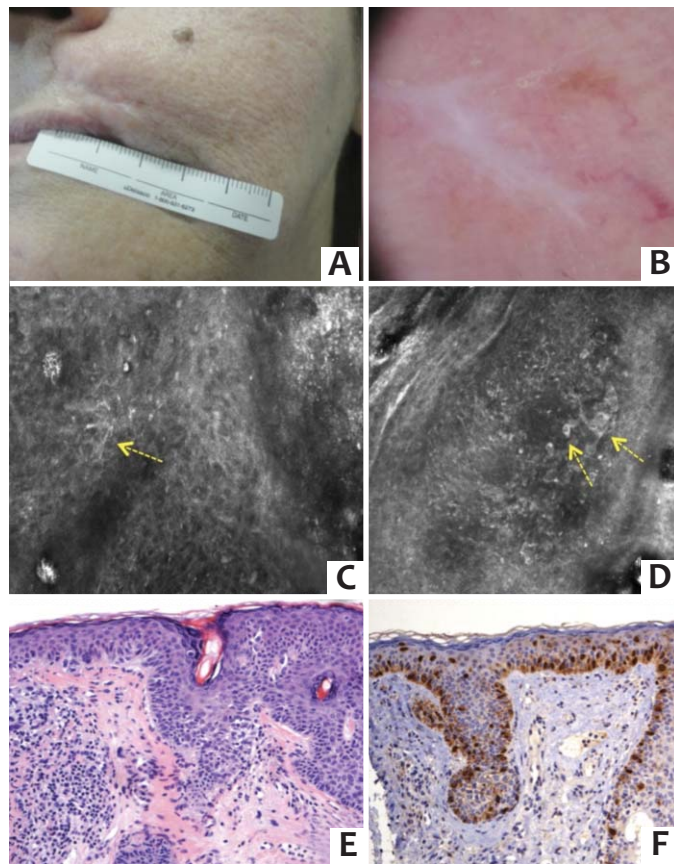
Intraepidermal Langerhans cells are visualized in CM examination as dendritic cells, with long and thin dendrites.



**FIGURE 1:** **A** (photograph of case 10): clinical photograph of hyperpigmentation in area of previously excised melanocytic nevus in the left leg and dermoscopic photograph with the presence of radiated striae in scar area; **B** (confocal microscopy, 2.5 x 2.5 mm mosaic): image of the entire lesion with heterogeneous brightness and dendritic cells arranged in a radial pattern; **C** and **D** (confocal microscopy, individual images 1 x 1mm and 0.5x 0.5 mm, respectively): intraepidermal dendritic cells in large amounts (yellow arrows); **E** (anatomopathology stained with hematoxylin-eosin 100X): presence of nests of nevus cells in the dermis; **F** (anatomopathology stained with hematoxylin-eosin 200X): proliferation of nevus cells in the dermal-epidermal junction and in the dermis (compound melanocytic nevus).

These cells are often difficult to differentiate from atypical melanocytes present in the suspicious melanocytic lesions, which are also visualized as dendritic cells or rounded and nucleated with pagetoid dissemination in the epidermis.<sup>5</sup> Therefore, the presence of those dendritic cells in scars of melanocytic lesions may indicate a reactional inflammatory phenomenon or proliferation of atypical melanocytes.<sup>1,2</sup> The cells of the recurrent nevus viewed through confocal microscopy examination (as illustrated in Figure 1) are probably intraepidermal Langerhans cells secondary to the healing process. One opportunity to document the presence of these cells in future studies would be through the use of immunohistochemistry with the marker CD1a, the main marker for Langerhans cells.

One criterion that can assist in the diagnosis of recurrence of melanocytic lesions in scar is the fact that dendritic cells (in cases of recurrent nevi) do not extend beyond the scar—



**FIGURE 2:** **A** (clinical photograph of case 8): hyperpigmentation in area of lentigo maligna previously excised in the left hand side of the upper lip; **B** (dermoscopic photograph): homogeneous focal hyperpigmentation in cicatricial area; **C** (confocal microscopy, individual 0.5 x 0.5 mm image): epidermis with atypical honeycomb pattern and some dendritic cells (yellow arrow); **D** (confocal microscopy, individual 0.5 x 0.5 mm image): presence of dendritic, and nucleated rounded cells in the dermal-epidermal junction, suspicious of atypical melanocytes (yellow arrows); **E** (anatomopathological examination stained with hematoxylin-eosin): in situ residual lentiginous type melanoma, presence of atypical melanocytes in the epidermis; **F** (MITF—Microphthalmia Transcription Factor based immunohistochemistry—nuclear marker for melanocytes): marker is frankly positive in the epidermis.



unlike with cases of recurrent melanoma. In figure 2, a CM examination of the pericatricial area of hyperpigmentation evidenced intraepidermal pagetoid cells and nucleated rounded dendritic cells in the dermal-epidermal junction that extended beyond the scar, suggesting the diagnosis of lentigo maligna, which was confirmed by the anatomopathologic examination.

Other authors who assessed hyperpigmentation areas in scars from melanocytic lesions, carried out cutaneous biopsies in all cases examined—even when the confocal microscopy findings did not evidence suspicious structures.<sup>1</sup> In contrast, in the present study, only the lesions with intraepidermal dendritic cells were removed, for as discussed above, the presence of those cells may suggest both atypical melanocytes and Langerhans cells. The CM avoided the need for cutaneous biopsies in 6 of the 14 patients evaluated, who remain under periodic dermatologic follow up. The limitation of the present study was linked to the small number of patients included in the sample.

CM is a useful auxiliary tool in the evaluation of hyperpigmentation in scars resulting from melanomas and melanocytic nevi, avoiding unnecessary excision of benign lesions and providing a good degree of safety to the dermatologist in the follow-up of those cases. ●

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# Mohs micrographic surgery: a study of 93 tumors operated on in a specialist center in Rio de Janeiro

*Cirurgia micrográfica de Mohs: estudo de 93 tumores operados em um centro de referência no Rio de Janeiro*

## Authors:

Frederico H. Sanchez<sup>1</sup>  
Juliany Lima Estefan<sup>2</sup>  
Lidiany Lima Estefan<sup>3</sup>

<sup>1</sup> Head of the Center for Micrographic Surgery of Rio de Janeiro, Policlínica Ronaldo Gazolla—Rio de Janeiro (RJ); Preceptor at the Dermatologic Surgery Fellow Program, Hospital Federal Bonsucesso—Rio de Janeiro (RJ), Brazil

<sup>2</sup> Dermatologist Physician, MSc in Clinical Medicine from the Universidade Federal do Rio de Janeiro (UFRJ)—Rio de Janeiro (RJ), Brazil

<sup>3</sup> Collaborating Physician at the Center for Micrographic Surgery of Rio de Janeiro, Policlínica Ronaldo Gazolla

## Correspondence:

Centro de Cirurgia Micrográfica do Rio de Janeiro  
Dr. Frederico H. Sanchez  
Rua da Assembléia 10 / sala 2807—Centro  
Cep: 20011-000—Rio de Janeiro—RJ, Brazil  
E-mail: fredhsanchez@gmail.com

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## ABSTRACT

**Introduction:** Mohs micrographic surgery is a treatment option that increases the cure rate in various types of skin cancer, offering greater tissue preservation and lower recurrence rates.

**Objective:** To describe clinically and histologically the tumors operated on with Mohs micrographic surgery, and to draw correlations to the number of stages and the type of surgical reconstruction performed. The operations were performed at a private clinic in the municipality of Rio de Janeiro, Brazil that is a specialist center for this technique.

**Methods:** Retrospective, observational, cross-sectional/transversal study was carried out based on the review of medical records.

**Results:** A study was conducted of 93 tumors in 84 patients, operated on between April 2010 and August 2012, and followed up with until August 2013 (12 to 42 months). Findings: 47.61% of patients were men and 52.38% were women, the mean age was 62.89 years; predominant phototypes: II (44%) and III (43%); 6 cases (6.45%) of squamous cell carcinoma, 87 (93.54%) of basal cell carcinoma; 74.19% were primary tumors; the nose was the most frequent site (46.24%); a single surgical stage was performed in most cases, with flaps (44%) being the more frequently performed type of closure. There was recurrence in one patient, who required reoperation in October 2012 and followed without new recurrence.

**Conclusions:** Mohs surgery has proven effective with high cure rates and a minimal recurrence rate, especially in lesions located in the face's H area of risk.

**Keywords:** Mohs surgery; carcinoma, basal cell; carcinoma, squamous cell.

## RESUMO

**Introdução:** A cirurgia micrográfica de Mohs é opção terapêutica que aumenta a taxa de cura de vários tipos de câncer de pele, com maior preservação tecidual e menores taxas de recidiva.

**Objetivo:** Traçar o perfil clínico e histológico dos tumores operados pela cirurgia micrográfica de Mohs, em serviço privado de referência nessa técnica no município do Rio de Janeiro, Brasil, e relacioná-lo com o número de fases e tipo de reconstrução cirúrgica realizada.

**Métodos:** Estudo retrospectivo, observacional, transversal, com revisão de prontuários.

**Resultados:** Foram relacionados 93 tumores em 84 pacientes operados no período entre abril/2010 e agosto/2012 e seguidos até agosto/2013 (12 a 42 meses). Dados encontrados: 47,61% homens e 52,38% mulheres; idade média de 62,89 anos; fototipos predominantes II (44%) e III (43%); seis casos (6,45%) de carcinoma espinocelular; 87 (93,54%) de carcinoma basocelular; 74,19% de tumores primários; nariz como localização mais frequente (46,24%); uma fase cirúrgica realizada na maioria dos casos, tendo sido o retalho (44%) o tipo de fechamento mais realizado. Houve recidiva em um paciente, que foi reoperado em outubro/2012 e segue sem recidiva.

**Conclusões:** A cirurgia de Mohs mostrou-se eficaz, com altos índices de cura e mínima taxa de recidiva, especialmente nas lesões da área de risco do H da face.

**Palavras-chave:** cirurgia micrográfica de Mohs; carcinoma basocelular; carcinoma espinocelular.

**INTRODUCTION**

Mohs micrographic surgery (MMS) is a therapeutic option for the treatment of various malignant neoplasms of the skin because it presents the highest cure rates combined with the lowest recurrence rates. It has the additional advantage of preserving the healthy tissue around the tumor, thus leading to less cosmetic and functional damage.<sup>1,2</sup> MMS is the gold standard for the treatment of recurrent basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), primary tumors of aggressive histologic subtypes, tumors in embryonic clefts areas or in areas of difficult surgical reconstruction.<sup>1-3</sup>

With the micrographic technique, the tumor is removed with minimal surgical margins through a topographical mapping of the sample relative to its location on the patient. The sample is then prepared in a way that allows the histological analysis of all surgical margins (lateral and deep) in the same plane. The surgical specimen undergoes stages of tissue inclusion, freezing and preparation of histological sections, which are then stained and analyzed with a microscope. When the histological slide evidences permanence of the tumor, a new Mohs phase is required. The surgeon then, through the surgical mapping of the lesion, selectively widens the compromised surgical margin. According to some authors,<sup>1,2,4</sup> while with the traditional freezing techniques (standardized by pathologists using the *bread loaf* or cut in cross techniques) the analysis covers only about 0.01% of the margins, the Mohs method allows the visualization of 100% of the surgical margins.

Although the Mohs micrographic technique was introduced in Brazil over 20 years ago and is the treatment of choice for many patients with aggressive or recurrent cutaneous tumors, it is still not widely used in the country, with only two articles found in the national literature about the use of this method in actual cases: Cernea<sup>4</sup> (1994, São Paulo, SP, Brazil) and Chagas and Silva<sup>1</sup> (2012, Aracaju, SE, Brazil). No articles discussing the Mohs technique in patients originating from the Brazilian state of Rio de Janeiro were found in the authors' literature search.

The purpose of the present article is to evaluate the clinical and histological profile of tumors operated through the Mohs micrographic method at a private MMS reference center in the municipality of Rio de Janeiro, studying its correlation to the number of phases and type of surgical reconstruction performed.

**METHODS**

Ninety-three tumors were evaluated in 84 patients treated with the Mohs micrographic method in the Centro de Cirurgia Micrográfica do Rio de Janeiro (Center for Micrographic Surgery of Rio de Janeiro), from April 2010 to August 2012. A retrospective, observational, cross-sectional, descriptive study was carried out, with the data being collected through the analysis of the medical records and preoperative, intraoperative and postoperative photographs of 84 patients.

An operative record containing key patient data, that is part of the service protocol, served as the database for the study

Mohs micrographic surgery			
<b>PATIENT</b>		NUMBER DATE	
AGE			
GENDER	F M		
<b>PHOTOTYPE</b>			
PREOPERATIVE DIAGNOSIS			
PRESENCE OF OTHER CUTANEOUS TUMORS	YES NO		SPECIFY
ALLERGY TO MEDICATIONS	YES NO		SPECIFY
<b>COMORBIDITIES</b>			
USE OF REGULAR MEDICATIONS			
OBS.			
<b>TUMOR</b>			
TUMOR	PRIMARY RECURRENT		
PALPABLE LYMPH NODES	YES NO		
LOCATION			
SIZE			
BIOPSY DIAGNOSIS			
DEFINITIVE DIAGNOSIS			
OBS.			
<b>SURGERY</b>			
ANESTHESIA	TUMESCENT LOCAL LOCAL GENERAL		
OBS.			
SEDATION	YES NO		
OBS.			
STAINING	HE TOLUIDINE BLUE OTHER		
OBS.			
PREVIOUS CURETTAGE	YES NO		
DEBULK	YES NO		
OBS.			
FINAL SURGICAL DEFECT SIZE			
MOHS SURGICAL TIMES			
OBS.			
NUMBER OF PIECES 1ST STAGE			
NUMBER OF PIECES 2ND STAGE			
NUMBER OF PIECES 3RD STAGE			
NUMBER OF PIECES 4TH STAGE			
OTHER STAGES			
RESOLUTION OF THE SURGICAL DEFECT			
SECOND INTENTION			
PRIMARY CLOSURE			
GRAFT			
FLAP			
OBS.			
<b>SURGICAL TEAM</b>			
1ST SURGEON			
2ND SURGEON			
HISTOLOGY TECHNICIAN			
ANESTHETIST			
PATHOLOGIST			

FIGURE 1: Surgical record containing data for statistical analysis

(Figure 1). The record form presented the following variables: date of surgery, patient age, gender, phototype, location of the tumor, histological type of tumor in the previous biopsy, histological type of the tumor assessed during surgery, classification in primary or recurrent tumor, number stages of Mohs surgery, type of surgical reconstruction, presence of lymph nodes, use of medication, comorbidities, dimensions of the tumor and of the resulting surgical defect after removal.

All patients signed a term of free and informed consent and a permission allowing the inclusion of personal data in the study, with guarantee of confidentiality.

All operated patients had previous biopsies, with tumors being classified according to histological type. The histological subtype was classified according to the previous biopsy or, where it was possible to detect the tumor remnant in the evaluated margins, according to the histological analysis carried out during the surgery. In case of inconsistency between histologic subtypes observed in the biopsy reports and in the blades analyzed during the surgery, the latter was chosen for assessment. Some tumors presented mixed characteristics, with more than one histological subtype in the same sample. In such cases, the

most aggressive subtype was deemed the main tumor.

The tumors were further divided into categories of primary, recurrent, or incompletely excised—the latter being those with compromised surgical margins according to the histopathology carried out after conventional surgery, being then referred to Mohs micrographic surgery for the widening of margins.

The authors classified the location of tumors as follows: trunk, upper limbs, nose, malar area, nasogenian sulcus, periauricular, periocular, scalp, temporal and forehead regions.

Regarding the type of surgical closure, the authors considered: primary closure, healing by secondary intention, flaps, simple grafts, and composite grafts.

**RESULTS**

Ninety-three tumors were analyzed in 84 patients—40 men (47.61%) and 44 women (52.38%), mean age of 62.89 years (SD ± 14.57), and median age of 65 years (minimum = 35 and maximum = 89 years).

The predominant Fitzpatrick skin phototypes in the study were II (44%) and III (43%). Phototypes I and IV were also observed in 11% and 2% of cases, respectively (Graph 1).

Regarding the histologic types, the study observed 6 (6.45%) SCC cases and 87 (93.54%) BCC cases, the latter being subdivided into 36 nodular BCC (one over a sebaceous nevus), 11 micronodular BCCs, 11 infiltrating BCCs, 10 superficial BCCs, 8 sclerodermiform BCCs, 4 metatypical BCCs, 2 adenoid BCCs, and in five cases the subtype has not been evaluated. (Table 1)

Of the 93 tumors operated through MMS, 69 (74.19%) were primary and 18 (19.35%) recurrent. In 6 cases (6.45%) there were no clinical recurrences of the lesions, nevertheless these cases were referred for expansion of surgical margins, due to the histopathologic diagnosis of BCC with compromised surgical margins after being operated with conventional techniques (Graph 2). Of these, in 5 cases (5.37%) it was not possible to identify the histological subtype, for the tumor was not observed during MMS, with previous reports showing no specification of the histological subtype. It was assumed that a tumor was not identified during Mohs surgery given that it is a peripheral technique, and surgical margins free of neoplasia were obtained in the initial stage of MMS.

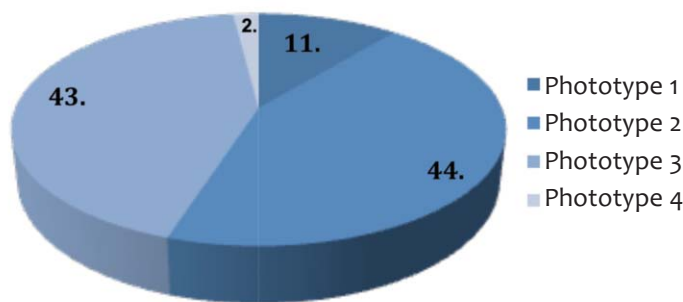
Histologic types	N	%
Nodular BCC	36	38.70
Micronodular BCC	11	11.82
CBC infiltrante	11	11.82
Infiltrating BCC	10	10.75
Superficial BCC	8	8.60
Sclerodermiform BCC	5	5.37
Not evaluated BCC subtype	4	4.30
Metatypical BCC	2	2.15
Adenoid BCC	6	6.45
<b>TOTAL</b>	<b>93</b>	<b>100</b>

Regarding the location of tumors, the majority (43/93, 46.24%) were located in the nose. Other locations were: 9 (9.68%) in the malar region, 9 (9.68%) in the periocular region, 8 (8.60%) in the frontal region, 7 (7.53%) in the temporal region, 7 (7.53%) in the periauricular region, 3(3.23%) in the scalp, 2 (2.15%) in the nasolabial folds, 2 (2.15%) in the upper limbs, 2 (2.15%) in the anterior thorax and 1 (1.08%) in the lip (Table 2).

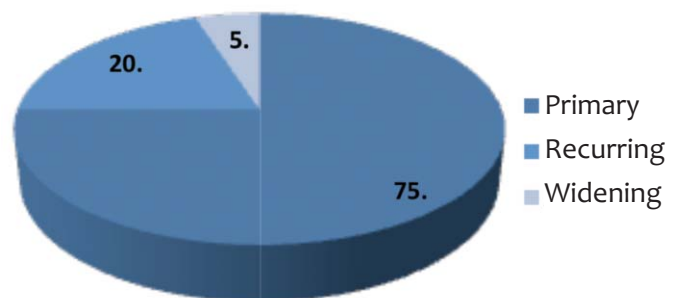
Regarding the number of stages of the MMS, only one was observed in the majority (46/93, 49.46%) of cases. Two stages were observed in 25 (26.88%) cases, 3 in 17 (18.27%) cases, 4 in 2(2.15%) cases, 5 in 2 (2.15%) cases and 6 in 1(1.07%) case.

Of the examined cases, surgical margins free of neoplasia were not obtained in 2 patients. One of those patients had a BCC in the nasal wing area that recurred four times on the prior cutaneous flap, with an infiltrative pattern, that invaded the nasal septum and bone up until the right choana. The other patient had a poorly differentiated SCC in the pre-auricular region. Extensive invasion of the parotid gland was verified during the Mohs surgery. These patients were referred to the head and neck surgery and oncology services for radical surgery and radiotherapy.

To date (August 2013), the postoperative follow-up of these patients ranged from 12 to 42 months. In 47 (50.53%) patients, the follow-up period was of one to two years, and in 46 (49.46%), it was more than two years.



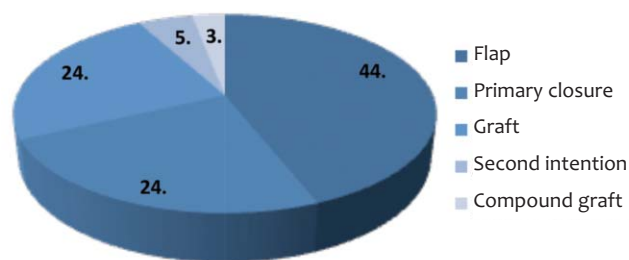
GRAPH 1: Prevalence of phototypes in operated patients



GRAPH 2: Profiles of studied tumors

TABLE 2: Types of tumors found in the 84 patients in the study

Histologic types	N.	%
Nose	43	46.24
Malar region	9	9.68
Periocular region	9	9.68
Forehead region	8	8.60
Temporal region	7	7.53
Preauricular region	7	7.53
Scalp	3	3.23
Nasogenian fold	2	2.15
Upper limbs	2	2.15
Anterior thorax	2	2.15
Lip	1	1.08
<b>TOTAL</b>	<b>93</b>	<b>100.00</b>



GRAPH 3: Types of surgical reconstruction carried out

Recurrence was observed in only one patient during this period, 16 months after the first Mohs micrographic surgery was performed. It was a predominantly micronodular BCC case in the ear pinna that had recurred several times after cryosurgery and conventional surgery. The patient was re-operated using the Mohs method in October 2012 and to date has had no recurrence.

Regarding the surgical closure, 41 flaps, 22 simple grafts, 22 primary closures, and 3 compound grafts were performed. Five surgical defects were left to heal by secondary intention (Figure 3).

**DISCUSSION**

The mean age of patients was 62.89 years (SD±14.57), with a predominance of Fitzpatrick’s skin phototypes II and III—findings that coincide with data found in the literature.

The literature describes male patients as the most affected by skin neoplasia.<sup>5,6</sup> In the present study there was a predominance of female patients, with 52.38% (44/84) of cases, while male patients accounted for 47.61% (40/84) of cases. This difference was not significant and can be justified by the small size of the sample and by the fact that it focused only on cases referred for Mohs surgery.

Regarding the histological type, SCCs accounted for 6.45% and BCCs accounted for 93.54%, with the nodular subtype being found in 38.7% of cases. This finding was consistent with the literature, which describes BCC as the most frequent malignant neoplasm.<sup>3,5</sup> Considering that the most aggressive histologic subtypes of BCC are the sclerodermiform, the infiltrative micronodular, and the metatypical, the present study included a large number of aggressive tumors (36.54%).

Of the 93 tumors studied, 74.19% were of the primary type and 19.35% were recurrent. This profile differs from the trend described by the Brazilian articles found in the authors’ research. Chagas and Silva (2012)<sup>1</sup> reported 62.7% recurrent tumors, and Cernea (1994)<sup>4</sup> showed 56.1% recurrent tumors operated on using the Mohs technique. This misalignment may be due to socio-economic and regional factors, considering that this study was carried out in a private practice in the city of Rio de Janeiro, which may explain the fact that most of the operated tumors were primary. The smaller number of recurrent tumors in the present study is reflected in the number of stages required to achieve free surgical margins,<sup>2,7</sup> even though as many as 50.54% of the analyzed tumors have required two or more stages.

Regarding the recurrence, although the follow-up time was still limited at the time the present article was written (12-42 months), recovery rates obtained were high, and when compared to those reported in the international literature corroborate the efficiency of the method in selected cases. Only one case of recurrence was detected, in an aggressive histological subtype tumor that had already recurred several times. Studies conducted with fewer than five years of followup demonstrated that recurring BCC lesions, when treated with traditional surgical techniques, achieved cure rates of roughly 82% after excision, while MMS increased that rate to 94.4%.<sup>7</sup>

The most common locations of the tumors analyzed in the present study were: nose, malar, and periocular regions, coinciding with the “H zone of the face” area of risk, known by the presence of embryonic clefts that result in lower resistance to tumor infiltration, providing greater subclinical extension of lesions.<sup>8,9</sup> There is a formal indication of MMS in those cases, for it allows precise histological control, achieving high cure rates with low tumor recurrence rates.<sup>10</sup>

**CONCLUSION**

The present study has some limitations, such as the relatively small size of the sample and the limited follow-up time with the patients (1 to 3.5 years). This is justified by the facts that the MMS technique is still not widespread in Brazil and that the study has been conducted at a relatively new private practice (operations commenced in February 2010).

Despite the limitations, the Mohs surgical technique has proven its efficacy by achieving high cure rates with minimal recurrence rates. It was especially helpful in lesions located in the “H zone of the face” risk area—the majority in the present study—and in tumors of the aggressive histological subtype.

The authors suggest that further papers should be written describing studies with larger sample sizes and longer followup times, since there are few Brazilian articles on the subject. ●

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## Article Original

# Increase in the minimum erythema dose level based on the intake of a vitamin supplement containing antioxidants

*Aumento da dose eritematosa mínima a partir da ingestão de um suplemento vitamínico contendo antioxidantes*

### Authors:

Flávia Alvim Sant'Anna Addor<sup>1</sup>  
Patrícia Camarano<sup>2</sup>  
Christiane Agelune<sup>3</sup>

<sup>1</sup> Dermatologist Physician, Technical Director, Medcin Instituto da Pele—Osasco (SP), Brazil

<sup>2</sup> Clinical Research Manager, Medcin Instituto da Pele

<sup>3</sup> Photoprotection Research Manager, Medcin Instituto da Pele

### Correspondence:

Dr. Flávia Alvim Sant'Anna Addor  
Rua Dr. Carlos de Moraes Barros, 304  
Cep: 06544-540—Santana de Parnaíba—  
SP, Brazil  
E-mail: flavia@medcinonline.com.br

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### ABSTRACT

**Introduction:** UV light-induced photodamage is an acute precipitator of solar erythema, which is the phenomenon measured to assess the protection against the sun provided by a particular product.

**Objective:** To investigate the ability of a dietary supplement containing antioxidants (carotenoids, trace elements/oligoelements, flaxseed oil, and vitamins E and C) to prevent photodamage, using as a parameter the minimum erythema dose level.

**Method:** The minimum erythema dose level of 28 volunteers (Fitzpatrick skin types 2 and 3) was measured with a solar simulator, before and after 30 and 60 days of supplement use.

**Results:** The daily use of the supplement was well tolerated. There was a significant increase in the minimum erythema dose level in the group evaluated ( $p = 0.017$ ).

**Conclusion:** The studied combination of antioxidants was demonstrated to increase the minimum erythema dose level with statistical significance, suggesting the presence of photoprotective activity.

**Keywords:** ultraviolet rays; antioxidants; carotenoids.

### RESUMO

**Introdução:** O fotodano induzido pela luz ultravioleta leva agudamente a eritema solar, que é o fenômeno medido para avaliar a proteção solar de um determinado produto.

**Objetivo:** Investigar a capacidade de um suplemento alimentar contendo antioxidantes (carotenoides, oligoelementos, óleo de linhaça e vitaminas E e C) para prevenir fotodano, usando como parâmetro a dose eritematosa mínima.

**Método:** Foi determinada a dose eritematosa mínima de 28 voluntários de fototipos 2 e 3 de Fitzpatrick, com um simulador solar, antes e após 30 e 60 dias do uso do suplemento.

**Resultados:** O uso diário do suplemento foi bem tolerado. Houve aumento significativo da dose eritematosa mínima no grupo avaliado ( $p = 0,017$ ).

**Conclusão:** A associação de antioxidantes estudada exibiu aumento estatisticamente significativo da dose eritematosa mínima, sugerindo a atividade fotoprotetora.

**Palavras-chave:** raios ultravioleta; antioxidantes; carotenoides.

## INTRODUCTION

Exposure to the ultraviolet range of solar radiation induces erythema and pigmentation that vary according to skin phototype.<sup>1</sup>

Solar-induced erythema occurs mainly in fair-skinned individuals, beginning two to four hours after sun exposure and reaching its greatest intensity after roughly 24 hours. It results from vasodilation and subsequent migration of polymorphonuclear leukocytes, characterizing an acute inflammatory reaction. Ultraviolet B radiation is the main determinant of the occurrence of erythema.<sup>2</sup>

Some standardized resources are used in the literature for quantifying individual susceptibility to erythema. The minimal erythema dose (MED) is defined as the lowest effective erythemogenic energy amount (i.e. sufficient to produce the first perceptible erythema reaction with defined borders). In order to determine the MED, the individual must be exposed to increasing doses of ultraviolet radiation generated by a device called Solar Simulator, which has a radiation spectrum similar to that of the sun. The reading of the erythema is carried out 24 hours after the exposure, with the MED being subsequently determined.<sup>3</sup>

The higher the MED, the greater the individual's resistance to the production of erythema.

The determination of the Individual Typological Angle—ITA—an index that relates to skin color, is calculated using measurements obtained from a colorimeter.<sup>4</sup>

The prevention of erythema is desired by individuals with acute sun exposure, given its obvious discomfort. In addition to topical sunscreens, certain oral agents may have photoprotective action, increasing the MED through antioxidant or anti-inflammatory mechanisms, since the pigmentation results from the melanin photooxidative process.

The association of nutrients with antioxidant and anti-inflammatory action can be beneficial in preventing erythema.<sup>5</sup> One way to evaluate the effect is by determining the MED 6 before and after the use of the supplement.

The present study was aimed at evaluating the efficacy of a vitamin supplement in reducing erythema, by increasing the MED, which was measured before and after use.

## METHODS

A prospective, controlled, blind, non-comparative study was carried out between April and July 2013, at a private clinical research laboratory, in the city of Osasco, in the Brazilian state of São Paulo.

The study population consisted of 33 adult female patients between 18 and 60 years old, with Fitzpatrick skin phototypes II and III. Patients using immunosuppressive or anti-inflammatory drugs, individuals with photodermatosis history, and pregnant and lactating women were excluded.

After signing the term of free and informed consent, all participating volunteers were evaluated clinically and had their inclusion and exclusion criteria checked. Subsequently, colorimetry measurements were taken with the colorimeter (Konica Minolta CR400, UK) on each patient's dorsum, the area chosen

for testing the ITA and then the Ultraviolet B radiation. In this manner, the patient's dorsal area was divided into six sites, with each being irradiated with progressive doses emitted by a solar simulator. The doses were predetermined using a UVB irradiation detector, with each dose being 12% higher than the previous one, following a geometric progression. This irradiation progression is the same as that recommended in the methodology for determining the sun protection factor.<sup>7</sup>

The solar simulator (Solar Light,<sup>®</sup> Solar Light Co, Glenside, PA, USA) is a device capable of emitting light in the range of the solar spectrum, and is a reference in studies aimed at determining sun protection factor (SPF) and other studies in photobiology, complying with the European and North American technical requirements regarding photoprotection directives.

The median dose (4<sup>th</sup> subsite exposure) corresponds to the MED, being thus defined based on the value obtained through the calculating of the ITA. The remaining doses were determined through the geometric progression, as shown below (Table 1).

After the exposure, the volunteer was observed for 15 minutes for possible immediate reactions to ultraviolet radiation, such as tanning, reflex erythema, and vesicular eruptions. After the 15-minute observation, patients were discharged and instructed to come back after 24 hours for an assessment of the test area.

After the assessment, 24 hours later, when the MED was determined through the analysis of the erythema using standardized lighting intensity, the volunteers received a sample of the vitamin supplement and were instructed to ingest one capsule per day.

Table 2 shows the content composition of each capsule.

The supplement was ingested in this dose for eight weeks. New measurements of the MED following the same standards were carried out after four and eight weeks, when the study ended.

TABLE 1: Progression of doses for the assessment of the Minimum Erythema Dose-MED.

1 <sup>st</sup> subsite exposure:	1 x MED	- 20%
2 <sup>nd</sup> subsite exposure:	1 x MED	- 10%
3 <sup>rd</sup> subsite exposure:	1 x MED	
4 <sup>th</sup> subsite exposure:	1 x MED	+ 10%
5 <sup>th</sup> subsite exposure:	1 x MED	+ 20%
6 <sup>th</sup> subsite exposure:	1 x MED	+ 30%

TABLE 2: Composition of the capsule contents

Linseed oil
Lutein
Tomato oil (lycopene)
Beta carotene
Ascorbic acid
Vitamin E Acetate
Zinc sulfate
Sodium selenite



## RESULTS

Of the 33 invited and included volunteers, 28 completed the study. Four dropped out for reasons unrelated to the protocol, and one was excluded due to the use of a medication not allowed during the study.

None of the volunteers showed any adverse reaction related to the supplement use during the study period.

The statistical evaluation of the results was performed using the Student's *t*-test, with a significance level of 5% ( $p = 0.05$ ).

### Evaluation of the Minimal Erythema Dose

Graph 1 shows the evolution of the mean values of the MED at intervals (in days) T0, T30 and T60. From Graph 1, it can be concluded that the daily use of the supplement led to a statistically significant increase ( $p = 0.017$ ) in the MED values as from 60 days. An important finding is noteworthy: four volunteers did not exhibit erythema in any of the irradiation sessions, suggesting there was considerable increase in the MED, even with increases of up to 30% in the irradiation amount.

## DISCUSSION

The combination of oral antioxidants as agents for reducing photodamage, based on increased levels of MED, is already known. In addition, the photoprotective effect of topical—or even systemic antioxidants—has already been demonstrated in several experimental studies.<sup>8,9</sup>

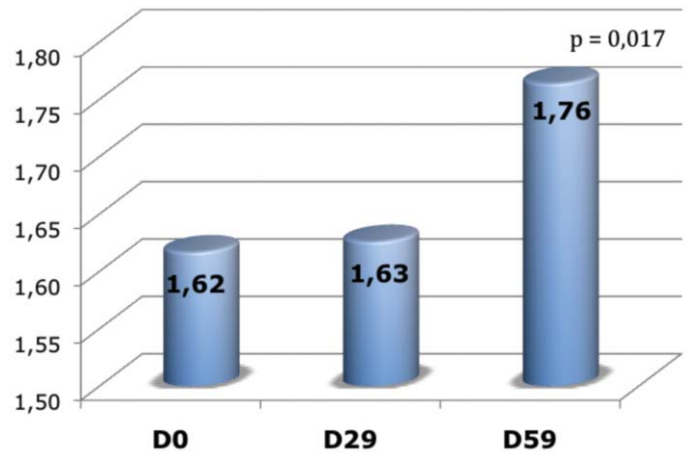
A clinical trial using the combination of vitamins E (in 500 IU doses) and C (in 1g doses) twice a day, showed a significant increase in MED from 90 days.<sup>10</sup>

The concomitant use has superior results, even reducing the formation of thymine dimers, what has been demonstrated in animal models.<sup>11</sup>

The synergistic effect among antioxidants is possible and can lead to increased quality of the protective effect not only against the immediate photodamage, but also against cellular phenomena typical of photodamage.<sup>12</sup>

The association of nutrients can also allow for the use of lower, alimentary doses, thus preventing effects such as hypervitaminosis.<sup>13</sup>

The oral supplementation evaluated in the present study combined antioxidants with diverse mechanisms, meaning that the protective effect can be enhanced as well as having an earlier action, which can be observed as from 60 days of use.



GRAPH 1: Mean values for Minimum Erythema Dose (MED)

Molecules, such as lutein and lycopene, already established as oral antioxidants with photoprotective effect,<sup>14,15</sup> may act in tandem, potentializing the antioxidant effects. Lycopene, for instance, can be associated with another carotenoid, with no competition in the absorption and utilization or pro-vitamin A activity. None of these is the human body not able to synthesize.<sup>16</sup>

Linseeds are rich in essential fatty acids, fiber, and phenolic compounds. These compounds exert antioxidant activity, being a significant source of essential fatty acids  $\omega$ -3 and  $\omega$ -6, both of which are crucial in the maintenance of the skin barrier and modulation of inflammatory activity.<sup>17</sup>

Minerals such as zinc and selenium are factors that constitute the fundamental enzymes for the antioxidative mechanism—such as superoxide dismutase and glutathione peroxidase, respectively.<sup>18,19</sup>

## CONCLUSION

The combination of nutrients with antioxidant value has the ability to provide protection against acute photodamage, measured in the present study through the increase in the Minimal Erythema Dose. Concentrations in dietary doses have an adequate safety profile, avoiding the risk of toxicity. ●

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## Article Original

### Authors:

Geraldo Magela Magalhães<sup>1</sup>  
 Maria de Fátima Melo Borges<sup>2</sup>  
 Amanda Gomes Dell' Horto<sup>2</sup>  
 Denise de Borba Carvalho<sup>2</sup>  
 Marcela Mattos Simões Mendonça<sup>3</sup>  
 Marcos Alvarenga de Souza Júnior<sup>3</sup>

<sup>1</sup> Associate Professor "A" of Dermatology, Medical School, Universidade Federal de Ouro Preto (UFOP)—Ouro Preto (MG), Brazil; Preceptor at the Cosmetic Dermatology Ambulatory, Santa Casa de Belo Horizonte—Belo Horizonte (MG), Brazil

<sup>2</sup> Preceptor at the Cosmetic Dermatology Ambulatory, Santa Casa de Belo Horizonte

<sup>3</sup> Dermatologist Physician—Belo Horizonte (MG), Brazil

### Correspondence:

Dr. Geraldo Magela Magalhães  
 Avenida do Contorno, 4747, sala 904—  
 Funcionários  
 Cep: 30110-090—Belo Horizonte—MG,  
 Brazil  
 E-mail: gergmagela@ig.com.br

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Conflict of interest: None

# Double-blind randomized study performed with 4% lidocaine cream and vehicle in the application of type A botulinum toxin: analysis of the pain during the procedure and of the interference with the efficacy and duration of the effect

*Estudo duplo-cego randomizado com lidocaína creme 4% e veículo na aplicação de toxina botulínica tipo A: análise da dor durante o procedimento e interferência na eficácia e duração do efeito*

### ABSTRACT

**Introduction:** For some patients, pain during the injection of botulinum toxin can represent a limitation for performing the procedure. There are doubts about whether the use of topical anesthetic decreases pain or interferes with the treatment's efficacy and duration of effect.

**Objectives:** To study the effect of 4% lidocaine cream in controlling pain during BoNT-A – Speywood Unit botulinum toxin application, comparing it to the vehicle. In addition, the study was aimed at verifying whether the cream influences the treatment's outcome and duration.

**Methods:** An experimental, prospective, double-blind, randomized study was carried out. The pain was assessed through a compartmentalized numerical rating scale (CNRS). The effect was assessed through a four-point contraction qualitative scale.

**Results:** After evaluating the pain scale, higher values were observed in the placebo group when compared to the group that used anesthetic, with statistical significance. Furthermore, there was no statistical difference in the efficacy and duration of effect over weeks 4, 8, 12, and 16.

**Conclusions:** BoNT-A – Speywood Unit toxin was effective and safe for the treatment of glabellar and frontal wrinkles. The use of topical anesthetics (4% lidocaine cream) reduced the pain during the procedure. In addition, there was no interference in the toxin's efficacy and effect duration.

**Keywords:** botulinum toxin type A; lidocaine; pain; therapy.

### RESUMO

**Introdução:** A dor durante a injeção da toxina botulínica pode representar, para alguns pacientes, uma limitação à realização do procedimento. Há dúvidas se o uso de anestésico tópico diminui a dor ou interfere no efeito e duração do tratamento.

**Objetivos:** Objetiva-se estudar o efeito da lidocaína 4% creme no controle da dor durante aplicação da toxina botulínica BoNT-A – Speywood Unit, comparando-a ao veículo. Ademais, deseja-se verificar se o referido creme influencia o resultado e a duração do tratamento.

**Métodos:** Estudo experimental, prospectivo, duplo-cego e randomizado. A dor foi avaliada por escala de graduação numérica compartimentada (EGNC), e o efeito, pela escala qualitativa de contração de quatro pontos. Resultados: avaliando-se a escala de dor observaram-se valores maiores no grupo placebo quando comparado ao grupo que usou anestésico, com diferença estatisticamente significativa. Além disso, não houve diferença estatística na eficácia e na duração do efeito ao longo das semanas 4, 8, 12 e 16.

**Conclusões:** A toxina BoNT-A – Speywood Unit mostrou-se eficaz e segura para tratamento de rugas glabulares e frontais. A aplicação de anestésico tópico (lidocaína 4% creme) reduziu a dor durante o procedimento sem interferir na eficácia e duração do efeito da referida toxina.

**Palavras-chave:** toxinas botulínicas tipo A; lidocaína; dor; terapêutica.

## INTRODUCTION

In 1817, Justinus Kerner first described the symptoms of a highly lethal, progressive paralysis associated with the ingestion of sausages, later known as botulism (from the Latin *botulus*, meaning sausage).<sup>1</sup> In 1895, Emile van Ermengen described the bacterial agent responsible for the disease and the agent's mechanism of toxic action.<sup>1</sup>

Botulinum toxin is one of the most potent bacterial toxins known to date. It is produced by the *Clostridium botulinum*, a gram-positive anaerobic bacteria in the form of a spore, commonly found in the soil and in marine environments. Eight immunologically distinct serotypes have been identified, of which seven (A, B, C1, D, E, F, and G) are neurotoxins. Although all neurotoxins are able to reduce the release of acetylcholine by the motor plate, they vary in size, cellular biosynthesis, and mechanism of action. Serotype A has the greatest neuromuscular blocking potency, with rare systemic effects, and has been used for several years with various therapeutic objectives, and is the first to be manufactured for clinical use.<sup>2</sup> In 1980, the serotype described was introduced in medical practice for the treatment of strabismus.<sup>3</sup>

In 1982, after a multicentric study on the use of botulinum toxin type A for correcting strabismus and other facial muscle problems, one patient reported a reduction of glabellar wrinkles. This was the landmark case for the treatment of glabellar wrinkles with this product, with its results being published in 1988.<sup>4</sup> Since then, botulinum toxin has seen increasing use, in isolation or associated with other facial rejuvenation techniques, and is currently one of the main procedures performed in dermatology practices.<sup>2</sup>

Several botulinum toxins are available in the market for clinical use: abobotulinumtoxinA (Dysport<sup>®</sup>, Ipsen Biopharm Limited—UK), onabotulinumtoxinA (Botox<sup>®</sup>, Allergan, Inc., Irvine, CA—USA), incobotulinumtoxinA (Xeomin<sup>®</sup> Merz Pharma, Frankfurt—Germany),<sup>5</sup> Lanzhou type A—LBTXA (Prosigne, Cristália, China), among others.<sup>6</sup> Botulinum toxin is manufactured from different strains of bacteria, undergoing various purification and stabilization processes, resulting in different chemical and biological properties.<sup>7</sup> Abobotulinumtoxina (Dysport—Ipsen Biopharm Limited—UK), a derivative of botulinum toxin A, has been used in Europe for the correction or mitigation of facial wrinkles for over two decades, and in April 2009 its use was approved by the U.S. FDA. It is measured in Speywood Units (s.U.), and collectively referred to as BoNT-A (Speywood Unit).<sup>8</sup> The product is sold in 300 s.U. and 500 s.U. vials.<sup>8,9</sup>

Neuromuscular diseases, the use of aminoglycosides and anticholinergic drugs, pregnancy and lactation, and allergy to cow's milk are reported as contraindications. Unrealistic expectations are a relative contraindication and must be thoroughly evaluated by the physician.<sup>10</sup>

Some adverse effects associated with the use of botulinum toxin type A in the treatment of dynamic wrinkles in the upper third of the face have been reported: headache, facial edema, sensation of facial swelling, palpebral ptosis, eyebrow

ptosis, local pain and bruising, mild pruritus, and nausea.<sup>6</sup> Local pain during the procedure is one of the most important and limiting side effects of the technique.<sup>6,10</sup>

For some patients, pain during the injection of the toxin may represent a limitation for undergoing the procedure. Topical anesthetic in the form of a dermatological cream offers a non-invasive and relatively safe analgesia in various dermatologic procedures, such as cutaneous fillings, curettage, electrocauterization, laser, and botulinum toxin application, among others.<sup>11,12</sup> The standard drug used is 4% lidocaine cream.<sup>12</sup>

The present study is aimed at determining whether the use of 4% lidocaine cream modifies pain during the application of botulinum toxin. In addition, it is intended to study whether the cream described affects the outcome and duration of treatment. The scarcity of scientific reports on the influence of the use of anesthetic cream and the effect of treatment justifies the study.

## METHODS

An experimental, prospective, double-blind, randomized study was conducted at the Cosmetic Dermatology Ambulatory of the Dermatology Clinic of the Santa Casa de Belo Horizonte, Minas Gerais—Brazil, in ambulatorial patients bearing glabellar and frontal hyperfunctional facial lines, from April 20–August 24, 2012.

Fifteen patients were included in the study, which was submitted to the Ethics Committee in Research, and all participants signed a Free and Informed Term of Consent.

The patients were randomized: half the glabellar and frontal region received topical anesthetic cream (4% lidocaine cream) applied to the injection points, and the other half received a pure cream vehicle (Figure 1).

Each vial containing 500s.U. of abobotulinumtoxinA (Dysport<sup>®</sup> Ipsen Biopharm Limited—UK) was diluted in 2 ml of 0.9% saline solution without preservatives, resulting in a concentration of 250 s.U./ml. The syringe used in the dilution process was the BD ultrafine II 100UI, with all vials used being from the same batch (D31307 exp. date 05/2013). The application was performed immediately after dilution.

Each patient received 100 s.U. of BoNT-A treatment, as



FIGURA 1: Aplicação de lidocaína creme 4% (lado direito) e placebo (lado esquerdo)

follows: eight points in the frontal muscle, each with 5 s.U. (0.02 ml of the dilution), totaling 40 s.U., and five glabellar points, totaling 60 s.U. (one point in the procerus muscle—20 s.U., 0.08 ml of the dilution and four points in the corrugator muscles—10 s.U., 0.04 ml each point). BD ultrafine II 30 UI syringes were used for injection.

The study was double-blind and the applications of the topical anesthetic and the vehicle were carried out by a research assistant. The injection of botulinum toxin was performed by the main investigator physician, who was also responsible for assessing the effectiveness and duration of effect of the botulinum toxin, and was unaware of which area was treated with topical anesthetic or placebo.

The patients were assessed immediately after the procedure for the verification of pain, through the compartmentalized numerical grading scale (EGNC) 13 and in weeks 4, 8, 12, and 16, for the verification of efficacy and duration of treatment effect through photographic analysis and qualitative scale of four-point contraction.<sup>14,15</sup>

The photographic analysis was carried out at each visit, with patients being photographed at rest and at maximal contraction of muscles. All photographs were taken with the same digital camera respecting parameters regarding body site, background, and distance.

The following inclusion criteria were observed: women with hyperfunctional glabellar and frontal lines, age over 18, and signature on a Free and Informed Term of Consent.

The following exclusion criteria were observed: pregnant and lactating women, patients with infection in the application site, patients with a known hypersensitivity to one of the contents of the anesthetic cream or botulinum toxin, patients with psychological instability and unrealistic desires regarding the treatment, patients who rely on facial mimicry for their work, patients bearing neuromuscular diseases such as myasthenia gravis or Eaton-Lambert syndrome, patients taking drugs such as aminoglycosides, penicillamine, kinins, or calcium channel inhibitors.

The studied variables—pain and degree of paralysis—were analyzed according to the presence or absence of anesthetic. Initially, a characterization of the sample by means of frequency distribution tables, and central tendency and variability measures, was performed. To check for differences between groups—control (placebo) and experimental (anesthetic)—the Pearson’s Chi-square test or Fisher’s exact test were employed for comparing proportions. To compare continuous variables, the nonparametric test of Mann-Whitney, suitable for comparing two groups, was used. The intraclass correlation coefficient was used to assess the correlation between the physician’s and the patient’s assessments. In all analyses a 5% significance level was adopted. The software SPSS 15.0 was used.

## RESULTS

Fifteen patients 26- to 52-years-old (mean = 37-years-old) (Table 1) were evaluated. All were originally from urban regions (information not shown in the table). Most had photo-

TABLE 1: Descriptive statistics of evaluated patients’ characteristics.

Phototype	N	%
II	3	20
III	7	46,7
IV	4	26,7
V	1	6,7
<b>Phototype</b>		
Ex-smoker	3	20
Smoker	1	6,7
Has never smoked	11	73,3
<b>Previous skin disease</b>		
Yes	3	20
No	12	80
<b>Active skin disease</b>		
No	4	26,7
Yes	11	73,3
<b>Systemic disease</b>		
No	5	33,3
Yes	10	66,7
<b>Use of medicaments</b>		
Yes	10	66,7
No	5	33,3
<b>Previous toxin</b>		
No	4	26,7
Yes	11	73,3
<b>Adverse reaction to toxin application</b>		
Yes	1	6,7
No	14	93,3
<b>Age</b>		
Mean	37,1	
Standard-deviation	9,3	
Maximum	26	
Maximum	52	
Percentile 25	29	
Median	35	
Percentile 75	47	

type III (46.7%) and 73.3% had never smoked. The prevalence of prior skin disease was 20% (73.3% of active disease and 66.7% of systemic disease). It is worth noting that the prior skin disease reported was acne, and the active disease was melasma. Arterial hypertension, asthma, lupus syndrome NEM-2 A were informed as systemic diseases. Pharmaceutical use was reported in 66.7% of cases, with contraceptives being the most frequently declared. The majority of respondents reported previous use of botulinum toxin (73.3%), and only one patient (6.7%) mentioned adverse reaction.

According to the results presented in Table 2, the values for the anesthesia duration were similar in both groups, with an average of 42 minutes (min = 30’ and max = 54’). On the pain scale, higher mean and median values were observed in the placebo group when compared to the anesthetic group, with a sta-

**TABLE 2: Comparison of anesthesia duration (in minutes) and pain scale between anesthesia and placebo groups.**

	Anesthesia	Placebo	p-value
<b>Duration of anesthesia</b>			
Mean	42	42	1,000***
Standard-deviation	6.9	6.9	
Minimum	30	30	
Maximum	54	54	
Percentile 25	36	36	
Median	42	42	
Percentile 75	47	47	
<b>Pain scale</b>			
Mean	2.8	6.7	<0,001***
Standard-deviation	1.9	2.7	
Minimum	1	2	
Maximum	6	10	
Percentile 25	1	4	
Median	2	7	
Percentile 75	5	9	

\*\*\* Man-Whitney test

tistically significant difference (p-value < 0.05).

According to the results shown in Table 3, the physician's assessment in week 4 attributed a score of 4 to both the anesthetic and the placebo group. In that same week, according to the patients' evaluation, 80% of the anesthetic group and 86.7% of the placebo group received a score of 4. In week 8, in the physician assessment, both groups had a score of 4. In the evaluation of patients, 60% of the anesthetic group and 46.7% in the placebo group received that score. In weeks 12 and 16 an identical percentage was observed in the comparison between the two groups. The prevalence of a score of 4 was 13.3% in both weeks, both in the physician's and the patients' evaluations. There were no significant differences between groups in any of the evaluations (p-values > 0.05).

Table 4 shows the correlation between the assessments carried out by the physician and the patient. Due to the fact that it is a case of correlation between two ordinal variables (physician's assessment x patient's assessment) the intraclass correlation coefficient was used. For weeks 4 and 8 it was not possible to carry out an estimate due to the lack of variability in the physician's assessment (which attributed a score of 4 for all patients).

As for week 12, the correlation between the two assessments can be classified as moderate (0.517) and in week 16, the correlation was good (0.764).

**DISCUSSION**

The mean age of the treated group was 37 years (range = 26-52 years). This finding reinforces the use of botulinum toxin for the correction of hyperfunctional wrinkles of the facial muscles, which was more frequent in that age group. Only one patient (6.7%) reported adverse reaction to the treatment: local pain for three days in the points of application and a sensation

**TABLE 3: Comparison of results between anesthesia and placebo groups.**

	Anesthesia	Placebo	p-value
<b>Week 4 (physician)</b>			
4	15	15	-
	100%	100%	
<b>Week 4 (patient)</b>			
3	3	2	1.000*
	20%	13.3%	
4	12	13	
	80%	86.7%	
<b>Week 8 (physician)</b>			
4	15	15	-
	50%	50%	
<b>Week 8 (patient)</b>			
2	1	-	0.462*
	6.7%	-	
3	5	8	
	33.3%	53.3%	
4	9	7	
	60%	46.7%	
<b>Week 12 (physician)</b>			
3	13	13	1.000*
	86.7%	86.7%	
4	2	2	
	13.3%	13.3%	
<b>Week 12 (patient)</b>			
2	2	2	1.000*
	13.3%	13.3%	
3	11	11	
	73.3%	73.3%	
4	2	2	
	13.3%	13.3%	
<b>Week 16 (physician)</b>			
2	5	5	1.000*
	33.3%	33.3%	
3	8	8	
	53.3%	53.3%	
4	2	2	
	13.3%	13.3%	
<b>Week 16 (patient)</b>			
1	2	2	1.000*
	13.3%	13.3%	
2	5	5	
	33.3%	33.3%	
3	6	6	
	40%	40%	
4	2	2	
	13.3%	13.3%	

\* Fisher's exact test

that the eyebrow had "sunk", a fact that was not confirmed by the dermatological clinical examination.

The visual analogue scale (VAS) and the compartmentalized numeric graded scale (EGNC) are commonly used to evaluate

TABLE 4: Assessment of the correlation between the physician’s and the patients’ evaluation per week.

Physician’s evaluation	Patients’ evaluation				CCI	
	1	2	3	4		
<b>Week 4</b>						
4			5	25		-
			16.7%	83.3%		
<b>Week 8</b>						
4		1	13	16		-
		3.3%	43.3%	53.3%		
<b>Week 12</b>						
3			4	20	2	0.517
		15.4%	76.9%	7.7%		
4		-	2	2		
		-	50%	50%		
<b>Week 16</b>						
2	4	4	2	-		0.764
	40%	40%	20%	-		
3	-	6	8	2		
	-	37.5%	50%	12.5%		
4	-	-	2	2		
	-	-	50%	50%		

ICC = intraclass correlation coefficient

luate the intensity and severity of pain. Its use is justified by the reproducibility, and can be used both clinically and in research. The VAS consists of a straight, not numbered, ten-centimeter line, presented on a blank sheet, where the left end means an absence of pain and the right end, the greatest level of pain perceived by the patient. It is one of the most-used scales for measuring pathological pain for scientific purposes, since it allows for the minimizing of the subjective factor. Another variation of this type of scale would be the EGNC, which is numbered from 0 to 10, in ascending order, from the left to right within a frame. The minimum value measured means absence of pain, and the maximum value, a greater intensity of pain; the patient chooses the number that best represents his or her perception of pain.<sup>13</sup>

In developing countries, the best option is the EGNC scale, which presents greater ease of interpretation and makes it therefore more accessible to patients with a low level of education. In EGNC pain is expressed in numbers and patients tend to prefer it to quantify their pain; 13 in this study, it was the chosen scale for the assessment of pain.

There was a significant reduction in pain in the group treated with a topical anesthetic versus the one treated with the placebo: in the first, the average pain was 2.8 and in the second 6.7 ( $p < 0.001$  %). The placebo group felt 2.4 times more pain than the anesthetic group. Anesthesia time ranged from 30 to 54 minutes (mean = 42 minutes).

Some studies tested the efficacy and safety of using topical lidocaine in botulinum toxin application. In 2010, Baumann et al. evaluated 26 patients regarding pain during botulinum toxin application, concluding that there is a statistically significant reduction in pain, with proven efficacy when applying 4%

lidocaine before the procedure.<sup>12</sup> In 2005, Carruthers A. et al. also found similar effectiveness in a randomized double-blind study involving 24 patients.<sup>16</sup> These observations were confirmed by the present study.

In addition, it aimed at studying the interference of the use of a topical anesthetic in the effectiveness and duration of the effect of the treatment with BoNT-A (Speywood Unit). There is anatomical variability of the muscles in the frontal and glabellar regions, a fact that has generated interest and stimulated the realization of recent studies describing different patterns of contraction in these areas. These studies have reinforced the need for individualization of the points of application of botulinum toxin, based on those anatomical variations.<sup>17,18</sup> For standardization, conventional doses and points of application for the treatment of glabellar and frontal regions were used, following the literature data.<sup>18</sup> In a recent study about the international consensus for the use of botulinum toxin type A (BoNT-A, Speywood Unit), the recommended dose for the frontal region ranged from 20 to 60 s.U., and for the glabellar region the recommendation was 50 s.U. In the present study, we used doses of 40 s.U. for the frontal region and 60 s.U. for the glabellar region.

The muscular mobility was evaluated both by the physician and the patient at each visit using a qualitative four-point scale (1 = unaltered, 2 = slightly reduced, 3 = moderately reduced, 4 = considerably reduced).<sup>14,15</sup> The physician assessed the patients directly, and the volunteers observed themselves in mirrors.

There was no statistical difference in efficacy and duration of effect when the anesthetic and placebo groups were compared, over weeks 4, 8, 12, and 16, as can be seen in Table 3.

The same table provides important information about the duration of the muscle paralysis throughout the study. It is possible to observe that in week 16, 66.6% of patients had moderately reduced muscle contraction (value = 3) or considerably reduced (value = 4), regardless of the side (anesthetic or pure vehicle), according to the physician's evaluation. In the patients' assessment, that ratio stood at 53.3%.

In week 16, the correlation between the observations relating to decreased muscle contraction assessed by the physician and the patients was good (intraclass correlation coefficient = 0.764). This demonstrates that at the end of four months there were no significant differences between doctor and patient in the evaluation of the BoNT-A, Speywood Unit's effect.

## CONCLUSIONS

The BoNT-A, Speywood Unit toxin was effective and safe for the treatment of glabellar and frontal wrinkles. The application of topical anesthetic (4% lidocaine cream) reduced pain during the procedure. Furthermore, there was no interference in the efficacy and duration of the toxin's effect. ●

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## Article Original

# Culture of human dermal fibroblasts in the presence of hyaluronic acid and polyethylene glycol: effects on cell proliferation, collagen production, and related enzymes linked to the remodeling of the extracellular matrix

*Cultura de fibroblastos dérmicos humanos na presença de ácido hialurônico e polietilenoglicol: efeitos na proliferação celular, produção de colágeno e enzimas relacionadas à remodelação da matriz extracelular*

### Authors:

Marcia Regina Monteiro<sup>1</sup>  
Ivarne Luis dos Santos Tersario<sup>2</sup>  
Sheyla Varela Lucena<sup>3</sup>  
Gioconda Emanuella Diniz de Dantas Moura<sup>4</sup>  
Denise Steiner<sup>4</sup>

<sup>1</sup> Dermatology Preceptor, Universidade Federal de Mogi das Cruzes (UMC)—Mogi das Cruzes (SP), Brazil

<sup>2</sup> Associate Professor, Department of Biochemistry, Universidade Federal de São Paulo (UNIFESP)—São Paulo (SP), Brazil

<sup>3</sup> Post-graduate Diploma Candidate, Department of Biochemistry, Universidade Federal de São Paulo (UNIFESP)

<sup>4</sup> Full Professor and Head of the Dermatology Department, Universidade de Mogi das Cruzes (UMC)

### Correspondence:

Dr. Marcia Regina Monteiro  
Rua Itapeva, 240 / cjs. 503 e 504  
Cep: 01332-000—São Paulo—SP, Brazil  
E-mail: dermarciamonteiro@yahoo.com.br

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### ABSTRACT

**Introduction:** Cutaneous fillings are a common procedure in today's dermatology, with the majority being carried out with hyaluronic acid isolated or combined with other substances.

**Objective:** To study the effects of adding hyaluronic acid and polyethylene glycol to cultures of human dermal fibroblasts.

**Methods:** The study evaluated: cell proliferation and production of type 1 collagen (COL1A1) in the presence or absence of anti-CD44 antibodies (membrane receptor for hyaluronic acid); the synthesis of metalloproteinase-1 (mmp-1), of tissue factor inhibitor of metalloproteinase-1 (TIMP-1) and of transforming growth factor- $\alpha$  (TGF- $\alpha$ ) through the analysis of gene expression via PCR (polymerase chain reaction); cell proliferation through the detection of the incorporation of a thymidine analogue in the cellular DNA.

**Results:** Increased proliferation of fibroblasts and collagen synthesis were observed in the cultures exposed to hyaluronic acid, partially inhibited by the presence of anti-CD44 antibodies in the cultures. The exposure of cultures to hyaluronic acid enhances the production of TIMP-1 and TGF- $\alpha$ , and reduces the expression of MMP-1. These effects were not noticed in the cultures exposed to polyethylene glycol.

**Conclusion:** In an in vitro setting, the addition of hyaluronic acid to cultures of human dermal fibroblasts increases proliferation and synthesis of COL1A1, TIMP-1 and TGF- $\alpha$ , decreasing that of MMP-1. The addition of anti-CD44 to the cultures reduces cell proliferation and collagen synthesis, which may indicate the role of that receptor in mediating those events.

**Keywords:** fibroblasts; hyaluronic acid; extracellular matrix.

### RESUMO

**Introdução:** Os preenchimentos cutâneos representam procedimentos comuns na dermatologia atual, sendo a maioria realizada com ácido hialurônico isolado ou associado a outras substâncias.

**Objetivo:** Estudar os efeitos da adição de ácido hialurônico e polietilenoglicol a culturas de fibroblastos dérmicos humanos.

**Métodos:** Foram avaliados: proliferação celular e produção de colágeno tipo 1 (COL1A1), na presença ou não de anticorpos antiCD44 (receptor de membrana de ácido hialurônico); síntese de metaloproteinase1 (MMP-1), fator tecidual inibidor de metaloproteinase1 (TIMP-1) e fator transformador de crescimento  $\beta$  (TGF- $\beta$ ), pela análise da expressão gênica via PCR (polymerase chain reaction); proliferação celular através da detecção da incorporação de um análogo da timidina no DNA celular.

**Resultados:** Observou-se aumento na proliferação dos fibroblastos, bem como da síntese de colágeno nas culturas expostas ao ácido hialurônico, inibido parcialmente pela presença dos anticorpos antiCD44 nas culturas. A exposição das culturas ao ácido hialurônico aumenta a produção de TIMP-1 e TGF- $\beta$  e reduz a expressão de MMP-1. Esses efeitos não foram notados nas culturas expostas ao polietilenoglicol.

**Conclusão:** In vitro, a adição de ácido hialurônico a culturas de fibroblastos dérmicos humanos aumenta a proliferação e síntese de COL1A1, TIMP-1 e TGF- $\beta$ , diminuindo a de MMP-1. A adição de antiCD44 às culturas reduz a proliferação celular e síntese de colágeno, podendo indicar o papel desse receptor na mediação desses eventos.

**Palavras-chave:** fibroblastos; ácido hialurônico; matriz extracelular.

## INTRODUCTION

Dermal fillings are one of the most commonly performed procedures in modern cosmetic dermatology. Most fillings are performed with various modalities of hyaluronic acid. More recently, a new filling material, polyethylene glycol (PEG) has been introduced. As a result, it has become necessary to evaluate the effect of exposing cultures of human dermal fibroblasts to two types of hyaluronic acid (HA)—one associated with a sugar and PEG. Furthermore, similar experiments were performed with the addition of an Anti-CD44 antibody to the cultures. HA is a glycosaminoglycan, which naturally forms the extracellular matrix of connective tissue and is present in the vitreous humor, synovial fluid, cartilage and fascia. It is constituted by the polyanionic repetition of disaccharide units of glucuronic acid and N-acetyl glucosamine, connected by alternate links.<sup>1</sup>

In order to increase the cutaneous filling capacity and longevity of results, manufacturers use substances to bind HA polymers—called cross-link agents—that prolong the degradation time of HA in the skin.<sup>2</sup> The most commonly used agent is BDDE (1-4 butanediol diglycidyl ether).

PEG is a synthetic material that has had several applications in medicine, including as the basis for the release of biomolecules and as a skeleton for the integration of cells in regenerative medicine.<sup>3,4</sup>

More recently, a new product for cutaneous filling that consists of a PEG hydrogel (whose cross-link agent is the diacrylate) has been introduced.

Finally, it is important to highlight that antibodies Anti-CD44, added to the cultures, were used in the present study in order to investigate whether the interaction of HA with fibroblasts via its receptor (CD44) would have any interference in the evaluated parameters.

CD44 is part of a family of transmembrane glycoproteins that mediate cellular responses to the micro-environment—more specifically, the interaction between cells and the extracellular matrix. CD44 family proteins are involved in cellular growth, differentiation, survival, and motility processes. One of the cellular interactions mediated by CD44 protein occurs with AH present in the extracellular matrix.<sup>5</sup>

The present *in vitro* study was aimed at evaluating the effects of the addition of compounds used in cutaneous fillings in cultured human dermal fibroblasts. To assess such effects, the following parameters were chosen: cell proliferation, and the expression of collagen type 1 (COL1A1), tissue inhibitor of metalloproteinases (TIMP1), metalloproteinase 1 (MMP1) and transforming growth transformation (TGF- $\beta$ ), by those cells. Cell proliferation and collagen production were also assessed in the presence of AntiCD44 antibody, which acts as a receptor of HA in the cell membrane of the fibroblasts.

References<sup>6-8</sup> indicating that the use of HA fillers may induce local fibroblasts to increase their collagen synthesis through mechanisms not yet fully known, can be found in the literature. In the present study, the addition of Anti-CD44 to the cultures reduced cell proliferation and collagen production. This result suggests that the CD44 receptor may be involved in the

stimulation of collagen production by fibroblasts when in the presence of HA.

## METHODS

Human dermal fibroblasts purchased from ATCC were incubated for one hour in a 5% CO<sub>2</sub> atmosphere at 37°C in DMEM supplemented with 10% fetal bovine serum (FBS), 100U/ml penicillin and 100 $\mu$ g/ml streptomycin.

The fibroblasts (105 cells/compartiment) were incubated in the presence of a product based on polyethylene glycol diacrylate (PEG)—(Scientech. Corp., Italy)—at 1/10 (v/v); isolated HA—(Allergan, Santa Barbara – CA, USA)—0.1 mg/ml or HA stabilized with DEAE Sephadex A25—Prolenium (HA+D)—(MEDICAL Technologies Inc, Ontario, Canada) – at 0.1 mg/ml for 24 hours at 37°C, with the parameters being compared with the control cultures.

After 24 hours of incubation, the following gene expression parameters were studied:

COL1A1 (collagen type 1)

TIMP-1 (tissue inhibitor of metalloproteinase 1)

MMP-1 (metalloproteinase1)

TGF- $\beta$  (transforming growth factor  $\beta$ )

After 96 hours in culture, the cell proliferation of fibroblasts was evaluated in the presence of the described substances and when incubated with antibodies Anti-CD44 (Clone DF1485)(Dako comp.). The expression of COL1A1 gene was analyzed through PCR with the aid of the primers 5'-GGGATTCCCTGGACCTAAAG-3' (forward primer) and GGAACACCTCGCT-CTCCAG (reverse primer). The expression of MMP1 gene was analyzed through PCR with the aid of the primers 5'-GCTAACCTTTGATGCTATAACTAC-GA-3' (forward primer) and TTTGTGCGCATGTAGAATCTG (reverse primer). The expression of TIMP1 gene was analyzed with assistance/the aid of the primers 5'-GAAGAGCCTGAAC-CACAGGT-3' (forward primer) and CGGGGAGGAGATGTAGCAC (reverse primer), and, finally, the expression of TGF- $\beta$ 3 was analyzed with the aid of the primers 5'-GAATTCTATGCACTTGCAAAGGGCTCTGG-3' (forward primer) and GTCGACTTATTATCAGCTGCACTTACAC (reverse primer). To evaluate the production of collagen, MMP, TIMP, and TGF- $\beta$ , total RNA was isolated (Trizol, Invitrogen) from cells at 70% confluence, transcribed and reversely amplified using Taqman Assay-on-Demand primers (Applied Biosystems) and One-Step Master Mix (Applied Biosystems). The amplified sequences were detected using the ABI Prism 7900HT detector (Perkin-Elmer-Cetus), according to the product instructions.

The gene expression of collagen type 1, MMP1, TIMP1, TGF- $\beta$ 3 were evaluated through the Real Time PCR technique, and cell proliferation was measured through BrdU incorporation into DNA and subsequent evaluation by detection with chemiluminescence using the Cell Proliferation ELISA BrdU kit (Roche). Cells were incubated with the compounds for 48 hours at 96-Black-F-Bottom well plates (Nunc, Roskilde, Denmark).

### Quantification experiments through real time PCR

These experiments were used to measure the expression rate of genes COL1, TIMP1, MMP-1, and TGF- $\beta$ 3 of fibroblast cultures exposed to the products (HA and PEG), compared to the cultures that were not exposed. Results were presented in terms of rates of variation in the gene expression or cell proliferation (increase or decrease) of the exposed cultures compared to those that had not been exposed. The gene expression of  $\beta$ -actin and GAPDH was used as a control of the experimental quantification variability.

### Statistical analysis

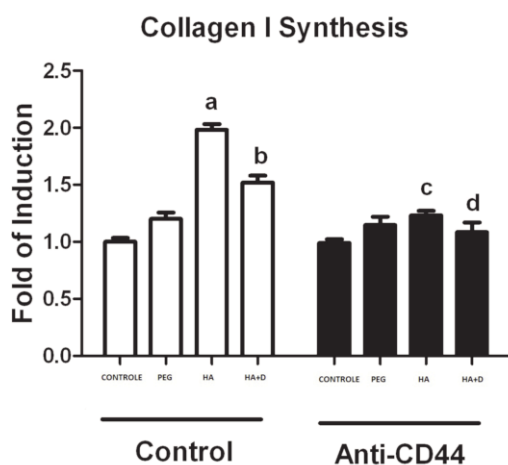
The comparison of gene expression and cell proliferation between treated and untreated samples was carried out in terms of the rate of increase (mean  $\pm$  SD) of independent experiments, performed three times, through the Tukey's post hoc test (ANOVA) with  $P < 0.05$ . The statistical analysis was performed with the Graph Pad Prism 5® software.

### RESULTS

Evaluation of type 1 collagen synthesis through the expression of COL1A1 gene

After 24 hours, a statistically significant increase in the gene expression of COL1A1 in cultures exposed to all compounds studied was observed when compared to the controls. The cultures exposed to the HA compound (a) were those which presented greater increase in the gene expression of collagen when compared to the control cultures, followed by the cultures exposed to the HA compound associated with the dextranomer (b).

When the Anti-CD44 antibody was added to the cultures, a significant reduction of COL1A1 gene expression was observed only in cultures exposed to the HA compounds (c, d). (Graph 1)



GRAPH 1: Compound containing polyethylene glycol (PEG); Isolated HA compound and compound containing AH associated with dextranomer (HA+D).

### Production of MMP -1, TIMP -1, and TGF- $\beta$

After 24 hours, a statistically significant increase in the gene expression of TIMP-1 (a) and TGF- $\beta$  (b) was observed only in cultures where HA had been added.

Likewise, after 24 hours, there was a statistically significant reduction in the gene expression of MMP1 only in the cultures exposed to the AHs (c).

These parameters showed no significant alteration in the cultures exposed to the PEG compound when compared with controls. (Graph 2)

### Cell proliferation

After 48 hours, a statistically significant increase of fibroblasts was observed when compared to controls, only in cultures with AH (c). This result became more pronounced after 96 hours (d).

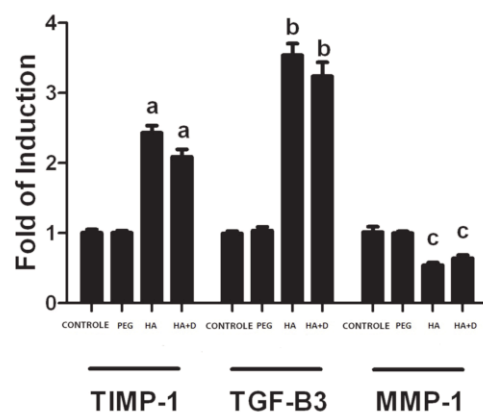
After 96 hours, the proliferation of fibroblasts exposed to compounds containing AH was significantly reduced when cultures were incubated with Anti-CD44 antibodies (e). However, despite this effect, the cell proliferation of these cultures was still greater than that observed in control cultures and in cultures exposed to PEG (a).

The cultures exposed to PEG (b) showed an initial reduction in fibroblast proliferation (48h) when compared to controls. After 96 hours, proliferation was comparable to that found in the controls (a).

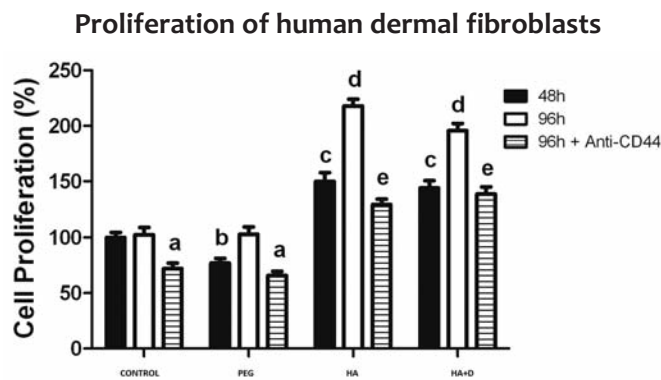
The proliferation of fibroblasts after 96 hours (with and without the addition of Anti-CD44) was similar in the controls and in cultures exposed to PEG. (Graph 3)

### DISCUSSION

This in vitro study demonstrated that 24 hours of exposure of cultured human dermal fibroblasts to the various com-



GRAPH 1: Compound containing polyethylene glycol (PEG); Isolated HA compound and compound containing AH associated with dextranomer (HA+D).



**GRAPH 1:** Compound containing polyethylene glycol (PEG); Isolated HA compound and compound containing AH associated with dextranomer (HA+D).

pounds used in cutaneous fillers led to an increase in collagen production, evidenced by increased expression of COL1A1 gene, as compared to the controls. It was also observed that the increased expression of collagen was more pronounced in cultures exposed to compounds of AH.

Concomitantly, gene expression was inhibited when cultures exposed to AHs were treated with the Anti-CD44 antibody, which is a cell membrane receptor of AH. This result suggests that the receptor CD44 may be involved in the mechanism of stimulation of collagen production by fibroblasts in the presence of HA.

An interesting observation is that the exposure of the cultures to HA increases production of TIMP-1 and TGF- $\beta$ , and reduces the expression of MMP-1. This data may indicate that the increased expression of collagen in the cultures exposed to AH is due to a greater stimulation from growth factors, coupled

with the reduction of degradation (decrease in MMP-1 and increase in TIMP-1).

The results of this *in vitro* study are in agreement with the findings in the literature.<sup>6,7</sup> Other studies show that the use of HA for dermal filling seems to stimulate the production of collagen at the site of its application.<sup>6</sup> There has been speculation about the possible mechanisms involved in this process. There is evidence that the mechanical distension of fibroblasts at the site of application of HA could be one of the stimuli.<sup>8,9</sup>

## CONCLUSION

The present study was an *in vitro* analysis in which human dermal fibroblast cultures were exposed to different compounds available for cutaneous filling. The authors studied the gene expression of collagen type I, metalloproteinase I, tissue inhibitor of metalloproteinase, and TGF- $\beta$ , as well as the proliferation of fibroblasts in these conditions.

It could be observed that the addition of HA to the cultures resulted in increased fibroblast proliferation and greater gene expression of collagen, TGF- $\beta$ , and TIMP-1, and decreased expression of MMP-1.

An important finding of this study links the reduction of fibroblast proliferation and collagen production to the addition of CD44 antibodies to cultures exposed to HA, indicating that this receptor may be involved in the mechanism leading to those effects.

The addition of PEG to the cultures did not lead to an increased proliferation of fibroblasts, nor did it alter the gene expression of studied proteins.

Further studies are needed to deepen the understanding of the role of the macromolecules used in cutaneous fillings in the biology of fibroblasts. ●

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## Article Original

# Cosmiatry from the perspective of women: a pilot-study in three Brazilian states

*A cosmiatria na perspectiva das mulheres: estudo-piloto em três estados do Brasil*

### Authors:

Gustavo Martins<sup>1</sup>  
 Fred Bernardes Filho<sup>2</sup>  
 Leticia Soares Sasso<sup>3</sup>  
 Marilda Aparecida Milanez Morgado de Abreu<sup>4</sup>  
 Omar Lupi<sup>5</sup>

<sup>1</sup> Dermatologist Physician—Rio de Janeiro (RJ), Brazil

<sup>2</sup> Post-graduate Candidate in Dermatology at Instituto de Dermatologia Professor Rubem David Azuly of the Santa Casa da Misericórdia do Rio de Janeiro (IDPRDA—SCMRJ)—Rio de Janeiro (RJ), Brazil

<sup>3</sup> Ophthalmologist Physician—Rio de Janeiro (RJ), Brazil

<sup>4</sup> Head of the Dermatology Service of the Hospital Regional da Universidade do Oeste Paulista (UNOESTE)—Presidente Prudente (SP), Brazil

<sup>5</sup> Associate Professor of Dermatology, Universidade Federal do Estado do Rio de Janeiro (UNIRIO); Permanent Post-graduate Instructor at the Universidade Federal do Rio de Janeiro (UFRJ); Full Professor and Head of the Dermatology Service of the Department of Dermatology at Policlínica Geral do Rio January (PGRJ)—Rio de Janeiro (RJ), Brazil

### Correspondence:

Dr. Gustavo Martins  
 Rua 38, nº 936—Progresso  
 Cep: 38302-010—Ituiutaba—MG, Brazil  
 E-mail: luizgustavodermatologia@gmail.com

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### ABSTRACT

**Introduction:** The beauty industry in Brazil ranks third in the world by size, second only to those of the U.S. and Japan. Paradoxically, the vast majority of studies on aesthetic treatments for the skin do not demonstrate a corresponding knowledge of the industry by the relevant population. Contemporary women, with their increasingly strong role in society, are the engine that drives the growth of the beauty and aesthetics industry.

**Objectives:** To obtain data related to the population's knowledge of cosmetic dermatology treatments.

**Methods:** A descriptive, multicentric study was carried out in the Brazilian states of São Paulo, Rio de Janeiro, and Santa Catarina with 600 women between the ages of 18 and 70 years old.

**Results:** The majority of the target population wants to correct skin imperfections, however there is great suspicion about the effectiveness of the treatments available. The dermatologist's practice is not the main source of information for the interested audience.

**Conclusions:** The consumer profile in the beauty market undergoes constant changes and to understand the public's knowledge, concerns, and challenges linked to these issues is key to allowing discussion with, and educating patients about the ever-expanding cosmetic dermatology field.

**Keywords:** esthetics; beauty culture; Lasers; botulinum toxins; skin cream.

### RESUMO

**Introdução:** A indústria da beleza no Brasil é a terceira do mundo, perdendo apenas para os Estados Unidos e o Japão. Paradoxalmente, os estudos sobre os tratamentos estéticos da pele, em sua maioria, não fazem menção ao conhecimento populacional. A mulher moderna, cada vez mais inserida na sociedade, é a locomotiva que puxa o crescimento do mercado de beleza e estética.

**Objetivos:** Obter dados do conhecimento da população sobre tratamentos cosmiátricos. **Métodos:** Realizado um estudo descritivo, multicêntrico, nos estados de São Paulo, Rio de Janeiro e Santa Catarina com 600 mulheres entre 18 e 70 anos.

**Resultados:** A maioria da população deseja corrigir as imperfeições de sua pele, porém há grande desconfiança sobre a eficácia dos tratamentos. O consultório dermatológico não é a principal fonte de informações das pessoas.

**Conclusão:** O perfil de consumo nesse mercado sofre constantes alterações, e saber quais são os conhecimentos, os anseios e as dificuldades da população sobre esse tema é imprescindível, pois assim é possível dialogar e orientar os pacientes sobre esse crescente campo dermatológico que é a cosmiatria.

**Palavras-chave:** estética; indústria da beleza; Lasers; toxinas botulínicas; creme para a pele.

## INTRODUCTION

The quest for beauty and youth is an enduring trend in contemporary culture — also called, by psychoanalysts of culture, ‘the spectacle and culture of the body’.<sup>1</sup> Beautiful, graceful, sublime, wonderful, and superb are adjectives often used to describe something that pleases. It seems that, in this sense, if it is beautiful then it is good—and in fact, a close link between the concepts of beauty and good has developed in various eras in human history.<sup>2</sup>

Traditionally, dermatologists and plastic surgeons are the specialists who have provided the best aesthetic interventions for an individual patient’s case. Currently, however, the Internet, printed media, and television are important sources of information for people seeking the most appropriate and viable interventions.<sup>3</sup>

Today, medical knowledge doubles every five years.<sup>4</sup> Some of the fruits of laboratory research will be put on shelves, becoming almost immediately available to potential consumers. In actuality, prescriptions are not required for the sale of most such products, a fact that establishes a direct relationship with the consumption market.<sup>5</sup>

In the face of the considerable amount of information available on products intended for aesthetic treatments, consumers seem ever more disoriented, and the vast majority do not realize that such information may come from unfounded sources.<sup>6</sup> Moreover, the classification of those products is controversial.

In 1938, the U.S. Congress passed a law known as The Federal Food, Drug, and Cosmetics Act (the FD&C Act), which established formal criteria for the classification of drugs and cosmetics.<sup>7</sup> In this document, cosmetics are defined as items that are meant to be spread, poured, sprayed, or nebulized, introduced into or otherwise applied to the human body or any part of it, for cleaning, beautifying, promoting attractiveness, or for the purpose of altering appearance. In contrast, a drug is defined as a substance that is aimed at affecting the body’s structure and function.<sup>8</sup>

It is important to note that every new drug must be clinically tested, following the guidelines of the Food and Drug Administration (FDA) for the registration of new drugs (New Drug Application—NDA) in the U.S., and of the National Health Surveillance Agency (ANVISA) in Brazil.<sup>9,10</sup> The drug approval process can last more than ten years and can cost hundreds of millions of dollars. Obviously, it is much easier for cosmetics manufacturers to avoid this obstacle by following guidelines that will keep their products classified as a cosmetic. As a result, these products can then be sold freely without the need for prescriptions, and thus consumers will try them with little guidance—and will likely experience disappointment and lack of results—due to the lack of information about them available to the medical community.<sup>8</sup>

The dilemma faced by cosmetics manufacturers must be taken into account: if they support a research study and the product is not proven to work, they will lose money and possibly face decreased sales and negative publicity. However if the product is effective, they will have their products categorized within

the regulations as drugs, and then face a delay until it is taken to the market.<sup>11</sup>

From an economic point of view, the Brazilian beauty care market (the third largest in the world, behind only those of the U.S. and Japan) quintupled its revenues between 1996 and 2009, according to the Brazilian Association of the Cosmetic, Toiletry, and Perfumery Industry (ABIHPEC).<sup>12</sup> In 2012, revenues reached R\$ 36.24 billion, with ABIHPEC estimating a jump to R\$ 50 billion in 2015. This data was researched by Pyxis Consumo—an Ibope Inteligência tool for gauging market sizes—and points to the C class as the largest consumer of the beauty ware sector’s products in the country.<sup>13</sup> Regarding the Brazilian geographic region, the Southeast concentrates 50% of the consumption potential of beauty care products, with a total estimated expenditure of R\$ 18.08 billion. However, the highest per capita expenditure per year is registered in the South region, which represents 16% of the total national consumption, with an average per capita consumption of R\$ 252.83.<sup>12</sup>

In 2009, the electronic journal *Fator Brasil* published data identifying the consumption habits of the Brazilian consumer and their respective behavior in light of the financial crisis that took place between 2008 and early 2009. In the survey, consumers answered a direct question about changes in their consumption habits due to the ongoing crisis, indicating whether such habits would change or not. The results showed that spending on beauty and health care suffered little impact with the crisis, ranging from 49% in 2008 to 51% in 2009.<sup>14</sup>

At present, most people seeking these treatments are female, however the male market has become increasingly significant, a fact important for the dermatologist physician to be aware, knowing their patients’ interests as well as their therapeutic options.<sup>15</sup>

Studies on aesthetic skin treatments mostly do not mention the general population’s knowledge about this subject—may be due to the scientific community’s old, pre-Internet-era habit of believing that it holds an exclusivity of knowledge about treatments for the skin. However, the cost of such treatments and a greater dissemination of information have led to an ever-increasing scrutiny of dermatological treatments.

Therefore, becoming familiar with the knowledge, doubts, and concerns of the population with which dermatologist physicians interact, is crucial.

## OBJECTIVES

The present study was carried out with an aim of answering the following questions:

- 1) What are the most common aesthetic skin problems for the population?
- 2) What is the percentage of people who buy products for the aesthetic treatment of the skin without medical prescriptions?
- 3) What is the population’s knowledge about the products’ formulation?
- 4) From whom are the products bought?

- 5) What are the difficulties in carrying out topical treatments?
- 6) What are the difficulties in carrying out procedures?
- 7) What is the source of information about aesthetic treatments?
- 8) What is the percentage of people who regularly use sunscreen?
- 9) What is the efficacy of treatments for people?
- 10) What is the education level of the respondents?
- 11) What is the monthly income of the respondents?

**METHODS**

A multicentric study was carried out in three different Brazilian states: São Paulo and Rio de Janeiro, in the Southeast Region, and Santa Catarina in the South Region. Participating cities are: São Paulo, Embu das Artes, Ribeirão Preto, Presidente Prudente, Barretos, Viradouro, Colina and Monte Azul Paulista in the State of São Paulo; Florianópolis in the State of Santa Catarina; Rio de Janeiro and Niterói in the State of Rio de Janeiro.

A pilot test was conducted with a questionnaire to assess the patients’ knowledge, the time required for filling it out, and possible difficulties in answering it. The questionnaire was applied to women between 18 and 70 years old.

Six hundred people were interviewed in the referred cities. Sixty-four forms were excluded due to the fact they had been incorrectly filled out (lack of signature, erasures, ambiguous answers in single alternative questions). Five hundred thirty-six forms were sent for statistical analysis (Figure 1).

The interviewer was not allowed to have any influence on the interviewee. The respondent was free to choose more than one alternative or write multiple answers for questions requiring complementary information. Therefore, in questions where more than one alternative could be chosen, the sum of the percentage might exceed 100%, for they were intended to

verify the more frequent alterations rather than the percentage sum.

From the occupational standpoint, the patients’ socio-economic status (SES) was measured using two indicators: educational level and income, based on the SES scale used in the Brazilian Classification of Occupations—CBO (Classificação Brasileira de Ocupações—CBO).<sup>16,17</sup>

All respondents signed a term of consent to participate in the study.

**RESULTS**

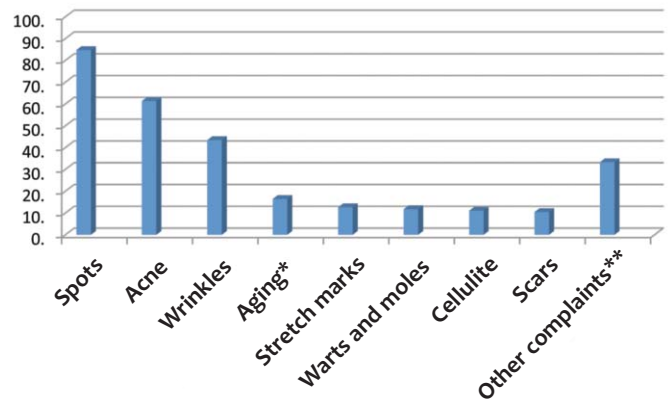
1) Major aesthetic complaints of the population (Graph 2A):

In decreasing order of frequency: 1st) spots (84.7%); 2nd) acne (61.3%); 3rd) wrinkles (43.4%); 4th) aging, rejuvenation, and “signs” of aging (16.4%); 5th) striae (12.6%); 6th) warts and moles (11.7%); 7th) cellulitis (11%); 8th) scars (10.4%).

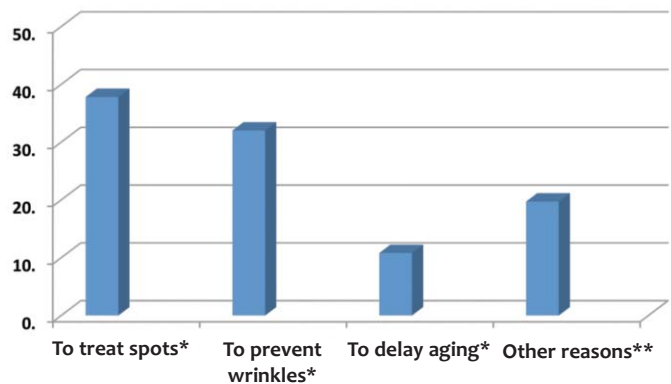
Other complaints such as dry skin, oily skin, or diseases, such as cancer and psoriasis, leveled at about 3% each.

2) On the purchase of creams\* for treatment of the skin (Graph 2B treatments):

Percentages: 37.8% of respondents had bought with a view to treating spots; 32.2% bought to prevent wrinkles; 27% bought to slow aging; 16% did not buy any cream for skin treatment; 19.7% bought for other reasons including: oily skin, acne,

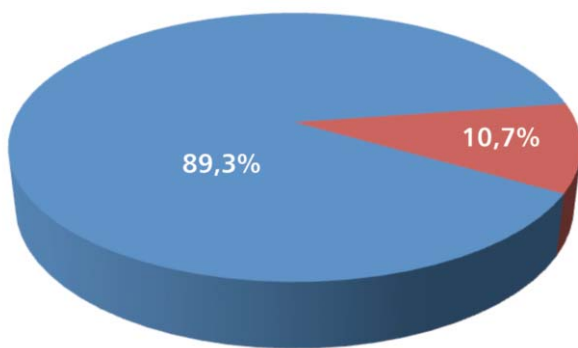


GRAPH 2: (A) Major aesthetic complaints of the population.



GRAPH 2: (B) Motivation for buying cream\* for treating the skin.

■ Included ■ Excluded



GRAPH 1: Persons interviewed in the states of Rio de Janeiro, Sao Paulo, and Santa Catarina.

dry skin, dark circles, cellulite, stretch marks, and hydration, ranging from 5% to 2%; 10.8% bought with a prescription, and 89.2% bought without a prescription.

3) Regarding the composition of products for cosmetic treatment of the skin (Graph 3A):

Percentages: 55.5% did not know the function of any component of the formulation; 28.7% knew the function of only a few the formulation's components; 11% knew the function of most of the formulation's components; 2.4% knew the function of all of the formulation's components.

4) Source from which the creams\* for aesthetic treatment of skin were bought:

Percentages: 57.4% bought from known door-to-door vendors; 20.3% bought directly from dispensing agents; 34.7% bought at pharmacies; 8.7% bought from other sources.

5) Desire to undergo treatments with creams\* to prevent skin aging (Graph 3B):

Percentages: 88.2% expressed a desire to undergo treatments with creams\*; 8.3% did not.

6) Limitations when undergoing treatment with creams\*

(Graph 4):

Price of treatment (59.3%); uncertainty regarding results (36.3%), concern about allergies (22%); other (3.4%); 9.8% answered that nothing limited the treatment.

7) Desire to undergo procedures (botulinum toxin, laser, peels) to prevent skin aging (Graph 5):

Percentages: 67.1% had one or more of these desires; 22.9% did not have these desires; 10% did not answer.

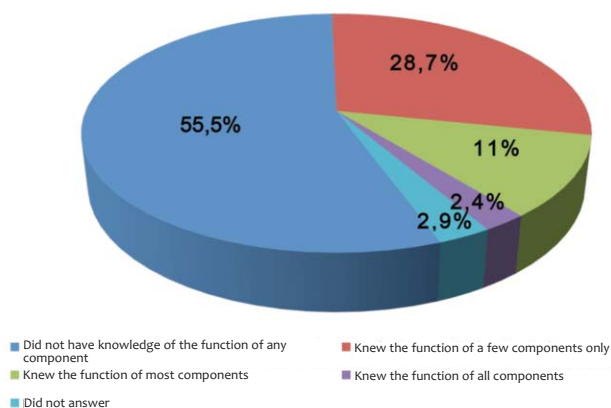
8) Limitations when undergoing these procedures (botulinum toxin, laser, peels) to prevent skin aging (Graph 6A):

Price of treatment (63.8%), uncertainty regarding results; (28.7%), fear of pain (19.1%); other (6.9%). For 8.3% nothing limited the treatments.

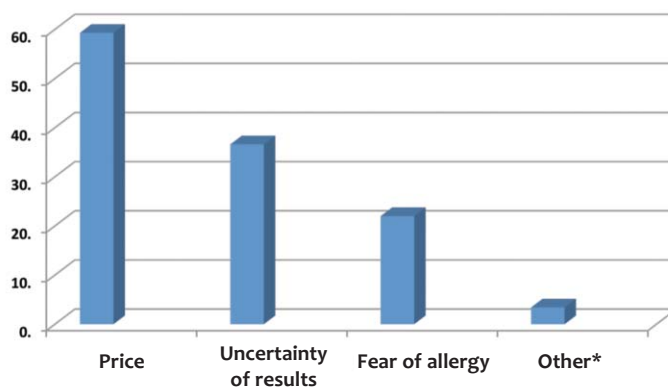
9) Source of information about aesthetic skin treatments (Graph 6B):

Internet (32.4%); beauty magazines (45.3%); medical practices (24.2%); conversations with friends (37.1); other (5.4%).

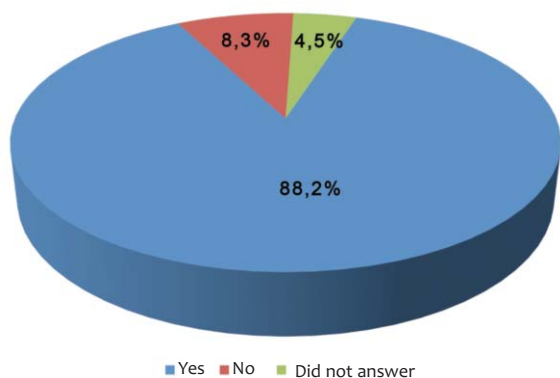
10) Knowledge about dermocosmetic or functional cosmetic products marketed for the treatment of aesthetic skin alte-



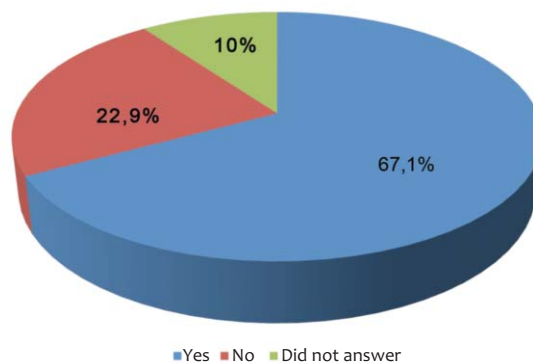
GRAPH 3: (A) Composition of cosmetic products for treating the skin.



GRAPH 4: Limitations to undergoing treatment with creams\*



Graph 3: (B) Desire to undergo treatments with creams\* in order to prevent the aging of the skin.



GRAPH 5: Desire to undergo procedures (botulinum toxin, laser, peelings) to prevent the aging of the skin.



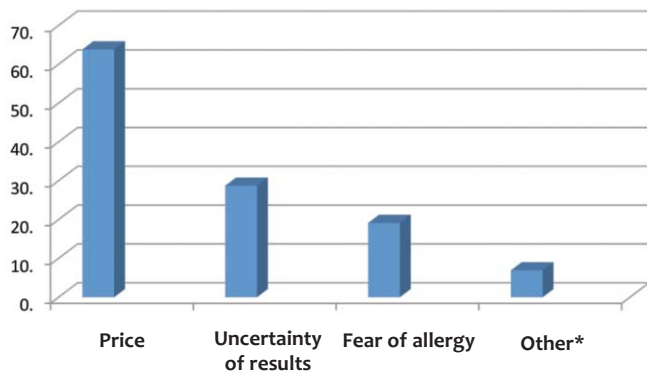


FIGURE 6: (A) Limitations to undergoing procedures (botulinum toxin, laser, peeling) to prevent aging of the skin.

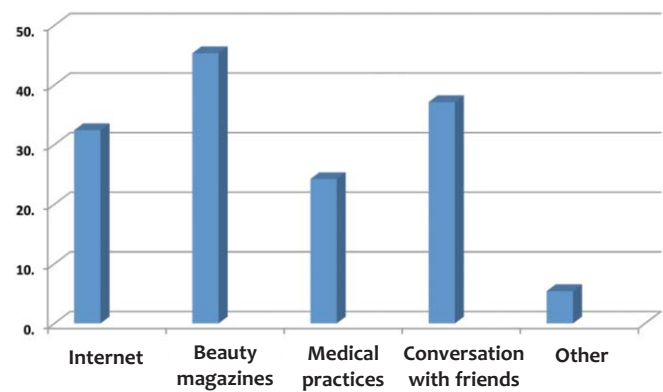


FIGURE 6: (B) Sources of information on aesthetic skin treatments.

rations (an explanation was provided) (Graph 7):

Percentages: 6.7% believed that the products do not work; 14.7% believed that most products work; 51.6% believed that only a few work; 1.3% believed that all function; 21.6% were unaware of functional cosmetics

11) Daily use of sunscreen (Graph 8):

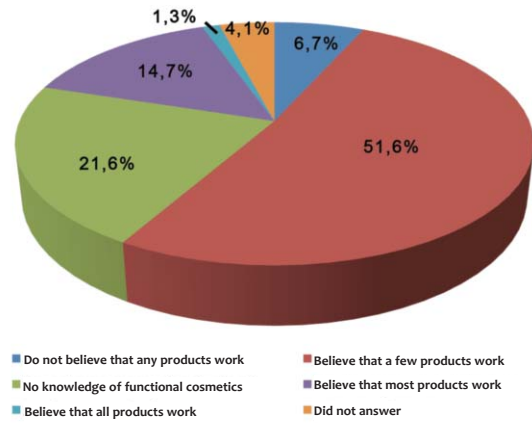
Percentages: 35.6% used sunscreen regularly; 60.2% did not use sunscreen regularly; 4.2% did not answer.

12) Educational level of respondents (Graph 9):

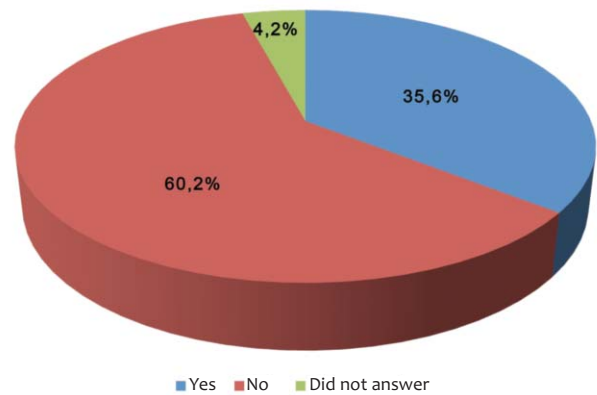
A) Illiterate (-); B) Incomplete primary education (3.1%); C) Complete primary education (3.3%); D) Incomplete secondary education (6.3%); E) Complete secondary education (4.1%); F) Incomplete tertiary education (5.7%); G) Complete tertiary education (38.8%); H) Incomplete higher education; (21%), I) Complete higher education (17.7%).

13) Monthly income of respondents (Graph 10):

A) Up to R\$545.00 (12.6%); B) from R\$545.00 to R\$1,090.00 (41.6%); C) from R\$1,090.00 to R\$1,635.00 (20.5%); D) from R\$1,635.00 to R\$2,725.00 (9.3%); E) from R\$2,725.00 to R\$5,450.00 (2.7%); F) from R\$5,450.00 to R\$10,900.00 (2.9%); G) over R\$10,900.00 (0.93%). 9.47% did not answer.



GRAPH 7: Knowledge of dermocosmetics (an explanation was provided) or functional cosmetics marketed for the treatment of aesthetic skin alterations.



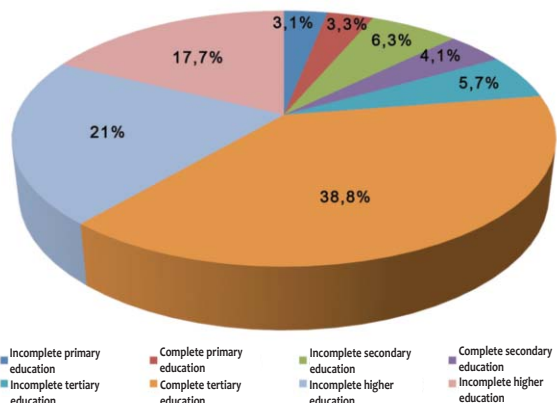
GRAPH 8: Daily use of sunscreen

## DISCUSSION

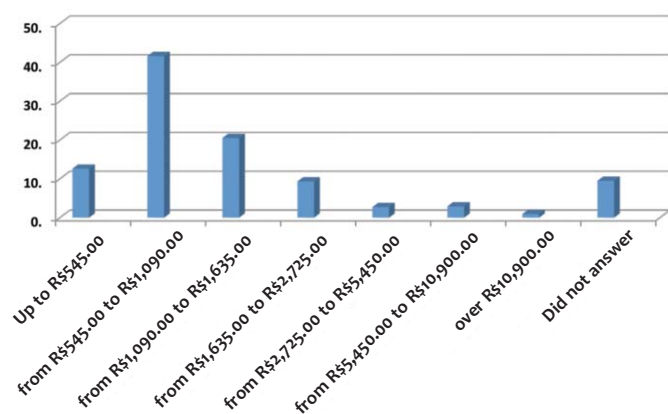
There has been a significant increase in the number of medical cosmetic procedures in the last decade. New products and techniques have been developed, and minimally invasive procedures, such as botulinum toxin injections and dermal fillings, have become popular.<sup>18-21</sup> On the other hand, an additional cost has emerged: the significant increase in complications related to the procedures.<sup>22,23</sup> Contemporary dermatologists should be able to implement procedures in a way that prevents complications.<sup>24,25</sup>

The importance of the correct cosmetic use of creams\* for the skin is due primarily to the search for satisfactory results, with the dermatologist being the professional who is most qualified to indicate them. The present study allows the assessment of the population's understanding of cosmetic dermatology, also providing information on the patients' motivations.

Considering that the percentage of the population that goes to dermatology practices is less than the total number of people who undergo cosmetic skin treatments, the authors chose not to research practices or medical outpatient clinics. Instead, volunteers were selected from the general public in the



GRAPH 9: Education level of respondents



GRAPH 10: Monthly income of respondents

selected cities. Due to the fact that patients in practices have evidently already made a decision for treatments overseen by a physician, a bias in the selection of volunteers was avoided.

When analyzing the study's results, it was possible to note that spots are the main aesthetic complaints of women, ahead of acne and of the wrinkle-aging signs group. However, the percentage of products bought to fight wrinkle-aging signs was higher (59.2%) than that bought to treat spots (37.8%). This data emphasizes the current concept of beauty, which is closely linked to younger-looking skin.<sup>26</sup>

The ratio for the purchase of creams\* without and with a prescription issued by a dermatologist is 9:1, with almost 90% of respondents buying without prescriptions and only 10.8% buying with prescriptions, meaning that the vast majority of aesthetic skin treatments are not overseen by a dermatologist.

The majority of respondents reported not knowing the function of most components of the products they buy. Only 2.4% said they knew the function of all components. Most of the products were bought from well-known vendors (57.4%).

Regarding the patients' motivations, the majority of respondents (88.2%) wanted to undergo topical treatments. The

price of treatments (59.3%) and the uncertainty of results (36.3%) were the most frequently mentioned limiting factors for undergoing topical treatments. Among respondents, 67.1% wanted to undergo some aesthetic procedure. Price was also a major limiting factor for undergoing cosmetic procedures (63.8%), followed by the uncertainty of results and fear of pain.

In the present study, it was possible to observe that beauty magazines were the main sources (45.3%) for respondents, followed by the Internet (32.4%), and lastly by physicians' practices. This confirms several citations about the fact that, with the increase in globalization experienced in recent decades, patterns in beauty trends have begun to be heavily influenced by the media.<sup>27-31</sup>

As for dermocosmetics, functional cosmetics, or cosmetics, 51.6% of the respondents reported to believe that most cosmeceuticals do not work. Another relevant and alarming fact that has arisen, due to its implication in the prevention of diseases such as skin cancer, is that 60.2% of respondents do not use sunscreen regularly.

In the economic and social sphere, there were important changes that have influenced the data collected. The 2010 Brazilian Census has shown that, in ten years, the educational level of women has continued to be higher than that of men, with the first group having gained more space in the labor market. According to the IBGE (the Brazilian Institute of Geography and Statistics), the analysis by age group showed that in 2011 approximately 63.9% of employed women were between 25 and 49 years old, whereas the percentage of people without education or with an incomplete primary education fell to 50.2% from 65.1%.<sup>32,33</sup>

The average real income of men rose from R\$1,450 in 2000 to R\$ 1,510 in 2010. Women saw an increase to R\$ 1,115 from R\$982, meaning real gains of 13.5% for women and 4.1% for men. The earning potential of women increased to 73.8% of the average income of men. In 2000, that percentage was 67.7%.<sup>32,33</sup> Both women and men understand that personal aesthetics are linked to quality of life, health, beauty, and physical and mental well-being. Nevertheless, women's important role in the beauty market is remarkable also due to their increasing access to the labor market.<sup>34</sup> Characterization of groups based on the SES parameters of education level and income appears to be considerably significant, as evidenced by the fact that the study covered all social classes.

Few scientific studies in Brazil focus on the population's knowledge about dermatology. The paper entitled "Dermatological diseases in Brazil: epidemiological and attitudinal profile" (*Doenças dermatológicas no Brasil: perfil atitudinal e epidemiológico*) published in 2010, is a pioneering work in which the perception of the lay public, their habits, and attitudes were evaluated in light of various dermatologic pathologies.<sup>35</sup>

As already mentioned, the objectives of the authors of the present study are to identify in the public's perceptions the major cosmiatric alterations—rather than pathologies—of the

skin, to list difficulties for the realization of dermatologic cosmetiatric treatments, and to find out which sources of information are consulted by the population. It is important to highlight the fact that although the present study was carried out only with female patients (unlike the research carried out by Lupi et al. who also addressed the male population) 35 both studies showed similar results, since some diseases were cited by respondents as aesthetic or cosmetiatric alterations—a fact which confirms and strengthens the consistency of the data presented.

In the study by Lupi et al., pigmentation disorders were the main single cause for a medical consultation for both genders, comprising slightly more than a quarter of consultations (27.6%). Forty percent are divided more or less evenly between allergies, mycoses, and acne, with a slight predominance of mycoses in the male subgroup and allergies in the female subgroup. Moreover, superficial infections, warts and scars stand out in the male subgroup. In the female subgroup, stretch marks/cellulite and wrinkles make up almost all consultations.<sup>35</sup>

In the present study, the pigmentation disorder referred to as “spots” by the patients, was also the population’s main cosmetiatric complaint. In both studies acne was the second most frequent complaint. The group wrinkles-signs-rejuvenation occupied third place, followed in descending order by stretch marks, warts and moles, cellulite, and scars. Mycoses and allergies amounted to a small percentage in the research on cosmetiatry. The opinion of the authors is that the majority of patients have recognized these entities as pathologies and not as aesthetics.

## CONCLUSIONS

Consulting with a dermatologist is of paramount importance, for doubts can be elucidated and patients who have become disbelievers due to ineffective and unassisted treatments, can be guided. It was also concluded that the Brazilian Society of Dermatology should take action in the media, such as printed media, Internet and television in the cosmetiatric field, in which there is biased and unsubstantiated information. ●

\*NOTA: A expressão “cremes” foi usada genericamente para todo produto de uso tópico, pois foi o termo que menos gerou confusão nos testes prévios à aplicação dos questionários.

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# Facial topography of the injection areas for dermal fillers, and associated risks

*Topografia facial das áreas de injeção de preenchedores e seus riscos*

## Authors:

Bhertha M. Tamura<sup>1</sup>

<sup>1</sup> Dermatology Coordinator, Ambulatório Médico de Especialidades Barradas—São Paulo (SP), Brazil

## Correspondence:

Dr. Bhertha M. Tamura  
Rua Ituxi, 58 / apt. 603  
Cep: 04055-020—São Paulo—SP, Brazil  
E-mail: bhertha.tamura@yahoo.com.br /  
bhertha.tamura@uol.com.br

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## ABSTRACT

**Introduction:** Filling techniques are an important procedure in modern therapeutic approaches to rejuvenation, and are currently in wide use.

**Objective:** To assist the practice of dermal filling procedures and reduce associated risks.

**Method:** Division of the face into 22 regions in which filling procedures are indicated, providing detailed description of the nervous and vascular structures of each.

**Results:** This didactic, practical, and detailed new division of the regions of the face highlights the possible risks related to anatomical features, thereby facilitating implementation, and reducing the risks and complications of filling techniques, such as the widely-feared amaurosis and tissue necrosis.

**Conclusion:** Only a thorough knowledge of facial anatomy enables the safe realization of dermal filling procedures.

**Keywords:** anatomy; risk zone; face.

## RESUMO

**Introdução:** As técnicas de preenchimento constituem importante procedimento na moderna abordagem terapêutica do rejuvenescimento, sendo largamente utilizadas na atualidade.

**Objetivo:** Auxiliar a prática dos preenchimentos e diminuir seus riscos.

**Método:** Divisão da face em 22 regiões nas quais se indicam preenchimentos, com descrição detalhada das estruturas nervosas e vasculares de cada uma.

**Resultado:** Essa nova divisão didática, prática e pormenorizada das regiões da face, evidenciando os possíveis riscos ligados às características anatômicas de cada região facilita a execução e diminui riscos e complicações das técnicas de preenchimento, tais como a tão temida amaurose e necroses teciduais.

**Conclusão:** Só o conhecimento profundo da anatomia facial permite a realização de preenchimentos com segurança.

**Palavras-chave:** anatomia; zona de risco; face.

**INTRODUCTION**

The classification of the face according to risk zones, when studying dermatologic surgery, can serve as a reference tool and assist in the new therapeutic rejuvenation practice of cutaneous facial filling. However, having only a generic, basic knowledge of anatomy might be insufficient and gives rise to doubts during the performance of this technique—especially regarding the areas and depth of injections.<sup>1-4</sup> The injection of fillers in the superficial layers of the skin, excepting the glabellar region, presents minimal risk. However, filling techniques have evolved and in most current cases the procedures are performed in the hypodermis and even in the supraperiosteal plane. In an attempt to better guide dermatologists and minimize complications, the present study is aimed at proposing a new didactic and practical classification of facial regions for implementing filling techniques, highlighting possible risks linked to specific anatomical features.<sup>5-12</sup>

**METHOD**

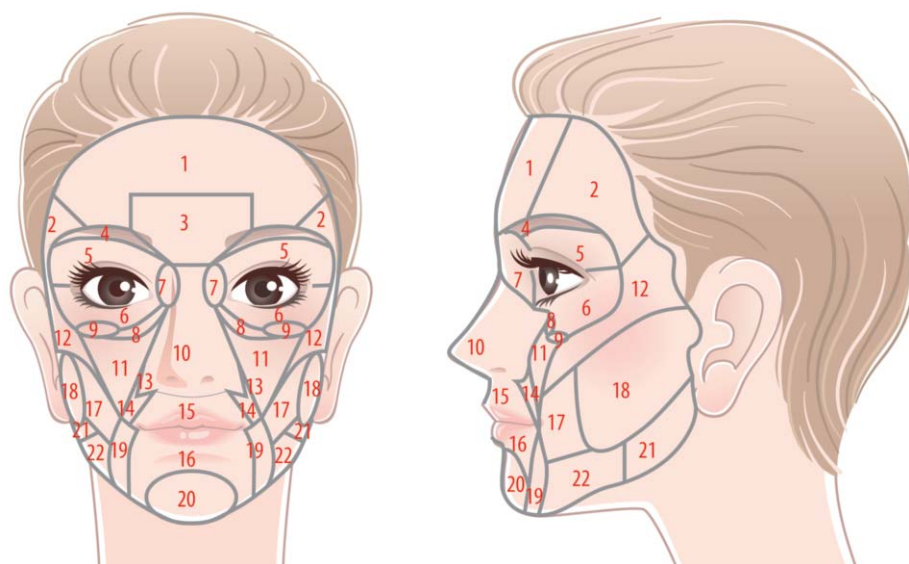
As opposed to what has been described in the literature, the face was divided into 21 regions, with a view to adjusting the areas where fillings are performed: frontal (1), temporal (2), glabellar (3), eyebrow (4), upper eyelid (5), lower eyelid (6), nasociliary (7), nasojugal sulcus (8), eyelid lateral sulcus (9), nasal (10), malar (11), zygomatic (12), canine fossa (13), nasolabial sulcus (14), upper lip (15), lower lip (16), cheek (17), preauricular (18), labiomental sulcus (19), mentonian (20), posterior mandibular region (21), (anterior border of the masseter up to the angle of the jaw) and anterior mandibular region (between the melolabial fold and the anterior border of the masseter). The boundaries of these areas are shown in figure 1, followed by a detailed description of each region.<sup>13-18</sup>

**FRONTAL REGION (1)**

This area was delimited excluding the glabella. An imaginary line was drawn above the eyebrow, originating in the mid pupillary regions and bilaterally reaching the hairline. It is important to note that when located on osseous structures, this area of skin, subcutaneous tissue, and muscle is relatively thin. Any filler injected in this region might result in lumps or a visibly linear texture. It is important to bear in mind that the aponeurosis of the frontal muscle—or that of the galea—begins at the level of the scalp’s border.

**TEMPORAL REGION (2)**

The temporal region has the mid pupillary line as a border in its cranial portion; the hair implantation line, in its lateral portion; a line passing above the eyebrows that extends and outlines the lateral orbital border; finally closing with the zygomatic arch as a reference for the lower border. This region presents risks due to the presence of the superficial temporal artery, in addition to the nerve and veins. The injection of dermal fillers in the dermis of this area would present low risk, however, the subcutaneous injection of substances may cause not only lesions in the veins (with hematoma or ecchymosis formation), but also in the nerve, if the procedure were to be performed in an intempestive manner. The structure that calls for the most attention is the temporal artery; its channeling and the intravascular injection of fillers can lead to tissue necrosis and embolization of the product, and may even cause amaurosis, as occurs with several other arterial branches in the upper region of the face due to the presence of anastomoses between superficial and deep arteries. In general, cutaneous fillings in this area can be carried out in the dermis, subcutaneous, or supraperiosteal planes. When a choice is made to fill the subcutaneous area, it is important to pay attention to the demarcation of the visible



**FIGURE 1:** frontal (1), temporal (2), glabellar (3), eyebrow (4), upper eyelid (5), lower eyelid (6), nasociliary (7), nasojugal sulcus (8), eyelid lateral sulcus (9), nasal (10), malar (11), zygomatic (12), canine fossa (13), nasolabial sulcus (14), upper lip (15), lower lip (16), cheek (17), preauricular (18), labiomental sulcus (19), mentonian (20), posterior mandibular region (21) = (anterior border of the masseter up until the angle of the jaw) and anterior mandibular region (between the melolabial fold and the anterior border of the masseter).

venous tree as well as of the arteries. When the injection is carried out in supraperiosteal planes, the risks of vascular channelling are lower, especially in the temporal fossa.

### **GLABELLAR AND EYEBROW REGIONS (3 AND 4)**

The limits of the glabellar region are: the superior area of the nasal dorsum and the medial portion of the eyebrow (inferiorly), and the line that links the 1.5 cm segments of the mid pupillary line in the cranial direction (superiorly). The eyebrow region corresponds to the region with hair, going along the eyebrow up until its lateral portion, where there is the possibility for cutaneous filling. The supraorbital artery (which arises through the supraorbital foramen and originates from the internal carotid artery) and the supratrochlear artery (a branch of the facial artery) must also be considered. Currently, it is no longer advisable to inject products for filling wrinkles or scars in the glabellar region, due to the possibility of arterial embolism with consequent amaurosis. In this region—as in the temporal region—there are arteries that can be anastomosed and have their blood flow directed to terminal arteries, such as the ophthalmic and retinal arteries. The embolization of these vessels can lead to immediate and irreversible amaurosis, which can even be bilateral. In addition to taking care not to channel the arteries, it is important to pay attention and avoid deep injections in the area of the supraorbital and supratrochlear foramina, preventing the ischemia of the structures that arise in this site. In addition to the treatment of the medial and lateral portions of the eyebrow, there is also the possibility that fillers can be injected in the medial portion (nasociliary region) for the treatment of epicanthus, bearing in mind that this area is not devoid of risks.

### **UPPER EYELID (5)**

The description of this area is especially important due to the fact that injections of fillers have been carried out throughout its upper portion (just below the eyebrow) aimed at correcting the “skeletonized gaze”. More specifically, through attempting to also correct the deficiency of the fat pad in that region and/or the loss of support that characterizes a “deep” gaze. The upper eyelid artery, in continuity with the angular artery, irrigates this area. There is little local supporting tissue, with the presence of skin and of the orbicularis oculi muscle, and below, the fat pads and the lacrimal gland, with the possibility of vascular accident.

### **LOWER EYELID, NASOJUGAL SULCUS (LACRIMAL GROOVE) AND NASOCILIARY REGION (6, 7 AND 8)**

There is indication for the correction of this region after a negative aesthetic result following the removal of fat pads in eyelid surgery, loss of support of the entire lower eyelid's orbital rim, or exacerbation of the medial, lower and/or lateral palpebromalar sulcus due to family characteristics. There is a close relationship between the lower eyelid area and the nasojugal sulcus (medial portion that goes along the medial inferior orbital rim) and the nasociliary region. It is important to pay attention to the anatomy of these regions and to consider them jointly.

Part of the angular artery, the inferior palpebral artery and the infraorbital artery (which unites with the dorsal nasal artery) are located underneath these areas, giving rise to the risk of tissue necrosis or embolism. When carrying out filling injections in these areas, the planes that bear lower risk of complications would be the muscular and the supraperiosteal—for the vessels are located under the skin and over the orbicularis oculi muscle. The procedure must be performed with delicacy and precision, either with cannulas or needles.

### **LATERAL PALPEBRAL SULCUS (9)**

It is located in the lateral portion of the lower eyelid, over the lateral inferior orbital rim. In this area, attention must be paid to the temporomaxillary vein, which lies under the skin (often visible when the skin is translucent) and crossing almost perpendicularly the infraorbital rim, between its medial region and lateral third. Its prior identification prevents complications such as echymoses and hematomas.

### **NASAL REGION (10)**

Some details must be taken into account when patients undergo nasal sculpture:

The dorsal nasal artery lies in the subcutaneous tissue, on a plane under the skin and over the dorsal nasal muscle, and can have branches that anastomose with the infraorbital and angular arteries.

Patients who have undergone rhinoplasty surgery concomitant with surgery in the septal region, might have had their blood supply compromised.

Reconstructive plastic or cosmetic surgery can greatly alter the vascularization of the nasal tip, nostrils, columella, and canine fossa, and it is possible that an embolization could affect the angular arteries. The manipulation of ethmoid arteries during surgical procedures increases the risk of occlusive vascular accidents.

The columella and lateral nasal branches irrigate the nasal ala, dorsum, and apex (tip). The lateral nasal veins are 2 or 3mm from nasal alar fold, and as the artery of the columella, arises deeply in the nasal base, ending at the tip, in the subdermal plexus. Fillings in this region—especially those used to sharpen, lengthen and minimize the nostril in an attempt to create a more Caucasian nasal profile for patients of African heritage—require lateral and deeper injections, as well as higher volumes, both conditions that increase the risk.

### **MALAR REGION (11)**

It is an infrapalpebral triangular area, limited medially by the nasal region up to the lower portion of the nasolabial fold, and from that point, by an imaginary line up until the zygomatic arch. The analysis of this area must consider the anatomical details described for the nasociliary region and lacrimal nasojugal sulcus, since its correction is many times carried out concomitantly with the treatment of these other regions.

The malar region is nourished by branches of the angular artery (facial/external carotid) and by another that arises

through the infraorbital foramen (branch of the internal carotid artery), together with the vein and the sensory neural system of the infraorbital nerve. When a choice is made for retrograde injection, the planes and location for the product can be well controlled. On the other hand, the bolus injection technique, when performed in an intempestive manner, especially with an aim at reconstituting volume in the supraperiosteal region, can lead to obstruction of the infraorbital foramen, and damage of the vasculature, possibly even resulting in neural necrosis. In this region there is a thick layer of subcutaneous tissue and fat. The mid-subcutaneous plane—which marks the transition between its looser and its denser part—is characteristic of this region and makes the injection of fillers safe, because the important neural structures are located at deeper levels and the main vessels go along the lateral line of the nasal region.

### ZYGOMATIC REGION (12)

As the nomenclature itself suggests, the zygomatic region is located laterally to the malar region, below the temporal region and anterior to the preauricular region. Its main structure is the zygomaticofacial nerve (branch of the trigeminal nerve) that emerges from the foramen located in the mid-lateral portion of the zygomatic bone. The considerations are similar to those related to the injection of fillers with consequent obstruction of the foramen. There is an important artery complex in deeper planes. The zygomatic palpebral vein is also located in this region and is most often visible with the stretching of the skin.

### CANINE FOSSA (13) AND NASOLABIAL FOLDS (14)

With the current technique for volumetric repair of the malar region, the canine fossa region and the nasolabial sulcus have been filled less frequently and with smaller volumes, reducing the risks. Nonetheless, there are several reports of necrosis in this region, including the nasal ala, nasal dorsum, and part of the paranasal region. The two main causes of this complication are the embolization or compression of the artery due to the great amount of product injected and, possibly, intempestive technique. Anatomical variations are very common and must always be considered when analyzing the anatomy of the face. The main blood vessels are the angular arteries and part of the superior labial artery, which may also be compromised depending on the portion of the nasolabial fold where the filler is injected.

### LOWER AND UPPER LIP (15 AND 16)

The arteries that irrigate the lips are the upper and lower lip arteries (branches of facial artery) that anastomose with those on the opposite side, forming an arterial circle around the rhyme of the mouth. The position of the arteries is unfavorable to the current techniques used to enhance the volume of and the convex shape of the lips. When performed on a superficial plane—in the skin, mucosa, or at the junction of the skin and mucosa—the lip contour injection brings few complications.

The labial arteries are curved and undulated, and therefore can be transfixed. In the anteroposterior view, they are loca-

ted in a posterior position to the orbicularis oris muscle, and are relatively superficial in the projection of the boundary between the wet and dry mucosae of the lips. This is the region of choice for many professionals to inject the filler when aiming at obtaining anterior projection and volume of the lips. Hematomas are frequent due to the absence of a firm tissue to contain arterial bleeding. As a result, compression of the vessel transfixed during the procedure must be firm and prolonged (three minutes or more). Cold compresses are useful.

### Cheek (17)

Corresponds to a free, “loose”, and unfixed region that is located up to the 1cm point laterally to the angle of the mouth. It is inferior to the zygomatic region, anterior to the pre-auricular region, inferior to the pre-mandibular region (“pre-jowl”) and lateral to the malar region.

The arterial branches originate from the facial artery that runs into the lips and around the nasal region (angular artery), including part of the parotid duct, distributed in this region. The loss of volume is common in individuals who practice sports intensely and frequently, can be constitutional, can be caused by ingestion of drugs, or by consumptive diseases. It is often the only area that needs correction.

### PRE-AURICULAR REGION (18)

It is an area posterolateral to the cheek border. It includes the zone that goes from a point 2cm anterior to the tragus muscle up until the same muscle. The superior limit is the zygomatic region, and the inferior limit is the zone of the mandibular angle 1.5 cm from the posterior mandibular border. In this region, in a point near the tragus, the facial nerve that innervates the various structures/regions of the face arises. There are deep vascular branches originating from the internal carotid artery, nevertheless the structure of greatest importance is the parotid gland, which lies under the subcutaneous tissue. Therefore, the filling of this region is carried out only in the skin and subcutaneous tissue. Between this region and the cheek, roughly one-third anterior to the angle of the mandible (between the anterior and posterior mandible), runs the path of the facial artery, which at this point is already branching and distributing into the perioral region, and a few others into the pre-tragus area.

### LABIOMENTAL SULCUS (19)

The labiomentale sulcus comprises a band that covers the area between the lateral angle of the mouth up to a point 1cm lateral to it (the lateral angle of the mouth). It runs caudally up until the mandibular border. In addition to the arterial branches that supply the upper and lower lips, this region presents an important superficial venous vasculature, with large diameter vessels. This vasculature can often be seen when distending the skin of patients with thin skin and phototypes I or II. Often there is ecchymosis and, not infrequently, hematoma, due to the fact that this portion is free and there are no compartments or boundaries that may contain the bleeding. In this site, transfixed vessels must receive firm compression for a few minutes.



### MENTONIAN REGION (20)

The mentonian region does not present risky structures, however the mental foramen may suffer inadvertent injection of filling substance with the compromise of the structures that run through this area. The localization of these structures is roughly made using the mid pupilar line—which is used to localize the main sensory foramina of the face. The arterial branch of the lower lip can be found in the labiomental sulcus region. The first crosses the region and venous system, which due to its proximity to the drainage system becomes more calibrous, with frequent presence of hematomas or ecchymoses.

### POSTERIOR MANDIBULAR REGION (21)

The posterior mandibular region, situated between the anterior border of the masseter and the angle of the mandible, was delimited as a risk zone. Close to the anterior border of the masseter, in the mandibular bone, a depression can be found where the facial artery lies. This depression is created throughout a patient's life by the artery pulsating on the bone. Therefore, due to the fact that fillers are injected into the skin or subcutaneous tissue, they usually do not cause trauma to it. Nonetheless, aggressive procedures performed without anatomical knowledge, can result in serious arterial lesions.

### ANTERIOR MANDIBULAR REGION (22)

This region is located 1cm posterior to the melolabial sulcus (as the labiomental region was delimited for didactic purposes) and the anterior border of the masseter, representing the region called “pre-jowl” or “bulldog”. This leaves free 1cm of the labiomental area, where fillers can be applied for the improvement of the facial contour. It does not present high risk structures, but in general filling procedures are not carried out in this area due to the fact that worsening of local sagging may occur, with the possibility of the weight of the filling substance causing a negative outcome when the objective is to obtain a rejuvenating facial contour.

### CONCLUSION

Only a detailed knowledge of facial anatomy can allow the professional to carry out procedures safely. Correlating different areas with procedural risks can be useful for the physician when starting to work with fillers. It is important to note, however, that the present study does not suggest a new anatomical classification, but only a segregation of facial regions that are usually treated with cutaneous fillers in order to analyze them in isolation. ●

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# Optical coherence tomography in the diagnosis of basal cell carcinoma

## Tomografia de coerência óptica no diagnóstico do carcinoma basocelular

### ABSTRACT

Early diagnosis of basal cell carcinoma—a cutaneous neoplasia with high incidence—can bring great benefits to the patient. Often, slightly pigmented lesions, small initial lesions, and superficial lesions can represent a clinical and dermoscopic diagnostic challenge for not having the typical findings of this neoplasia. In such cases, optical coherence tomography—a promising technology in dermatology—is an auxiliary, non-invasive resource that can be incorporated into the clinical practice.

**Keywords:** basal cell carcinoma; diagnostic imaging; optical coherence tomography.

### RESUMO

*O diagnóstico precoce do carcinoma basocelular, neoplasia cutânea de alta incidência, pode trazer grandes benefícios ao paciente. Muitas vezes lesões pouco pigmentadas, lesões iniciais pequenas e lesões superficiais podem representar um desafio diagnóstico clínico e dermatoscópico por não apresentar os achados típicos dessa neoplasia. Nessa situação, a tomografia de coerência óptica, tecnologia promissora na dermatologia, é recurso auxiliar não invasivo que pode ser incorporado à prática clínica.*

**Palavras-chave:** carcinoma basocelular; diagnóstico por imagem; tomografia de coerência óptica.

### INTRODUCTION

Basal cell carcinoma (BCC) is the most common malignancy in the fair-skinned Caucasian population. Its morbidity results from the invasion and destruction of local tissues, rarely causing metastases. Epidemiological data show increasing incidence, even affecting young people.<sup>1</sup> The importance of early diagnosis is in its value for targeting the best treatment option, leading to less operative morbidity, lower costs, lower recurrence rates, and better patient prognosis. Often easy to identify at a clinical examination, BCC is difficult to diagnose—especially in early, small, and superficial lesions.

In the last two decades there has been a progressive increase in the number of non-invasive techniques to assist in the early diagnosis of skin lesions, such as dermoscopy, *in vivo* confocal microscopy, and optical coherence tomography (OCT),<sup>2</sup> a promising imaging diagnostic technique, which provides images of the morphology of biological tissues *in vivo* and in real time with micro-resolution power. It was first described

## Diagnostic imaging

### Authors:

Elimar Elias Gomes<sup>1</sup>  
Tatiana Cristina Moraes Pinto Blumetti<sup>1</sup>  
Mariana Petaccia de Macedo<sup>2</sup>  
Marcela Pecora Cohen<sup>3</sup>  
Maria Dirlei Bergami<sup>2</sup>  
Gisele Gargantini Rezze<sup>1</sup>

<sup>1</sup> Assistant Dermatologist Physician, Skin Cancer Nucleus/Nucleon, A.C. Camargo Cancer Center—São Paulo (SP), Brazil

<sup>2</sup> Assistant Pathologist Physician, Department of Pathologic Anatomy, A.C. Camargo Cancer Center

<sup>3</sup> Assistant Radiologist Physician, Department of Radiology, A.C. Camargo Cancer Center

### Correspondence:

A.C. Camargo Cancer Center—Núcleo de Câncer da Pele  
Dr. Elimar Elias Gomes  
R. Professor Antonio Prudente, 211—Liberdade  
Cep: 01509-900—São Paulo—SP, Brazil  
E-mail: egomes.dermato@uol.com.br

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in dermatology by Welzer et al. (1997) and has since been offering advances in technical and image resolution.<sup>3</sup> This technology is based on the physical principle of interferometry, and its functionality is analogous to that of the ultrasound. However, with this technology the ultrasound pulses are replaced by a low-coherence source of light, with a wavelength of 1,300nm (close to infrared frequency). An optical system allows for the acquisition of images—in black and white, in two or three dimensions, and perpendicular to the skin’s surface—similar to those obtained by histology, and without causing harm to the patient.<sup>3,4</sup>

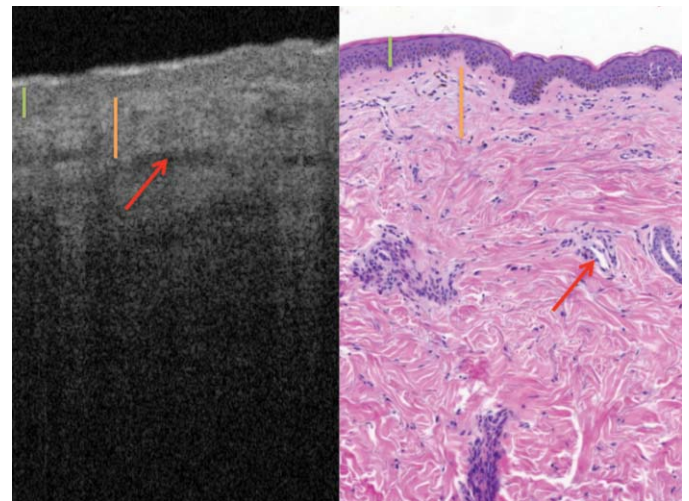
**CASE REPORT**

A thirty-eight-year-old female patient, phototype 3, complained of an erythematous lesion in the right sternum region, which had arisen six months before. At the examination, she showed an erythematous, shiny scaly plaque, roughly 7.0 mm in diameter. Through dermoscopy, a lesion with rosy background, no evident pigmentation, and the presence of short linear vessels distributed throughout the lesion could be observed (Figure 1). Based on the clinical and dermoscopic aspects, the main diagnosis was that of a superficial BCC. In the absence of conclusive dermoscopic criteria for the diagnosis of BCC, the differential diagnoses of actinic keratosis, squamous cell carcinoma in situ, and dermatosis of inflammatory character could not be discarded. In an attempt to elucidate the case, the authors decided to carry out an optical coherence tomography using the OCT Vivosight® device (Michelson Diagnostics, Orpington, England, UK). During this examination, unlike the normal structure of the skin shown in Figure 2, they observed a complete disorganization of the dermal-epidermal junction (Figure 3). In some areas it was possible to observe hyporeflective blocks (darker) contiguous with the epidermis and projecting towards the superficial dermis (Figures 4 and 5). It was still possible to identify hyporeflective areas modifying the structure of the

papillary dermis, which can correspond to inflammatory infiltrate. It was also possible to identify dark linear areas in the reticular dermis that correspond to vascular proliferation (Figure 5). In light of these findings, which were consistent with the description of BCC already published in the literature, the patient underwent surgical excision of the lesion with safety margins. The anatomical pathological examination confirmed the superficial BCC diagnosis, free of neoplastic involvement of resection margins.

**DISCUSSION**

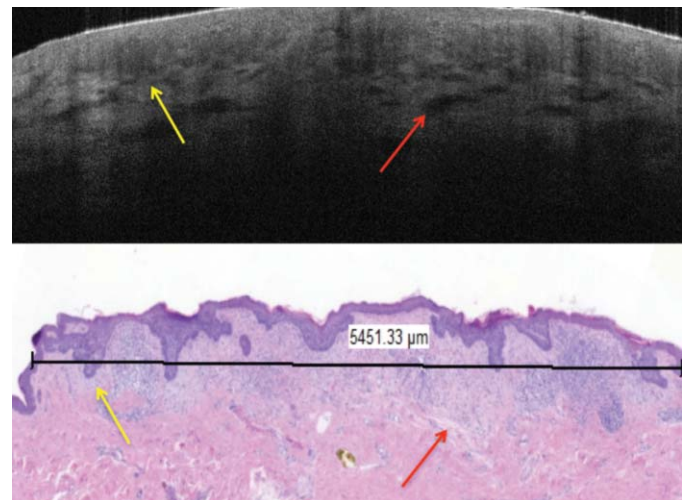
Inexpensive, easy to perform, and widely disseminated, dermoscopy has become an indispensable tool for dermatologi-



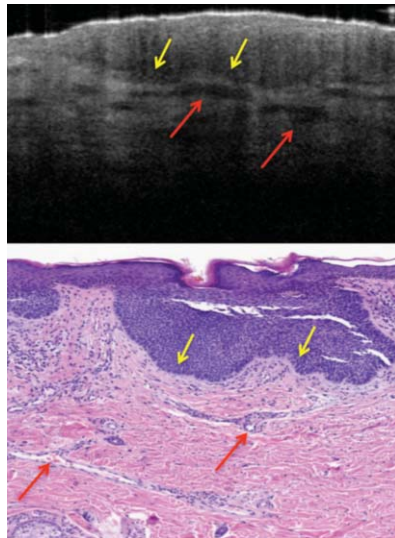
**Figure 2:** Normal skin adjacent to the lesion. Comparative images of optical coherence tomography (left) with histology. The green line represents the thickness of the epidermis, and the orange line delimits the area corresponding to the papillary dermis (hyperreflective by the collagen bundles). In the tomography image, the red arrow indicates a linear hyporeflective area corresponding to a blood vessel.



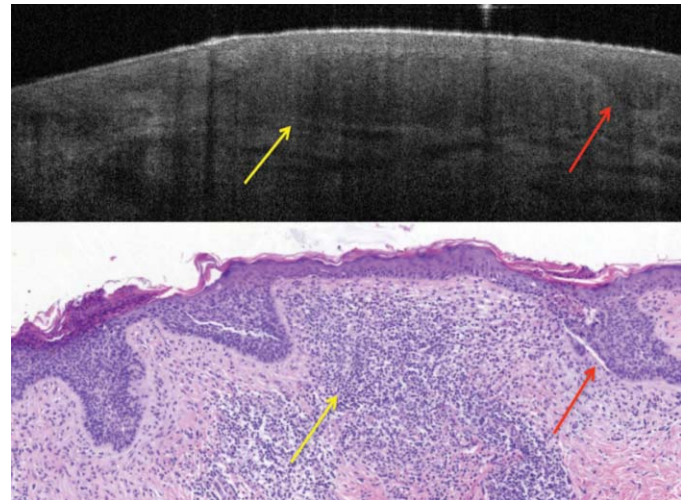
**FIGURE 1:** Clinical photograph and dermoscopy (polarized light dermatoscope with contact—Dermlite II Pro-HD 3Gen).



**FIGURE 3:** Superficial BCC—panoramic view comparing optical coherence tomography and histology images. The yellow arrow shows the loss of definition of the dermal-epidermal junction. The red arrow shows blood vessels in the reticular dermis.



**FIGURE 4:** Superficial BCC. Histologically, it is possible to observe the proliferation of basaloid cells in more detail—observed in the optical coherence tomography as a darkened (hyporeflective) well-defined area, starting from the corresponding area of the epidermis and invading the papillary dermis. In the histology, yellow arrows show the peripheral palisade typical of this tumor and the evident delimitation of the normal epidermis and tumor block. Red arrows show a blood vessel in the reticular dermis.



**FIGURE 5:** Superficial BCC. The proliferation of basaloid cells is observed in greater detail in the optical coherence tomography and histology images (red arrows). Yellow arrows show inflammatory infiltrate seen as a granulated hyporeflective area (darker when compared to the epidermis) separated from the epidermis by a band of collagen (hyperreflective, white area) from the papillary dermis.

cal evaluation, promoting a significant increase in the sensitivity of the clinical examination for early detection of various cutaneous neoplasias.<sup>2</sup>

In 2000, Menzies et al. developed a model for the dermoscopic diagnosis of pigmented BCC that showed a sensitivity of 97% and a specificity of 93%.<sup>5</sup> This model was based on the absence of a pigmentary network and the presence of at least one of the following dermoscopic features: ulceration, large blue-grayish ovoid nests, multiple blue-grayish globules, leaf-shaped areas, wheel spokes areas and arboriform telangiectasia. In 2010, Altamura et al. retrospectively studied 609 cases of various histological subtypes of BCC, pigmented or not, and assessed the variability and diagnostic relevance of diverse dermoscopic findings.<sup>6</sup> In that study, the findings reported by Menzies were deemed classic BCC dermoscopic patterns, with other dermoscopic findings, called non-classic, having been included.<sup>5,6</sup> The findings described as non-classic were very short, superficial telangiectasias, small multiple erosions, concentric structures, and nests of multiple blue-grayish dots.<sup>6</sup> In this context, lightly pigmented, initial and superficial BCC lesions may represent a clinical and dermoscopic diagnostic challenge due to the fact that they do not present dermoscopic findings typical of BCCs.

The OCT is a non-invasive, quick, and easy to perform examination. Images obtained are perpendicular to the skin, similar to the standard histological specimens, which facilitates interpretation. Widely used in other medical areas such as oph-

thalmology, cardiology, and gastroenterology, this new technology has only recently been introduced in dermatology. Nevertheless it has already yielded promising results in the differential diagnosis of non-melanoma cutaneous tumors.<sup>3,4</sup>

The first studies on the pattern of BCC images in optical coherence tomography are recent and show a loss of the normal architecture of the different skin layers and structures resembling hyporeflective tumor blocks (darker when compared to epidermal tissue) surrounded by dark silhouettes (linear areas close to the black color). These findings were correlated with histology, corresponding to basaloid tumor cells blocks, characteristic of this neoplasm. The dark silhouettes correspond to the slit surrounding the tumor blocks, and the presence of a white band encircling the darkened lobes corresponds to the tumoral stroma.<sup>4,7-9</sup>

In a study carried out by Mogensen et al., the main features observed in tomography's images of BCC were the loss of lamellar structure in the epidermis (mainly in the superficial BCCs), focal alterations of the epidermis with white striae and dots in some lesions, and lobular grayish or darkened structures surrounded by whitish borders.<sup>10</sup>

In the present case, the OCT showed findings consistent with those described in the literature for this new technology. This fact indicates the reproducibility of the examination, the good histological correlation and, more importantly, it has brought benefits to the patient since it avoids incisional biopsy, reducing costs and streamlining the definitive treatment. ●

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# Anatomy of the periorbital region

## Anatomia da região periorbital

### ABSTRACT

A careful study of the anatomy of the orbit is very important for dermatologists, even for those who do not perform major surgical procedures. This is due to the high complexity of the structures involved in the dermatological procedures performed in this region. A detailed knowledge of facial anatomy is what differentiates a qualified professional—whether in performing minimally invasive procedures (such as botulinum toxin and dermal fillings) or in conducting excisions of skin lesions—thereby avoiding complications and ensuring the best results, both aesthetically and correctively. The present review article focuses on the anatomy of the orbit and palpebral region and on the important structures related to the execution of dermatological procedures.

**Keywords:** eyelids; anatomy; skin.

### RESUMO

*Um estudo cuidadoso da anatomia da órbita é muito importante para os dermatologistas, mesmo para os que não realizam grandes procedimentos cirúrgicos, devido à elevada complexidade de estruturas envolvidas nos procedimentos dermatológicos realizados nesta região. O conhecimento detalhado da anatomia facial é o que diferencia o profissional qualificado, seja na realização de procedimentos minimamente invasivos, como toxina botulínica e preenchimentos, seja nas exéreses de lesões dermatológicas, evitando complicações e assegurando os melhores resultados, tanto estéticos quanto corretivos. Trataremos neste artigo da revisão da anatomia da região órbita-palpebral e das estruturas importantes correlacionadas à realização dos procedimentos dermatológicos.*

**Palavras-chave:** pálpebras; anatomia; pele.

### INTRODUCTION

To have a comprehensive knowledge of palpebral and orbital anatomy may sound excessive for dermatologists, given that they do not perform procedures in the deep levels of the ocular and orbital region. However, in light of the remarkable advances in procedures that encompass the orbital region, it has become important to recognize the crucial role of anatomical knowledge in ensuring better outcomes. Following are the main structures that make up the anatomy of the orbitopalpebral region:

#### Structures of the orbitopalpebral anatomy:

- Bone margins
- Innervation
- Irrigation
- Skin and subcutaneous tissue
- Musculature
- Orbital septum
- Fat pads

## Review article

### Authors:

Eliandre Costa Palermo<sup>1</sup>

<sup>1</sup> Dermatologist Physician, *Lato sensu* post-graduate diploma in Dermatologic Surgery from the Faculdade de Medicina do ABC - Santo André (SP), Brazil

### Correspondence:

Dr. Eliandre Costa Palermo  
Av. São Gualter, 615  
Cep: 05455 000 Alto de Pinheiros—São Paulo—SP, Brazil  
E-mail: eliane.palermo@uol.com.br

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## BONE MARGINS

The main function of the orbit is to give support and protection to the eyeball and its structures.

The volume of the orbital cavity of an adult is approximately 30cc. The border of the orbit measures about 40mm horizontally and 35mm vertically.<sup>1</sup> Due to the fact it is a compartment with a fixed cavity that cannot be widened, bleeding in the region may increase eye pressure and lead to disastrous consequences.

The orbit is composed of seven bones: ethmoid, sphenoid, zygomatic, frontal, maxillary, lacrimal, and palatine, which anastomose to form an osseous quadrilateral in the shape of a pyramid.<sup>1,2</sup>

The upper portion of the orbit is formed by the orbital process of the frontal bone, and the lesser wing of the sphenoid. At about 2.5 cm from the midline, a small notch in the bony edge can be felt through palpation: the supraorbital notch (supraorbital foramen in 25% of cases).<sup>3</sup> It passes through the eyebrow arch on the midpupillary line about a third of the distance from the medial aspect of the orbital margin. The supraorbital artery and nerve pass through it.<sup>2,3</sup> Right above and parallel to the supraorbital margin is the superciliary arch, which sits just below the eyebrow and above the frontal sinus passage. This is more prominent in men and often absent in women, frequently contributing, in the latter, to the sagging of the eyebrows in their lateral portion.<sup>3</sup> Subperiosteal filling with hyaluronic acid in this region can help to raise the lateral third of the eyebrow.

Medially, there is the frontal process of the maxillary, lacrimal, sphenoid bones, and a portion of the ethmoid. In the inferomedial border of this area there is a depression called the lacrimal fossa, which is formed by the maxillary and lacrimal bones and houses the nasolacrimal sac.<sup>1</sup> At its anterior end there is the nasolacrimal groove, which is approximately 16 mm long, 4 to 9 mm wide and 2 mm deep. This groove becomes the nasolacrimal canal, which in turn flows into the nasal cavity. This fossa integrates with the nasolacrimal canal through the nasolacrimal duct.<sup>1,3</sup> The lateral wall is formed by the greater and lesser wings of the sphenoid bone, the zygomatic bone, and the frontal portion.<sup>2</sup>

Inferiorly, there is the orbital plate of the maxilla, contiguous to the orbital plate of the zygomatic bone and the orbital plate of the palatine bones. At about 1 cm from the inferior margin, on the slope of the maxilla, is the infraorbital foramen. This opening is directed from above and downwards and is located medially, approximately 2.5 cm from the midline, transmitting infraorbital nerves and vessels.<sup>3,4</sup> (Figure 1)

## INNERVATION OF THE ORBIT AND PALPEBRAE

The sensory innervation of the upper and lower eyelid are respectively achieved by branches of the ophthalmic and maxillary nerves—both are ramifications of the trigeminal nerve.<sup>5</sup>

The motor innervation is achieved with branches of the facial nerve (VII pair) that act on the orbicularis oculi, procerus, corrugator, and frontalis muscles. However, the structures responsible for the elevation of the upper eyelid are the levator palpebrae superioris (innervated by the oculomotor nerve—III pair), and Müller muscle (innervated by the sympathetic nervous system). On the other hand, the frontalis muscle exerts only a small auxiliary lifting action on the upper eyelid. The orbicularis oculi muscle acts both in the upper as in the lower eyelids, promoting the occlusion of the palpebral fissure with the blinking and voluntary eyelid closure movements.<sup>5,6</sup>

For didactic reasons, the nerves of the eye and the orbit can be classified as the following:

**Somatic motor:** innervate the eye and the eyelid. The superior division of the oculomotor nerve (III) innervates the superior rectus and the levator palpebrae superioris muscle, while the inferior division innervates the inferior and medial rectus, and the inferior oblique muscles. The facial nerve (VII) innervates the facial expression muscles. Its frontal and zygomatic branches innervate the orbicularis oculi muscle, while the frontal branch innervates the muscles of the forehead.<sup>4,7</sup>

**Sensory:** trigeminal nerve or the 5th cranial nerve (V) is the main sensory nerve of the face and of the anterior part of the scalp. Its main sensory branches are the ophthalmic, maxillary, and mandibular nerves, usually referred to as V1, V2, and V3, respectively.<sup>3,8</sup> (Table 1)

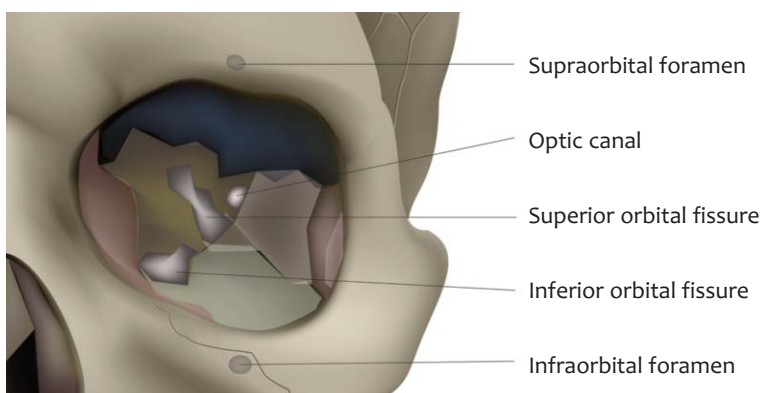


FIGURE 1: Bones of the orbit

TABLE 1: Branches of the Trigeminal Nerve

SENSITIVE INNERVATION: Branches of the trigeminal nerve that innervate the orbit	
1 - OPHTHALMIC NERVE	Goes through the superior orbital fissure, and upon reaching the orbit it originates three terminal branches (nasociliary, frontal and lacrimal nerves). It is the first division of the trigeminal nerve (V). It is an afferent nerve responsible for the sensitivity of the orbital cavity and its contents. It innervates the bulbus oculi, conjunctiva, lacrimal gland and sac, nasal mucosa, frontal sinus, external nose, upper eyelid, forehead and scalp.
BRANCHES	<p><b>Lacrimal:</b> lacrimal gland, conjunctiva, and skin of the upper eyelid.</p> <p><b>Frontal:</b> emits the main branches to the eyelid, forehead, and scalp.</p> <ul style="list-style-type: none"> <li>• Supraorbital: forehead, scalp, upper eyelid, and frontal sinus.</li> <li>• Supratrochlear: Forehead and upper eyelid.</li> </ul> <p><b>Nasociliary:</b> It is the sensory nerve of the eye.</p> <ul style="list-style-type: none"> <li>• Communicating branch to the ciliary ganglion.</li> <li>• Long ciliary nerves: uvea and cornea.</li> <li>• Infratrochlear nerve: eyelids, skin of the nose, and lacrimal sac.</li> <li>• Posterior ethmoid nerve: ethmoid and sphenoid sinus.</li> <li>• Anterior ethmoid nerve: skin of the nose and nasal mucosa.</li> </ul>
2 - MAXILARY NERVE	<b>Infraorbital nerve:</b> runs on the floor of the orbit, through the infraorbital sulcus, canal, and foramen, where it emerges. Innervates the soft parts located between the lower eyelid (inferior palpebral nerve), nose (nasal nerve), and upper lip (superior labial nerve). The infraorbital nerve is responsible for the sensitivity of part of the orbit and of the middle third of the lower eyelid.

Ophthalmic branch (V1) ÷ frontal branch: supratrochlear and supraorbital nerves, responsible for sensory innervation of the upper eyelid, eyebrow, and forehead, and lacrimal gland (lateral orbital region). The nasociliary branch extends into long and short ciliary nerves innervating the eye and the medial region of the orbit;

Maxillary branch (V2) ÷ infraorbital nerve innervates the inferior eyelid.<sup>4,5</sup> (Figures 2 and 3)

Visceral motor - autonomous - parasympathetic: oculomotor nerve (III), inferior branch for the ciliary ganglion located laterally to the posterior 1/3 of the optic nerve. The ciliary ganglion is a small ganglion located near the orbital apex, lateral to the ophthalmic artery and medial to the lateral rectus muscle, innervating the ciliary muscles and the pupil sphincter.<sup>4,9</sup>

The nerves present in the inner structure of the orbit are: oculomotor, trochlear, abducens, and the ophthalmic root of the trigeminal nerve.<sup>9</sup> The ophthalmic nerve is one of the three branches of the trigeminal nerve and has itself three main branches in the orbit: the lacrimal nerve, the frontal nerve, and the nasociliary nerve.

The trochlear nerve enters the orbit through the superior orbital fissure, above the common tendon of the rectus muscles. It runs medially in the orbit, above the levator muscle of the upper eyelid to innervate the superior oblique muscle.<sup>9</sup>

The abducens nerve enters the orbit through the superior orbital fissure, within the Annulus of Zinn, innervating the lateral rectus muscle.<sup>2</sup> (Table 1)

## IRRIGATION

The orbital vascular irrigation system is actually very complex, with numerous interindividual variations. The blood supply of the eyelids derives primarily from the internal carotid artery via the ophthalmic artery, and secondarily from the external carotid artery, through the branches of the infraorbital, facial, and superficial temporal arteries.<sup>2,3</sup>

## External and internal carotid arteries (ICA and ECA)

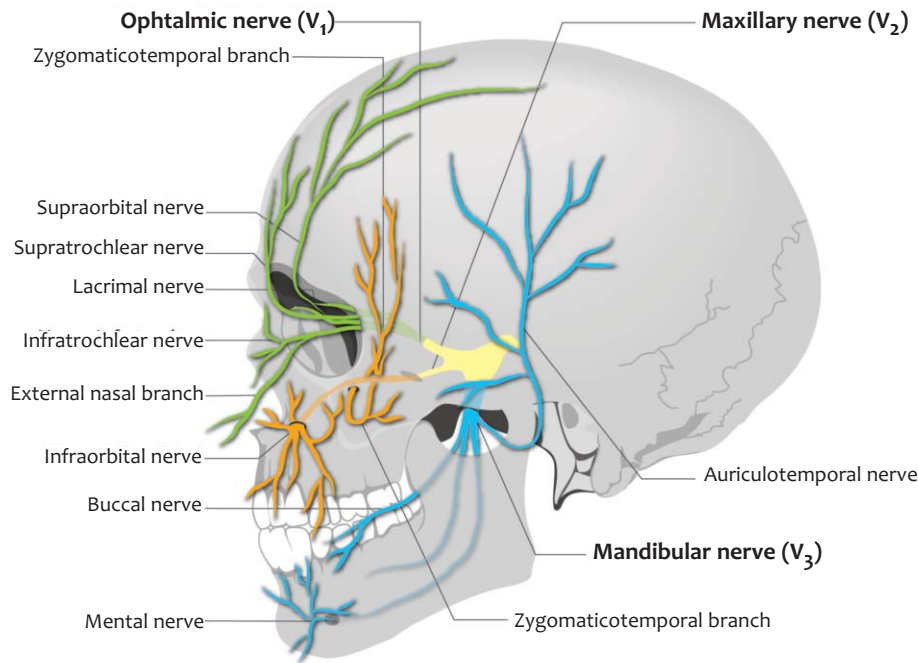
In general, the blood supply of the face derives primarily from the external carotid artery. Nevertheless, in the orbital region ÷ where one of the points of anastomosis of the two systems occurs ÷ the internal carotid dominates local irrigation. The internal carotid artery (ICA) provides a further arterial contribution to irrigation of the upper portion of the face and scalp.

The ICA emits numerous branches, however the present article will only cover the main branches and tributaries that irrigate the orbit. Collateral circulation does occur from the ICA to the middle meningeal artery and lacrimal and ethmoid anastomoses.<sup>10</sup>

The external carotid artery usually contributes only a small extension to the blood supply of the orbit, through the infraorbital artery and the orbital branch of the middle meningeal artery.<sup>8</sup> The infraorbital branch is a secondary or indirect blood supply of the eyelids.<sup>3</sup>

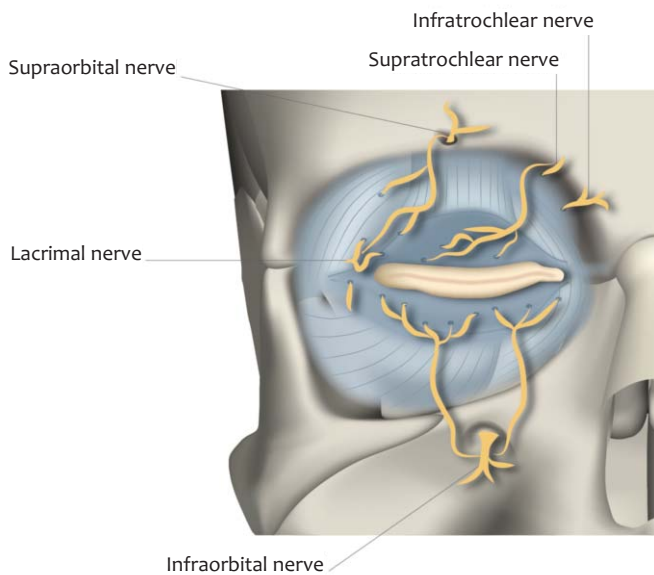
The infraorbital artery ÷ a branch of the internal maxillary artery ñ passes through the inferior orbital fissure in the infraor-





**FIGURE 2:** Sensory innervation of the face and eyelid—ophthalmic branch in green

Adapted source: EC Palermo, 2012.<sup>5</sup> -  
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**FIGURE 3:** Innervation of the orbit and eyelid

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bital groove and emits branches into the orbital fat and the orbital muscles that irrigate the inferior rectus and inferior oblique muscles.<sup>8</sup> Laterally, the superficial temporal branch of the external carotid artery contributes to the superior and inferior palpebral arterial arch through the zygomatic-orbital and transverse facial arteries.<sup>3,8</sup>

Filling procedures in the ocular region, nasal dorsum, and glabella, with accidental intravascular injection in one of the distal branches of the ophthalmic artery, can lead to a rare, but very serious complication, with embolization of the central artery of

the retina, resulting in blindness. This means that it is important to know in detail the orbital region's irrigation and its ramifications.

### OPHTHALMIC ARTERY

The ophthalmic artery, the first major branch of the internal carotid artery, is the main source of irrigation of the orbital region. It is responsible for the blood supply of the orbital structures, including nerves, muscles, lacrimal apparatus, the optical channel, part of the eyelid irrigation, part of the dorsum and superior region of the nose, and the frontal portion of the orbit.<sup>11,12</sup> Several studies have shown that there is a very high rate of anatomical variability of the ophthalmic artery and its branches.<sup>11</sup> Moreover, it is very important to bear in mind that, since the ophthalmic artery is one of the secondary axes that connect the external carotid system with the internal carotid system, some situations may predispose a retrograde flow of ocular irrigation, increasing the risk of complications, such as embolization.<sup>12,13</sup>

In 1887, Meyer carried out one of the first studies on the anatomical description of the ophthalmic artery, especially its branches and its variations. Notwithstanding the fact that his observations were based on only 20 cases, they were accepted as the norm by most anatomy books. Later on, studies have shown a wide variation regarding Meyer's initial descriptions.<sup>2</sup>

In most cases, it is a branch of the supra clinoid portion of the internal carotid artery. Approximately 8% of the ophthalmic arteries arise in the cavernous sinus, rather than in the subarachnoid space.<sup>11</sup> The ophthalmic artery may also arise as duplicate arteries of similar size and rarely originate from the middle meningeal artery or the anterior communicating artery.<sup>8,11</sup> The origin of the ophthalmic artery is usually medial to the anterior clinoid process, below the optic nerve, where it runs parallel to

the optic nerve, in the optic canal. The ophthalmic artery penetrates into the orbit through the optic canal, crosses from the lateral to the medial above the optic nerve in about 80% of cases and beneath that nerve in about 20% of cases.<sup>8-12</sup> The artery runs forward horizontally, below the lower border of the superior oblique muscle, and divides into two terminal branches: the frontal and nasal dorsal.<sup>10</sup>

### BRANCHES OF THE OPHTHALMIC ARTERY

**Central retinal artery:** This is the first and one of the shortest branches of the ophthalmic artery. It arises near the orbital apex and enters the optic nerve about 1 cm behind the eye, eventually occupying a central position within the optic nerve.<sup>8</sup>

**Ciliary arteries:** The long and short posterior ciliary arteries perforate the sclera to irrigate the ciliary body, the iris, and the choroid. Its branches penetrate bulbus oculi around the optic nerve.<sup>6</sup> Two or three posterior ciliary arteries are subdivided into about 15 short posterior ciliary arteries (that supply the optic nerve head and the choroid) and two long posterior ciliary arteries (that supply the ciliary body and iris).<sup>8</sup>

**Lacrimal artery:** This is one of the largest branches derived from the ophthalmic, running along the path of the lacrimal nerve. Its branches supply the lacrimal gland, the eyelids, the conjunctiva, and the superior and lateral rectus muscles. The lateral superior and inferior palpebral arteries are terminal branches of the lacrimal artery. They run from lateral to medial in the upper and lower eyelids, forming an anastomosis with the medial palpebral arteries and forming the superior and inferior arterial arch of the eyelids.<sup>8-12</sup>

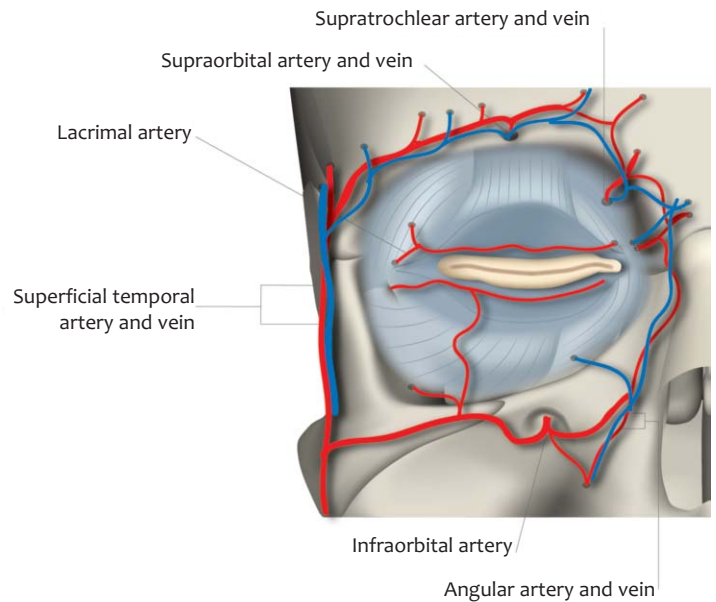
The lacrimal artery also emits the zygomatic branches. One of the branches arises in the face through the zygomatic-facial foramen and through anastomoses with the transverse facial artery; the other branch passes through the zygomatic-temporal foramen and irrigates the temporal fossa, where it forms an anastomosis with the deep temporal arteries.<sup>10</sup>

**Medial superior and inferior palpebral arteries:** The ophthalmic artery passes between the oblique superior and medial rectus muscles toward the orbit, dividing into superior medial and inferior palpebral arteries, forming a superior and an inferior irrigation arches between the orbicularis muscle of eyes and the tarsus.<sup>10</sup>

The marginal arch lies opposite the tarsus at 3 mm from the palpebral margin. The peripheral arch is located between the aponeurosis of the levator palpebrae muscle and the Mülleris muscle, above the superior border of the tarsus in the upper eyelid. In the lower eyelid, its position may vary.<sup>3,14</sup>

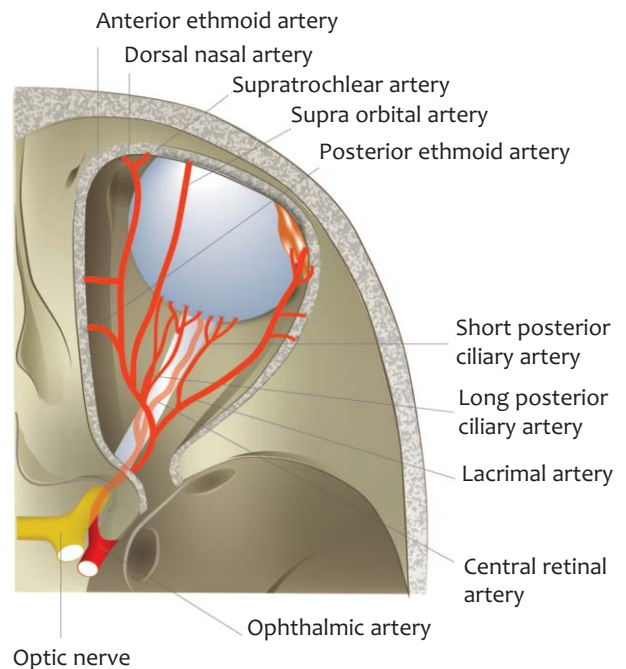
The superior palpebral artery passes around the medial aspect of the nasal fat into the pretarsal space, where it divides into a lesser marginal arch and a greater peripheral arch that forms an anastomosis with palpebral lateral branches of the lacrimal arteries.<sup>3</sup> The inferior palpebral artery passes through the medial canthal tendon, superior to the fat pad of the lower eyelid, to reach the pretarsal space, where the peripheral and marginal arterial arch are also formed.<sup>3</sup> (Figures 4 and 5)

Posterior and anterior ethmoid arteries (PEA and AEA):



**FIGURE 4:** Irrigation of the orbital region

Adapted source: Palermo EC, 2012.<sup>3</sup> Reproduction authorized by Elsevier Editora.



**FIGURE 5:** Irrigation of the orbital region

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The PEA passes along the medial wall, between the superior oblique muscle and the medial rectus muscle, crossing the posterior ethmoid canal. In the orbit, this vessel can irrigate the superior oblique muscle, the superior and medium rectus muscles, and the superior eyelid levator muscle. The AEA, in turn, runs along the nasociliary nerve and exits the orbit through the anterior ethmoidal foramen. In the orbit, it irrigates the superior oblique muscle, the anterior and middle ethmoid portion, the frontal sinus, the lateral nasal wall, and the nasal septum.<sup>10</sup>

The cutaneous branches of the ophthalmic artery are:

**Supraorbital artery:** This artery route supwards medially to the superior rectus and the superior eyelid levator muscles, irrigating them and following the path along the supraorbital nerve. As the artery passes through the supraorbital foramen, it divides into a superficial and a deep branch, which supply the integument, muscles, and pericranial tissues of the eyebrows and forehead. It forms an anastomosis with the supratrochlear artery and the frontal branch of the superficial temporal artery, and with the supraorbital artery of the opposite side.

**Supratrochlear artery<sup>10</sup>:** One of the terminal branches of the ophthalmic artery, the supratrochlear artery or frontal artery, leaves the orbit in its medial angle above the trochlea with the supratrochlear nerve, going upward into the forehead, and irrigating the lower forehead and scalp. The supratrochlear artery forms an anastomosis with the supraorbital artery and contralateral vessels.<sup>10,12</sup>

**Dorsal nasal artery:** This artery emerges from the orbit above the medial palpebral ligament, irrigates the root and dorsum of the nose, crosses the nasal root and extends into two branches. One of these anastomoses with the contralateral artery and with the lateral nasal artery. The other anastomoses with the angular artery, which is the terminal branch of the facial artery.<sup>10,12</sup>

Below are the different points of anastomosis in the orbital region:

#### Anastomosis between the ECA and ICA systems

The periorbital region has a huge network of arterial anastomoses, and numerous anatomical variations that make it impossible to predict with certainty the exact locations of their occurrence. Nevertheless, with prior knowledge of the location of the main connection points between the systems, it is possible to minimize the risks of applications in those locations using cannulas to perform fillings, for instance.

The orbital region has some points of anastomosis of the external carotid system with the internal carotid system. One of the most important is the anastomosis of the dorsal nasal artery with the angular artery. The facial artery, a branch of the external carotid artery, leads into the angular artery after superficially crossing the medial canthal tendon, where it anastomoses with

the dorsal nasal branch of the ophthalmic artery, which in turn is a branch of the internal carotid artery. One of its branches joins the angular artery at the root of the nose, and the other runs downward, anastomosing with the external nasal artery, which is a branch of the infraorbital artery.<sup>10,15</sup>

Another point is the anastomosis of the superficial temporal artery with branches of the supraorbital artery. From the external carotid artery, there is the superficial temporal artery, which anastomoses medially with branches of the supraorbital artery, which in turn is a branch of the ophthalmic artery that derives from the internal carotid artery.<sup>3,10</sup>

The zygomatic artery that derives from the lacrimal artery anastomoses with the transverse facial artery, a branch of the superficial temporal artery.<sup>10</sup>

The lacrimal artery gives rise to a recurrent meningeal branch that anastomoses with the middle meningeal artery, forming another communication axis between the internal and external carotid arteries.<sup>10,13</sup>

The lateral and medial palpebral arteries anastomose with each other, forming two sets: the marginal and peripheral arch. The superior medial palpebral artery anastomoses with the zygomatic-orbital branch of the temporal artery in the lateral angle of the orbit. That artery also anastomoses with the superior portion of the two lateral branches of the lacrimal artery.<sup>13</sup> (Figure 6)

#### VEINS

The venous system of the orbital region is highly variable and complex. Unlike in other sites of the body, there is no correspondence between arteries and veins, except for the superior ophthalmic vein, which has correspondence with the ophthalmic artery.<sup>12</sup>

Venous drainage of the orbit is performed by the inferior and superior ophthalmic veins, which are located within the connective septum of the orbit. The superior ophthalmic vein is formed near the root of the nose with the union of angular, supratrochlear, and supraorbital veins. Divided into three sections, the vein runs along the path of the ophthalmic artery, passes through the superior orbital fissure and ends in the cavernous sinus. The first section passes along the medial border of the

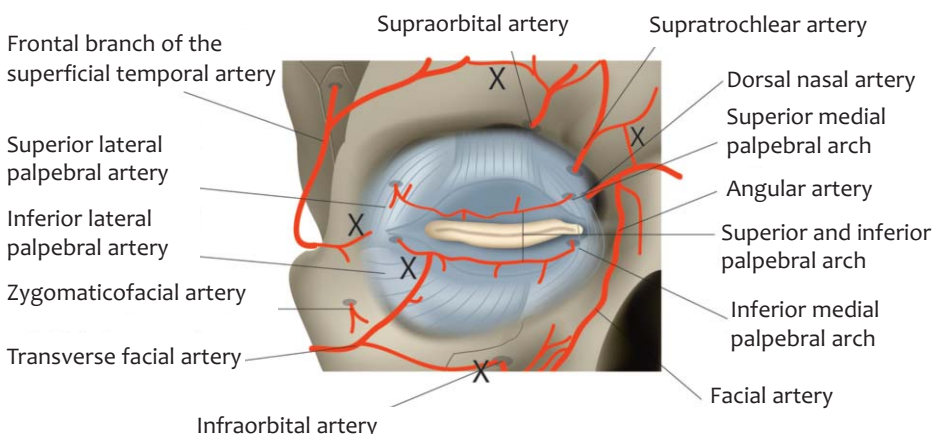


FIGURE 6: Areas of anastomosis of the branches of the ICA and ECA

superior rectus muscle, the second section passes near the superior rectus muscle and the third section passes posteriorly along the lateral border of the superior rectus muscle to enter the superficial orbital fissure, outside the annulus of Zinn, draining into the cavernous sinus.<sup>8</sup> The inferior ophthalmic vein is more variable, and usually is formed anteriorly as a plexus in the inferomedial orbital fat. The four vorticosae veins pierce the sclera obliquely and end in the ophthalmic veins. The central retinal vein is identified contiguous to the central retinal artery, often entering the cavernous sinus directly, and may join one of the ophthalmic veins.<sup>8,13</sup>

The drainage of the eyelids is carried out by the pre-tarsal and post-tarsal veins. The pre-tarsal veins are more superficial and connect latero-superiorly with the superficial temporal and lacrimal veins, and medially with the angular vein. The post-tarsal section connects the orbital veins with the deep branches of the anterior facial vein and the pterygoid plexus. The main venous drainage of the eyelids flows into the superficial temporal, angular, and facial veins, connecting superiorly with the supraorbital frontal system, and with the facial vein inferiorly. As in the arterial system, there are venous arch that drain into the main venous drainage systems.<sup>3</sup>

### Lymphatic drainage

The lymphatic vessels of the eyelids have systems similar to those of the veins, being divided into pre-tarsal and post-tarsal. The pre-tarsal vessels provide lymphatic drainage of the eyelid's skin and of the orbicularis oculi muscle. The post-tarsal deep plexus provides lymphatic drainage of the tarsal plates, glands and other structures of the palpebral margins, including the conjunctiva and lacrimal glands.<sup>3</sup> The palpebral lymphatic vessels drain two main areas. The lateral lymphatic drainage group provides drainage of the lateral aspect of both eyelids, as well as of the deep vessels that drain the conjunctiva and lacrimal glands of the upper eyelids. They drain into the superficial and deep parotid lymph nodes (pre-auricular). The medial aspects of both eyelids and lacrimal sac run parallel to the lacrimal vein into the submandibular lymph nodes.<sup>3</sup>

### EYELID

The eyelids are specialized structures with unique anatomical components. The skin of the eyelid is the thinnest on the human body, with a thickness of 700 $\mu$  to 800 $\mu$ .<sup>6</sup> The stratigraphies of the eyelids can differ according to the section assessed, with 4 layers in the tarsal portion and 7 layers in the tarsal region, above the orbital septum. In the tarsal portion there are: (1) skin and subcutaneous tissue, (2) orbicularis oculi muscle, (3) tarsus, and (4) conjunctiva. In the proximal portion there are: (1) skin and subcutaneous tissue, (2) orbicularis oculi muscle, (3) orbital septum, (4) post-septal or orbital fat, (5) aponeurosis of the levator muscle of the superior eyelid, (6) Müller muscle, and (7) conjunctiva.<sup>3</sup>

The upper eyelid extends superiorly to the eyebrow, which separates it from the forehead. The lower eyelid extends below the inferior orbital border, forming folds where the eye-

lid's loose conjunctive tissue is juxtaposed to the thicker tissue of the cheek.<sup>5</sup>

The palpebral skin is still divided into two parts: the orbital portion (between the tarsal portion and the orbital border), and the tarsal portion (between the free border and the orbito-palpebral sulcus). The subcutaneous tissue is composed of loose conjunctive tissue, which is very scarce in the skin of the eyelid. The tarsal portion is very thin and vascularized, with an absence of subcutaneous tissue. The transition from that portion of the tarsal skin to the orbital portion is clinically evident in thickness and color, being delimited by the superiorpalpebral-sulcus. The eyelids are the protective covering of the ocular globe. The palpebral borders enter in contact during the closure and the blinking movement of the eyelids. The eyelids help in creating and maintaining the lacrimal film, the mucus and the oil that are necessary for the cornea's survival.<sup>5</sup>

With an elliptical shape, they measure between 28mm and 30mm in width, and from 7mm to 12mm in height in men (from 8mm to 12mm in women). The space between the superior and inferior eyelids is called palpebral fissure. When opened, the superior eyelid should usually cover about 1mm to 2mm of the iris, with the inferior edge of the lower eyelid slightly brushing the inferior limbus.<sup>16</sup> (Figure 7)

In the case of a decrease of that distance due to the lowering of the upper eyelid, palpebral ptosis is configured. The so-called scleral show occurs when the palpebral fissure is enlarged due to malocclusion of the lower eyelid.<sup>5,16</sup>

Although similar, the upper and lower eyelids have different characteristics.

The lower eyelid has three sulci: inferior palpebral, malar, and nasojugal. The inferior palpebral sulcus begins at the medial canthus, bends down and passes over the inferior border of the tarsus, ending in the lateral canthus. The nasojugal sulcus begins below the medial canthus, and runs downward and laterally at an angle of 45°. The malar sulcus begins laterally at the malar prominence and curves medially and downwardly until it intersects the nasojugal sulcus. The nasojugal and malar sulcus attach to the periosteum through a fascia.<sup>3,17</sup>

The upper eyelid has an orbito-palpebral sulcus or superior palpebral sulcus. It divides the eyelid into two parts: the palpebral and tarsal portion below and the orbital portion above. The sulcus is formed by the insertion of the levator muscle's aponeurosis in the upper eyelid, in the orbicularis septum. The sulcus begins medially at 3mm from the ciliary border (measuring, on average, from 6mm to 8mm in its central portion in women and from 7mm to 10mm in men) and ends in the lateral portion, at 4 to 5mm from the ciliary border.<sup>5,17</sup> (Figure 8)

In people of East Asian heritage, it is located lower, at about 2 to 4mm from the tarsus. That palpebral sulcus is very important for it is used as reference in the marking and removal of skin in the superior blepharoplasty. The blepharoplasty technique with Westernization consists of building this sulcus which is absent in this case carrying out a plication in the muscle.<sup>3,14</sup>

It is important to bear in mind these measurements as well as some pre-existing conditions before carrying out proce-

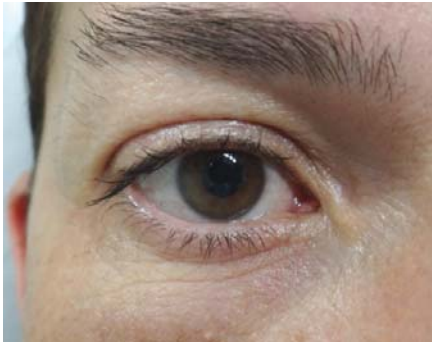


FIGURE 7: Normal palpebral fissure



FIGURE 8: Superior palpebral sulcus

dures that can lead to changes in the ocular closure. Below are some of the common problems related to eyelids:

**Palpebral ptosis:** Decrease of the palpebral fissure due to lowering of the upper eyelid.

**Apparent sclera:** Occurs when the palpebral fissure is increased due to malocclusion of the lower eyelid.

**Lagophthalmos:** Excessive exposure of the eye, with inability to close it.

**Dermatochalasis:** Excess of skin in the upper, lower, or both eyelids, associated with the aging of the eyelid and eyebrow.

The palpebral borders are 2mm thick and are the junction between the skin and the mucous membrane of the eyelid—the conjunctiva. They are located in the gray line, near each palpebral border's posterior border, and can be readily identified through a change in the color of the skin. The so-called gray line is the line of union between the skin and orbicularis muscle (anteriorly) and between the tarsus and the conjunctiva (posteriorly). The gray line is also an anatomical structure that identifies the junction of the eyelid's anterior and posterior lamellas.<sup>3,17</sup> The caruncle and the semilunar fold are located in the medial region, where there is an elevation called lacrimal papilla, whose central orifice presents the lacrimal punctum. The Meibomian glands' orifices are located behind the gray line.<sup>17</sup> There are approximately 40 Meibomian glands in the upper eyelid and 20 to 30 in the lower eyelid.<sup>3</sup>

The eyelashes form two or three layers anteriorly to the gray line, being more numerous and thick in the upper eyelid. There are approximately 100 to 150 eyelashes in the upper eyelid and half that number in the lower eyelid.

## MUSCLE LAYER

### Orbicularis oculi muscle

The second palpebral layer is the orbicularis oculi muscle, a striated muscle formed by the palpebral and orbital portions. The orbital portion has voluntary contraction, while the palpebral portion can have voluntary and involuntary movements. Innervation of the upper portion of the orbit occurs through the temporal branch of the facial nerve, while in the lower portion it occurs through the zygomatic branch of the facial nerve. The orbital portion covers the orbital border and its fibers are intermingled medially with the procerus muscle and superiorly with the frontal muscle. The central portion of the orbicularis oculi muscle covers the eyelid and is referred to as the palpebral portion.<sup>3,14</sup>

The palpebral portion of the orbicularis muscle is divided into two parts:

- **Pre-tarsal portion:** It is located over the tarsal plate of the orbicularis muscle and is tightly adhered to the tarsus. It begins in the lateral canthus and inserts in the medial canthus. Its superficial portion forms the anterior part of the medial canthal tendon. Its deep portion inserts into the bone of the posterior lacrimal crest, forming the posterior medial canthal tendon. When contracted, the eyelid closes, bringing the lacrimal punctum close to the lacrimal sac.<sup>7,17</sup>

- **Pre-septal portion:** It is loosely attached to skin and covers the orbital septum of the upper and lower eyelids, with its fibers bundling laterally to form the lateral palpebral raphe. The pre-septal portion inserts in the lacrimal fascia, on the lateral part of the lacrimal sac, and when contracted, produces a tear in the lacrimal sac. When the muscles relax, the lacrimal fascia returns to its normal position and the tear drains directly into the nasolacrimal duct.<sup>14,17</sup>

The superior and inferior medial canthal tendons originate in the medial aspect of the tarsal plates, which coincides with the location of the papilla and the lacrimal punctum. The superior and inferior medial canthal tendons, as well as the common medial canthal tendon, can be seen through thin eyelids as white, firm structures that extend from the medial canthus up to the medial aspect of the orbit.<sup>3</sup>

The lacrimal canaliculus lies deep to the common medial canthal tendon, and is therefore protected from traumas in that location if the tendon is not sectioned. The angular artery and vein cross the tendon at its medial aspect and anastomose with branches of the ophthalmic vessels above the superior border of the tendon.<sup>3,17</sup>

### Extraocular muscles

The main extraocular muscles are the superior eyelid levator muscle, the four rectus muscles (superior, inferior, lateral, and medial) and the two oblique muscles (superior and inferior).<sup>5</sup>

### Superior eyelid retractor muscle

The superior eyelid retractor muscles consist of the frontal muscles, superior eyelid levator muscle, superior tarsal muscle (or muscle of Müller), and also the Whitnall ligament. The supe-

rior eyelid levator muscle originates from the lesser wing of the sphenoid bone and, later on, dividing into aponeurosis and the superior tarsal muscle. The aponeurosis inserts and overlaps with the fibers of the orbicularis muscle to form the palpebral sulcus.<sup>5</sup>

### Superior eyelid levator muscle and muscle of Müller

The fourth layer of the upper eyelid is formed by the superior eyelid levator muscle and aponeurosis. It is innervated by the oculomotor nerve (3rd cranial pair). When it shifts into a diagonal-vertical direction, it divides into anterior aponeurosis and posterior tarsal muscle of Müller. It is responsible for lifting the upper eyelid and therefore opening the eye. The aponeurosis merges with the superior transverse ligament in the superior orbit, which acts as a restraint ligament that provides additional support for the aponeurosis.<sup>3</sup> The aponeurosis merges with the orbital septum and then inserts in the anterior surface of the tarsus. It is firmly attached to the orbicularis oculi muscle and to the skin by fibrous bands. The superior border of this insertion is marked by the lower crease of the upper eyelid (superior eyelid sulcus). During blepharoplasty, when operating in the postseptal space, it is necessary to take care in order to avoid trauma of the aponeurosis and the resulting ptosis.

The Müller muscle (controlled by the sympathetic nervous system), inserts in the superior margin of the tarsal plate. It contributes to the tonic elevation of the eyelid by 2 to 3mm.<sup>17</sup> The innervation of the superior tarsal muscle (Müller) is achieved by the sympathetic nervous system.<sup>14</sup>

### Lower eyelid retractor muscles

The lower eyelid retractor muscles are composed of a layer of fibrous tissue originating from the sheath of the inferior rectus muscle that attaches to the inferior border of the tarsus. In both morphology and function this tissue resembles the aponeurosis of the upper eyelid levator muscle. It extends along the inferior rectus muscle, intertwines with the inferior suspensory ligament (of Lockwood) of the bulbus oculi and runs toward the inferior border of the tarsus, accompanied by fibers of the inferior tarsal muscle. The retractor muscles are responsible for lowering the lower eyelid when looking downward. The same similarity exists between the lower tarsal and upper tarsal muscles. The tarsal plate is a dense conjunctive tissue that provides structure to the eyelid, stabilizing the palpebral border. As the superior tarsal plate measures approximately 11mm, it can be used as a donor source for tarsal-conjunctival graft. On the other hand, the inferior tarsal plate, measuring about 4mm, does not offer that possibility. The medial canthal tendon is formed by the insertion of pre-tarsal and pre-septal muscles. Its superficial portion inserts in the anterior lacrimal crest, while its deep portion inserts in the posterior lacrimal crest. The lateral canthal tendon is a tendon that gives rise to the pre-tarsal muscles.<sup>3,5</sup>

### ORBITAL SEPTUM

The third layer of the eyelids in their upper portion is the orbital septum. It is a fibrous conjunctive tissue membrane that separates the orbital fat pads and deep orbital structures from the

eyelid itself. It originates from the orbital marginal insertions of the thick fibrous band (arcus marginalis), which is formed by the junction of the orbital and periorbital periosteum with the insertion of the deep layer of the aponeurotic galea.<sup>3</sup> The septum merges laterally with the lateral canthal tendon and medially with the aponeurosis of the upper eyelid levator muscle. In the upper eyelid, the orbicularis septum inserts in the levator muscle, however, in the lower eyelid, the septum and the aponeurosis of the retractor muscle insert in the inferior border of the tarsus and of the inferior fornix.<sup>14</sup> Behind the septum are the fat pads. In blepharoplasty it is necessary to make small incisions in this septum in order to remove the fat pads. With aging, both the septum and the orbicularis muscle and skin become looser and thinner, causing orbital fat prolapse, making it prominent. Blepharoplasty is usually performed to correct that defect, however filler injections in the nasojugal sulcus region can alleviate the problem and delay the necessity of surgery.

### POST-SEPTAL LAYER

#### Fat pads

The palpebral fat pads are located behind the orbital septum and in front of the palpebral retractor muscles. There are three compartments in the lower eyelid: nasal, central, and lateral. The nasal fat pads are more whitish in appearance than the others. These fat pads are surrounded by a thin fibrous fascia, which separates them into distinct compartments. There are two compartments in the upper eyelid: the pre-aponeurotic fat pad and the nasal fat pad. The lacrimal gland lies laterally, and may be mistaken with the adipose body. Therefore, one should be careful not to inadvertently injure the gland during surgical procedures.<sup>3-14</sup>

The large superior and inferior medial palpebral vessels run on the surface of the respective nasal fat pads and can be carefully dissected or clamped when the fat pad is excised during blepharoplasty. Although the vessels of pre-septal and muscle areas are well supported by connective tissue and muscle, the orbital vessels are virtually unsupported. As a result, despite the fact that they can withstand some tension, orbital vessels can be easily traumatized and even suffer severe strain during blepharoplasty.<sup>14</sup> Bleeding in these vessels can lead to increased intraocular pressure and even blindness. The inferior oblique muscle is also vulnerable to trauma during such procedures, during the removal of the inferior medial fat pad.<sup>17</sup> (Figs. 9 and 10)



**FIGURE 9:** Two fat pads, upper eyelid



FIGURE 10: Threefat pads, lower eyelid

### Tarsal blade

Tarsus are structural elements of the eyelids composed of dense fibrous tissue, and measuring approximately 29mm in width, 10–12mm in height at its medial point, and 1mm in thickness. The inferior tarsus has the same width and thickness, but is 5–6mm high. The tarsus begins medially in the lacrimal punctum, extending up to the lateral commissures. The Meibomian sebaceous glands are embedded vertically in the tarsal plate and extend toward their marginal aspects. Thirty to 40 glands are present in the upper eyelids, and 20 to 30 are present in the lower eyelid.<sup>3</sup>

### ANATOMY OF THE ORBITAL REGION—CORRELATION WITH RISKY AREAS

The glabella and nasal root region is a location of major risk in the face when performing cutaneous filler injections. Despite being highly vascularized, this region differs from other areas of the face for presenting two separate events. Although it contains a rich vascular network, many of the vessels in the region are superficial and some have terminal branches. This leads to a higher risk of necrosis due to both ascending embolization in the forehead and ischemia by external compression.

The supraorbital artery which leaves the orbit through the supraorbital foramen and the supratrochlear artery which surfaces through the superior and medial portion of the orbit—merge in the glabella anteriorly to the corrugator supercilii muscle, and posteriorly to the orbicularis oculi muscle. Subsequently, both arteries cover a short path towards the frontal muscle and become superficial.

Another important event concerns the anastomoses network present in the glabellar region and across the periorbital region—especially in the medial portion—that ultimately increases the risk of embolism of the central retinal artery. Cutaneous filling applications in this region might reach vessels that have anastomosis with the internal carotid system, reaching the ophthalmic artery in retrograde and then to the central retinal artery.

The control of the flow of the ophthalmic artery depends on the autonomic nervous system. In cases of stimulus of the cervical sympathetic receptors, the flow in the ophthalmic artery is reduced, while in sympathectomy an increase in the

flow occurs. In contrast, the central retinal artery is a terminal vessel that has a characteristic mechanism of self-regulation and is not subject to the action of the autonomic nervous system. Thus, alterations in the flow of the ophthalmic artery directly affect the central retinal artery. The anastomoses between the systems help to regulate and maintain the blood support to the central nervous system.<sup>13</sup> Nevertheless, in situations where the flow is reduced, the secondary vascular axis is activated. In the presence of internal carotid artery stenosis, for example, reversal of the flow occurs and, hence, the patient in this situation, even if asymptomatic, has a greater chance of an embolization that might reach the central retinal artery.<sup>13</sup>

Risks of cutaneous filling techniques in the orbital region.

The most common complications regarding cutaneous fillings are related to circulatory issues. The more frequently affected sites, and those of greater risk of ischemia or embolization in the orbito-palpebral region concerning blindness are:

Nasojugal sulcus: as seen earlier, blood circulation in the eyelid happens through an anastomosis of the branches of the ophthalmic artery, laterally through the lacrimal artery (originating from the lateral palpebral branches) and medially through the branches of the medial palpebral artery (originating from the upper and lower eyelid artery). The medial and lateral palpebral arteries anastomose with each other, forming two sets of marginal and peripheral arches. (Figure 11) The marginal arch lies opposite to the tarsus at 3mm from the palpebral margin. The peripheral arch lies between the aponeurosis of the eyelid levator muscle and the Müller muscle, above the superior border of the tarsus, in the upper eyelid. In the lower eyelid, its position may vary. This inferior and medial region is therefore one of the areas of risk regarding embolization during application of cutaneous filling in the nasojugal sulcus.

Glabella: The supraorbital and the supratrochlear arteries are superficial in this region. Moreover, vascularization in the glabellar region is poor because it is predominantly a terminal circulation. Thus, obstruction of these small arteries can easily occur with injections of materials used for both external and internal filling. This superficial pathway is the most vulnerable point of these arteries, and is where there is a high risk of intravascular injection (Figure 12).



FIGURE 11: Anastomoses in the orbital irrigation



**FIGURE 12:** Arteries and veins of the orbital region

**Medial portion of the orbit:** In this specific region of the orbit, more precisely contiguous with the final and superior part of the nasojugal sulcus and the lateral portion of the nasal root, passes the angular artery—the final branch of the facial artery (a branch of the external carotid artery), which anastomoses with the dorsal nasal artery (the final branch of the ophthalmic artery). At this point, in patients who have thin skin, it is possible to visualize the angular vein, which runs slightly more centrally than the angular artery. The angular artery and vein cross the medial canthal tendon and anastomose with branches of the ophthalmic vessels above the superior border of the tendon. These sites contain one of the carotid system's anastomoses, a fact that also enables clots to access the central artery of the retina in retrograde.

Since the palpebral artery is a branch of the ophthalmic artery, in the case of intravascular injection with the release of clots of the filling product, there is a chance for those clots to move and reach the central retinal artery in retrograde, causing counter flow in the circulation of the ophthalmic artery.

Some studies demonstrate that this secondary vascular axis of anastomosis between the ICA and ECA (that reverse the flow of the ophthalmic artery) is activated when there is hemodynamically significant stenosis of the ICA, as evidenced by Doppler records of retrograde flow in the ophthalmic arteries.<sup>13</sup>

As a result, this calls into question whether some patients, even asymptomatic ones, might have a retrograde flow permanently activated and thus have an increased risk of complications related to cutaneous fillings in this region, affecting the central retinal artery.

Therefore, it is of paramount importance to be aware of the early signs of embolic or ischemic complications, including pain, local whitening, followed by hyperemia or blueness, visual blurring, and loss of vision.

As previously seen, the thickness of the palpebral skin and its correlation with the orbicularis muscle and the quasi-absence of subcutaneous tissue, also make the site risky for less serious—but undesirable—complications, such as the implant being visibly apparent in the palpebral region.

In order to avoid this problem, it is important to assess the site thoroughly before application and, where possible, work at deep and intermediate planes, preferably with the use of cannulas or micro-cannulas.

### **Botulinum toxin risks in the orbital region**

Rare complications, however related to ocular anatomy, are diplopia and strabismus after botulinum toxin injection, with the probable cause being the toxin's effect on the extrinsic muscles of the eye, such as the inferior oblique and the lateral rectus.<sup>18</sup>

The paresis of the inferior oblique muscle is caused by the migration of the toxin applied to the glabella and nasal region to the muscle, since the insertion of the inferior oblique muscle occurs in a small depression just behind the orbital border lateral to the lacrimal duct. As for the paresis of the lateral rectus muscle, the explanation would be the migration of the toxin applied in periorbital wrinkles (crow's feet), due to the anatomical proximity of that muscle to the region treated with the toxin.

The feared post-botulinum toxin ptosis, in turn, relates to the toxin's effect on the upper eyelid levator muscle, while the fall of the brow or pseudo ptosis relates to its action in the frontal muscle.

Due to the great local vascularization of the eyelids, there is a high risk of bleeding and echymosis. Furthermore, the lymphatic drainage system is very fragile, leading to the very common emergence of edema in this region after the application of cutaneous fillers and botulinum toxin. In the case of toxin applied to the glabella, some patients frequently complain of swelling in the eyes, especially in the morning, with edema in the upper eyelid that may be related to excessive relaxation of the superficial musculature that aids in local drainage. The same can occur in cases where cutaneous fillers are applied in the orbital region, due to the hydrophilic nature of the products, with edema that can be intermittent and prolonged, worsening after exposure to heat. In general, this problem resolves spontaneously, however it can be aided by manual drainage. In the specific case of cutaneous filling, the recommendation is to evaluate whether only edema occurred or if there was indeed superficialization of the filler—a situation where it can then be treated with applications of hyaluronidase.

### **Care in anesthesia and orbital surgery**

Regarding anesthesia in dermatological procedures, given that multiple cutaneous sensory nerves assist in the innervation of the orbit and eyelid, local infiltration or nerve blocks are good methods for anesthesia of the region. Local infiltration must be initiated by the lateral canthus, in the subdermal plane, with thin needles in order to avoid hematoma. Since the skin above the tarsus is loose, the needle can be advanced smoothly in the medial direction, as the injection of anesthetic elevates the epidermis and separates it from the dermis and from the orbicularis muscle.

If the surgery comes in contact with the tarsus or a chalazion forceps is used, the cornea must first be anesthetized with



a topical ophthalmic solution. The patient should be warned and the surgical team must be constantly aware of the fact that there is no corneal reflex, resulting therefore in the possibility of a significant lesion of the eye during the effective period of the local anesthesia. In the case of nerve blocks, the indication is to follow the midpupillary line as a reference, for it is the exit site of the supra and infraorbital nerves. Alternatively, intraoral nerve block can be carried out in the case of the lower eyelid. There is a risk of intravascular injection, however cases of serious complications are rare.

The lower eyelid has less redundant skin and is less tolerant to excessive tissue removal than the upper eyelid. Vertically oriented defects may result in ectropion if the tarsus is not well evaluated prior to the procedure. If located in the medial region of the palpebral margin, minor lesions can heal well by secondary intention, avoiding retraction of the tarsus. It is always crucial to evaluate in advance the local laxity.

The potential for development of ectropion can be estimated by pulling the defect with skin hooks or toothed forceps while instructing the patient to look up with his or her mouth open. This maneuver exerts maximum tension on the lower eyelid. If an impending ectropion is evident, an alternative such as a skin graft or flap should be considered. Pre-operative laxity of the lower eyelid can be estimated through the *isnaptesti*, in which a seated patient has their lower eyelid seized and moved away from the eyeball.

In the same way, the skin laxity of the proximal tarsal eyelid allows the (generally important) accumulation of fluid and edema, so blood or pus may also accumulate. Patients should be warned about the possibility of significant edema or ecchymosis after eyelid, forehead, or scalp surgery.

## CONCLUSIONS

There are several studies and publications demonstrating serious complications in the use of cutaneous fillers in the orbital region, glabella, nasal dorsum, and ala and even in the nasogenian sulcus and lips. Precisely because of the vast network of anastomoses between the superficial and deep carotid system, there is a risk of embolization even during application of products in seemingly safe areas.

The existence of this vascular complex helps to maintain an adequate blood flow to the central nervous system in case of any failure in the circulatory supply. Notwithstanding, this same system may be the cause of serious complications such as clots reaching the central retinal artery, leading to blindness, large edema, and ecchymosis.

The orbital region has a challenging and delicate anatomy, where even procedures that seemingly do not present risks (such as dermatological procedures), may suffer complications. Many cases of blindness and necrosis after filling applications are unfortunately irreversible. Therefore, only prevention and knowledge of risk areas can provide good results and low complication rates. ●

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# Treatment of dermatophyte onychomycosis of the haluces with 1064 Nd: YAG laser

*Tratamento de onicomicose dos háluces por dermatófito com laser Nd: YAG 1064nm*

## ABSTRACT

Onychomycosis is a very common condition in Brazil and one whose current treatments yield low cure rates, potential adverse effects, and drug interactions that limit their use. Recent studies have demonstrated laser therapy as a new, safe, and effective treatment option. This treatment was performed in 12 patients (with a total of 20 affected nails), with 3 application sessions of 1,064nm long pulse Nd:YAG laser, in two-week intervals. The results corroborate the current data of good clinical response and safety.

**Keywords:** onychomycosis; lasers; advanced treatment.

## RESUMO

*A onicomicose é uma doença muito prevalente em nosso meio, cujos tratamentos atuais apresentam baixas taxas de cura, potenciais efeitos adversos e interações medicamentosas que limitam seu uso. Estudos recentes apresentam a laserterapia como uma nova opção terapêutica segura e eficaz. Foi realizado este tratamento em 12 pacientes, num total de 20 unhas acometidas, com 3 sessões de aplicação do laser Nd:YAG 1064nm pulso longo, com intervalo de duas semanas entre elas. Os resultados corroboram os dados atuais de boa resposta clínica e segurança deste novo método.*

**Palavras-chave:** onicomicose; lasers; tratamento avançado.

## INTRODUCTION

Onychomycosis is a fungal infection of the nail bed or nail matrix. It is estimated that about 4–18% of the world population might be affected.<sup>1–3</sup>

The treatment of the condition involves the use of topical and systemic drugs. In recent studies, the use of 8% ciclopirox olamine enamel showed effective cure (mycological cure and <10% of the nail affected) of 6.5–12.0% and total cure (mycological cure and and <0% of the nail affected) of 5.5–8.5%.<sup>4</sup> Systemic agents, such as itraconazole, terbinafine, and fluconazole are more effective in treating onychomycosis,<sup>5</sup> howe-

## New Techniques

### Authors:

Renata Heck<sup>1</sup>  
Cristina Rossi<sup>2</sup>  
Isabel Cristina Palma Kuhl<sup>3</sup>  
Lucio Bakos<sup>4</sup>

<sup>1</sup> MSc Dermatology Candidate at the Post-graduate program in Medical Sciences from the Universidade Federal do Rio Grande do Sul (UFRGS)—Porto Alegre (RS), Brazil

<sup>2</sup> Physician, Universidade Federal do Rio Grande do Sul (UFRGS)—Porto Alegre (RS), Brazil

<sup>3</sup> Preceptor at the Dermatology Service of the Hospital de Clinicas de Porto Alegre—Porto Alegre (RS), Brazil

<sup>4</sup> Full Professor of Dermatology, Universidade Federal do Rio Grande do Sul (UFRGS)

### Correspondence:

Dr. Renata Heck  
Rua Ramiro Barcelos 1891/404  
Cep: 90035-006—Porto Alegre—RS, Brazil  
E-mail: reheck2@yahoo.com.br

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ver adverse effects and drug interactions limit their use. Cure rates of those drugs are respectively  $59\pm 5\%$ ,  $76\pm 3\%$ , and  $48\pm 5\%$ .<sup>6</sup>

Recent publications report laser therapy as a treatment option for onychomycosis,<sup>4,7</sup> which can be of great therapeutic value due to its absence of potential for drug interactions and renal/hepatic toxicity.

The non-ablative 1,064 nm Nd:YAG long pulsed laser (Neodymium Yttrium Aluminum Garnet), whose chromophores are melanin, hemoglobin, and water, acts on the dermis, reaching a depth of up to 5mm.

A recent study has shown that the 1,064 nm Nd:YAG laser had a significant effect on *T. rubrum*, inhibiting the growth of colonies *in vitro*.<sup>8</sup> The melanin present in the wall of the fungal cells acts as the chromophore, justifying the action of the laser. Another mechanism involved can be the action of short duration pulses that would lead to microcavitation and acoustic shock waves, resulting in the mechanical damage of the fungi.<sup>8</sup>

Other studies have demonstrated mycological cure rates of 87.5% after 2 or 3 sessions with 1,064 nm Nd:YAG laser in onychomycosis in the halluces,<sup>7</sup> and clinical improvement in 79% of patients after a single session, without any severe adverse effects.<sup>4</sup>

Gupta et al. treated 71 patients (128 nails) with a single laser session and observed a statistically significant improvement in 65.0% of them after six months.<sup>4</sup>

## METHODS

After approval by the Ethics Committee, the authors conducted a prospective, open, uncontrolled study, which included the first 12 patients who met the inclusion criteria, who did not present any exclusion criterion and had agreed to take part in the assessment.

Inclusion criteria were: patients from the Dermatology Service's Ambulatory Clinic of the Hospital de Clínicas de Porto Alegre (HCPA) and from the Universidade

Federal do Rio Grande do Sul (UFRGS) Porto Alegre (RS), Brazil – diagnosed with onychomycosis of halluces, confirmed by direct mycological examination and/or culture compatible with dermatophyte infection, and who were capable of reading, understanding, and signing the Term of Informed Consent (TIC).

Exclusion criteria were: use of systemic antifungal drugs in the previous 6 months, alteration in the nail pigmentation due to topical therapy, presence of subungual hematoma or nevi, bacterial infection, or nail diseases concomitant to pregnancy.

Selected patients signed the TIC and underwent pre-treatment photographic documentation (Sony® DSC H20). An evaluation of pre-existent comorbidities and treatments was carried out. 1,064 nm Nd:YAG laser (platform Etherea®, Industria Technologies Br) was applied, spot size = 6 mm, pulse duration = 40 ms, fluence = 50–80 J/cm<sup>2</sup>, in crossed passes (horizontal passes followed by vertical passes), 2 passed with 1 minute

intervals between them, covering the entire surface of the nail using the technique described by Hochman.<sup>7</sup> All patients underwent 3 sessions at biweekly intervals. Adverse effects were recorded during application and on the following day through a telephone call, rating the pain symptoms as mild, moderate, or severe.

Ninety days after the last session, the patients underwent a final clinical evaluation and photographic documentation. Images were recorded following the same regimen and photographic techniques used previously.

The evaluation of results was carried out by analyzing pre-treatment photographs and comparing them to the final images. The images were magnified to better assess and subjectively quantify the percentage of improvement. New, direct mycological examination and culture were carried out after the third session.

## RESULTS

The 12 patients (9 women and 3 men, 75% and 25% respectively, age range between 39 and 73 years with a mean value of 58 years) received treatment in 20 affected nails. The timing of the unguis alterations varied from 6 months to 10 years, with a mean value of 3.5 years. Of all patients, 7 (58%) had already undergone previous treatments: 2 (17%) oral treatments, 4 (33%) topical treatments, and 1 (8%) topical and oral treatments. Eleven patients (92%) had comorbidities, the most common being: hypertension, depression, and diabetes mellitus, with only one smoker. The fungal agent was identified through culture in only 5 cases (2 *Trichophyton mentagrophytes* and 3 *Trichophyton rubrum*). As for the affected area, 5 patients had up to 20% of the nail plate affected, 7 patients had 21–40%, 3 patients had 41–60%, 2 had 61–80% and 3 patients had 80–100%. (Table 1)

The immediate adverse effects included local pain (mostly described as a mild burning sensation reported by 9 of 12 patients (75%)) and local heat (reported by 7 patients (58%)). Only one patient (8%) had a delayed adverse effect, reported as mild local pain, which subsided after 24 hours.

All patients included in the study completed the evaluation. The mycological examination collected 3 months after the last session was negative in 3 patients (25%). In the other 9 patients, the samples remained positive, with the causative agent being identified in 3 cases.

The affected area 3 months after the last session was calculated based on the analysis of the photographs. One nail was excluded from the analysis for having been cut during the collection of mycological examination.

Of the 19 nails analyzed, 12 (63%) showed improvement in the affected area, 3 (16%) remained unaltered and 4 (21%) showed increased fungal infection. When there was an improvement of the affected area, it varied between 20–60% (mean value = 43.7%). (Figure 1)

The nails that presented negative results in the mycological examination also had clinical improvement. (Table 2)

TABLE 1: Clinical and demographic characteristics.

	Total =	12 patients
	n=	20 treated fingernails
<b>Sexo</b>		
male	9 patients	(75%)
female	3 patients	(25%)
<b>Age</b>		
range	39 - 73 anos	
mean value	58,1 anos	
<b>Ungual alteration duration</b>		
range	0,5 a 10 anos	
mean value	3,5 anos	
<b>Previous treatments</b>		
no	5 patients	(42%)
yes		
topical	4 patients	(33%)
oral	2 patients	(17%)
topical + oral	1 patient	(8%)
<b>Comorbidities</b>		
ASH*	6 patients	(50%)
depression	3 patients	(25%)
diabetes mellitus	3 patients	(25%)
dyslipidemia	2 patients	(17%)
GERD*	2 patients	(17%)
nephrolithiasis	2 patients	(17%)
hepatic hemangioma	1 patient	(8%)
prior CVA*	1 patient	(8%)
allergic rhinitis	1 patient	(8%)
osteoarthritis	1 patient	(8%)
BPH*	1 patient	(8%)
prior bariatric surgery	1 patient	(8%)
prior melanoma	1 patient	(8%)
<b>Fungal identification</b>		
Total	5 patients	(42%)
<i>T. rubrum</i>	3	
<i>T. mentagrophytes</i>	2	
<b>% of the nail plate affected</b>		
0 - 20%	5 patients	
21 - 40%	7	
41 - 60%	3	
61 - 80%	2	
81 - 100%	3	

ASH\* - arterial systemic hypertension, GERD\* - gastroesophageal reflux disease, CVA\* - cerebral vascular accident, BPH\* - benign prostatic hyperplasia

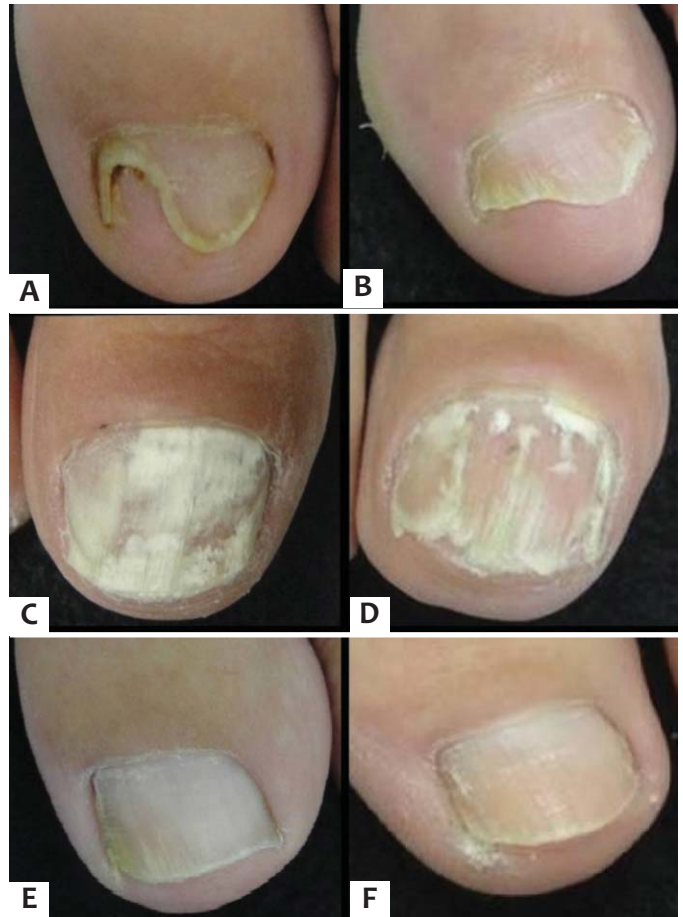


FIGURE 1: A, C, and E: Nails with onychomycosis before treatment. B, D, and F: The same nails 3 months after the last laser session.

TABLE 2: Results

	Total =	12 patients
	n=	20 treated fingernails
<b>Immediate adverse effects</b>		
local pain	9 patients	(75%)
local heat sensation	7 patients	(58%)
<b>Delayed adverse effects</b>		
local pain	1 patients	(8%)
<b>Post-treatment mycological examination</b>		
negative	3 patients	(25%)
positive	9 patients	(75%)
<b>Effects in the affected area* (%)</b>		
worsening	4 nails	(21%)
unaltered	3 nails	(16%)
improvement	12 nails	(63%)
20 - 30%	1 nails	(8%)
31 - 40%	4 nails	(33%)
41 - 50%	5 nails	(42%)
51 - 60%	2 nails	(17%)

\* One nail was excluded from the final analysis due to the alteration of its anatomy following collection for the final mycological examination.

## DISCUSSION

Due to the limitations of treatments for onychomycosis, some studies have demonstrated the use of laser for that purpose with promising results.<sup>4,7,8</sup> Among its benefits are: a shorter treatment duration, a low rate of occurrence of local adverse effects, the absence of systemic adverse effects, and a high patient adherence.

The present study demonstrated clinical improvement in 63% of the treated patients 3 months after the last session. The mean improvement in the affected area was 43.7%.

Poor response was observed in the nails that presented important initial pachyonychia, with that being possibly considered a limiting factor for the laser in reaching the fungal wall, and also suggesting the necessity of further studies on the need of unguis abrasion prior to treatment.

Depending on the angle of the nail bed, the coupling of the tip may have compromised the outcome in patients with predominantly lateral onychomycosis, which was already considered as having the worst prognosis.

There are no studies that are encompassing enough to establish the optimal number of sessions, the parameters to be used in the laser application, and the most appropriate thickness of the nail plate for obtaining better results. Future research may provide more reliable data for effective treatment of onychomycosis through the method described in the present paper.

## CONCLUSION

The present study corroborates the current data from the literature on the potential use of 1,064 nm Nd:YAG laser for the safe and effective treatment of onychomycosis. The optimal treatment regimen remains to be defined and further research is needed to verify whether the complete clinical cure can be achieved with this therapeutic modality. For now, the laser-based treatment constitutes an option for those patients with contraindications to standard treatments, due to its absence of significant adverse effects, ease of application, and good patient acceptance. ●

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# Pyogenic granuloma: description of two unusual cases and review of the literature

*Granuloma Piogênico: descrição de dois casos incomuns e revisão da literatura*

## ABSTRACT

Pyogenic granuloma is a common, benign, vascular proliferation, usually secondary to other events, such as cutaneous trauma. It is known that some lesions can mimic melanoma and vice versa, and it is recommended that the lesion be surgically removed and analyzed histologically. The advent of technologies—such as dermoscopy—that amplify the image recognized by the eye through the identification of certain structures and specific patterns, can facilitate this differentiation and assist in decision-making. In rare situations, its clinical presentation is unusual. The current article is aimed at demonstrating this fact and reviewing the medical literature on the subject, focusing on dermoscopic findings.

**Keywords:** pyogenic granuloma; dermoscopy; melanoma.

## RESUMO

*Granuloma piogênico é proliferação vascular benigna e comum, geralmente secundária a eventos como trauma cutâneo. É sabido que algumas lesões podem mimetizar o melanoma e vice-versa, sendo recomendadas remoção cirúrgica e análise anatomopatológica. O advento de tecnologias que ampliam a imagem reconhecida pelo olho, como a dermatoscopia, através da identificação de algumas estruturas e determinação de padrões específicos, pode facilitar essa diferenciação e ajudar na tomada de decisões. Em situações raras, sua apresentação clínica mostra-se inusitada, e o objetivo deste artigo é demonstrar esse fato e revisar a literatura médica sobre o assunto, com foco nos achados dermatoscópicos.*

**Palavras-chave:** granuloma piogênico; dermatoscopia; melanoma.

## INTRODUCTION

Pyogenic granuloma is a common, benign, acquired vascular proliferation that affects the skin and mucous membranes.<sup>1-4</sup> It usually presents as a single nodule or papule of rapid growth, bleeds easily with only a minimum of trauma, and may develop into an ulcer.<sup>1-4</sup> It occurs commonly on the hands (especially on the fingers), face, lips and feet, however it can also involve other body sites such as the trunk and perianal mucosa.<sup>1-4</sup>

It was first described by Poncet and Dor in 1897, being called botryomycose humaine. The expression pyogenic granuloma was subsequently proposed by Hartzel in 1904, however other names, such as telangiectaticum granuloma, granuloma pediculatum and lobular capillary

## Case Reports

### Authors:

Alessandra Yoradjian<sup>1</sup>  
Luciana C. Maluf Azevedo<sup>1</sup>  
Luciana Cattini<sup>1</sup>  
Ricardo Alves Basso<sup>2</sup>  
Deborah Krutman Zveibil<sup>3</sup>  
Francisco Macedo Paschoal<sup>4</sup>

<sup>1</sup> Dermatologist physician - São Paulo (SP), Brazil

<sup>2</sup> Pathologist Physician, Instituto Brasileiro de Controle do Câncer—São Paulo (SP), Brazil; Assistant Professor at the Faculdade de Medicina do ABC (FMABC)—Santo André (SP), Brazil

<sup>3</sup> Full Professor of Pathology, Faculdade de Medicina do ABC (FMABC)

<sup>4</sup> Assistant Professor of Dermatology, Faculdade de Medicina do ABC (FMABC)

### Correspondence:

Dr. Alessandra Yoradjian  
Rua Sampaio Viana, 580  
Cep: 04004-002—São Paulo—SP, Brazil  
E-mail: alessandraderma@gmail.com

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hemangioma have emerged. The denomination pyogenic granuloma was established in the United States, for it was believed to be the term that best described the pathologic process.<sup>1</sup> However, these lesions are neither pyogenic (for it was not possible to prove the involvement of bacterial infection) nor granulomatous. According to Zaballos et al., the best designation for these lesions would be lobular capillary hemangioma, which, however, is still subject to debate.<sup>5</sup>

The lesion seems to be reactive, but its exact mechanism of onset is uncertain. One possibility is that it might occur due to a reactional hyperproliferative vascular response to a variety of stimuli such as infectious organisms, cutaneous trauma, hormonal factors, and drug therapy such as retinoids.<sup>1,4,5</sup>

Histologically, it shows capillary proliferation close to the surface, with a radiated pattern and a loose edematous collagen matrix, with the epidermis extending down into the base of the lesion, producing an epidermal collar and in some cases causing the formation of peduncles. Mixed inflammatory infiltrate can occur—and fibrosis with septa that intersect the lesion, producing a lobular pattern that can take place in more severe cases.<sup>1</sup>

Its diagnosis is usually facilitated by analysis of history and clinical aspects, however it may mimic benign or malignant tumors in some situations.<sup>1-4,6</sup> The main differential diagnoses are: keratoacanthoma, squamous cell carcinoma, basal cell carcinoma, inflamed seborrheic keratosis, common warts, melanocytic nevus, Spitz nevus, metastatic carcinoma, Kaposi's sarcoma, true hemangioma, vascular tumors of intermediate malignancy, and amelanotic melanoma.<sup>1</sup>

Previous studies have found 38% of cases incorrectly diagnosed.<sup>1-3</sup> Some papers focusing on dermoscopy were designed to better study the characteristics of pyogenic granulomas with a view to facilitating the differentiation from similar lesions. Dermoscopy has been a useful tool in the diagnosis of not only pigmented but also non-pigmented lesions due to the capacity of recognition of

vascular patterns not visible to the naked eye.<sup>7</sup> Particularly in the case of pyogenic granulomas, dermoscopic patterns have been described.

In the present article, two cases of pyogenic granuloma with atypical clinical manifestations are presented with their dermoscopic images, followed by a review of the literature on the subject.

## CASES

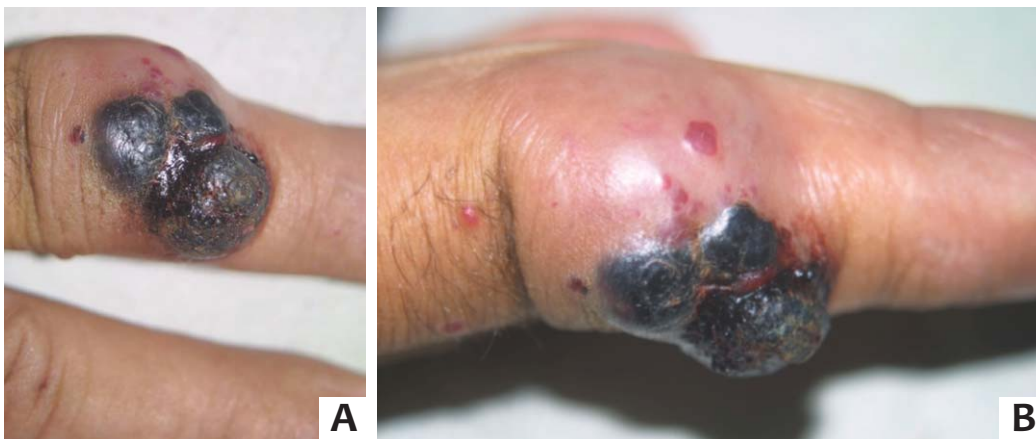
**Patient 1:** female, mulatto, 60-years-old, with a friable, asymptomatic tumor in the dorsal region of the third left finger for six months, recurring after previous treatments (surgical excision and electrocoagulation) (Figure 1).

**Patient 2:** female, Caucasian, 76-years-old, bearing a vegetating lesion with necrotic surface on the dorsum of the left hand, and wine colored satellite papules reaching the palm, for six months, with pain and bleeding (Figure 2).

Dermoscopy of the lesions showed a well-delimited raised nodular lesion, without melanin pigment, and characteristics compatible with melanocytic lesion (Figures 3 and 4).

Histological examination of Patient 1 revealed a raised, well-defined nodular lesion with conservation of epidermal areas and others with epidermal ulceration, inflammatory mononuclear cells, lymphocytes, intact and lysed polymorphonuclear neutrophils, with recent hemorrhage in the papillary dermis just beneath the ulcerated areas. In the deep and superficial papillary dermis, various capillary blood vessels were identified, proliferating in lobular arrangement, with thin walls overlaid by flattened endotheliocytes without atypia and containing red blood cells in the lumen. Capillaries had a radiated layout with some elongated vessels and others displaying obtuse angles (Figures 5 and 6).

A histopathological examination of Patient 2 revealed a lesion similar to that of Patient 1, in its nodular and lobulated arrangement, formed by a microvascular blood proliferative lesion with capillaries in a radiated disposition, and endothelial overlay without atypia. In deeper



**FIGURE 1: A e B.** Clinical picture of Case 1.

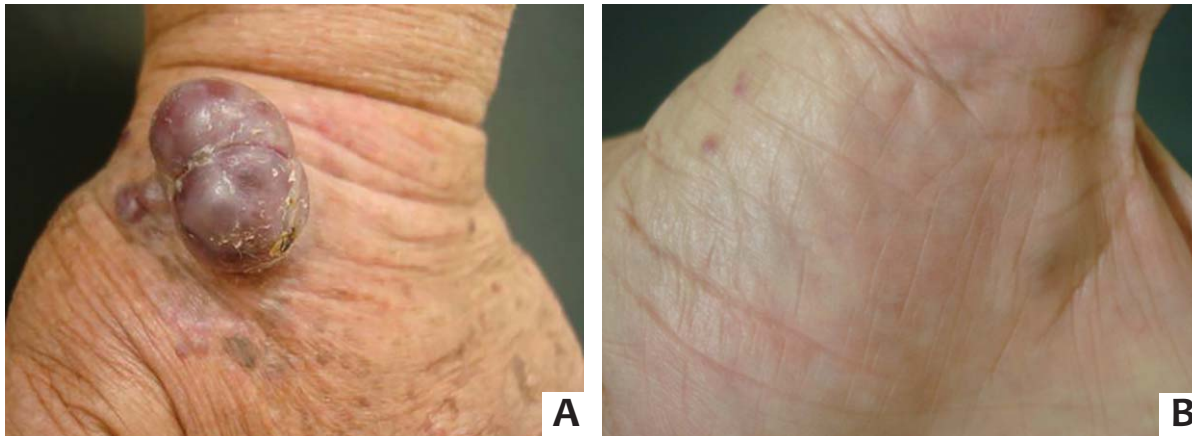


FIGURE 2: A e B. Clinical picture of Case 2.

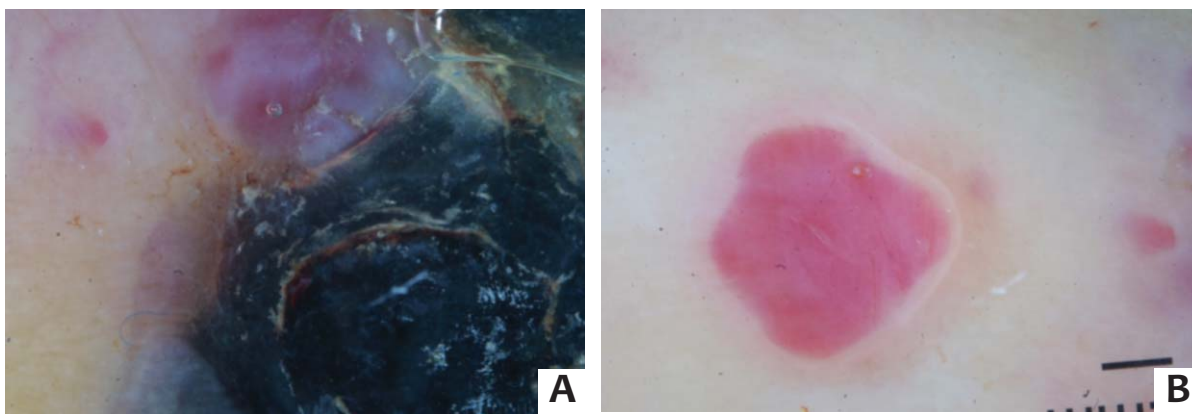


FIGURE 3: A e B. Dermoscopy of the lesion in Case 1.

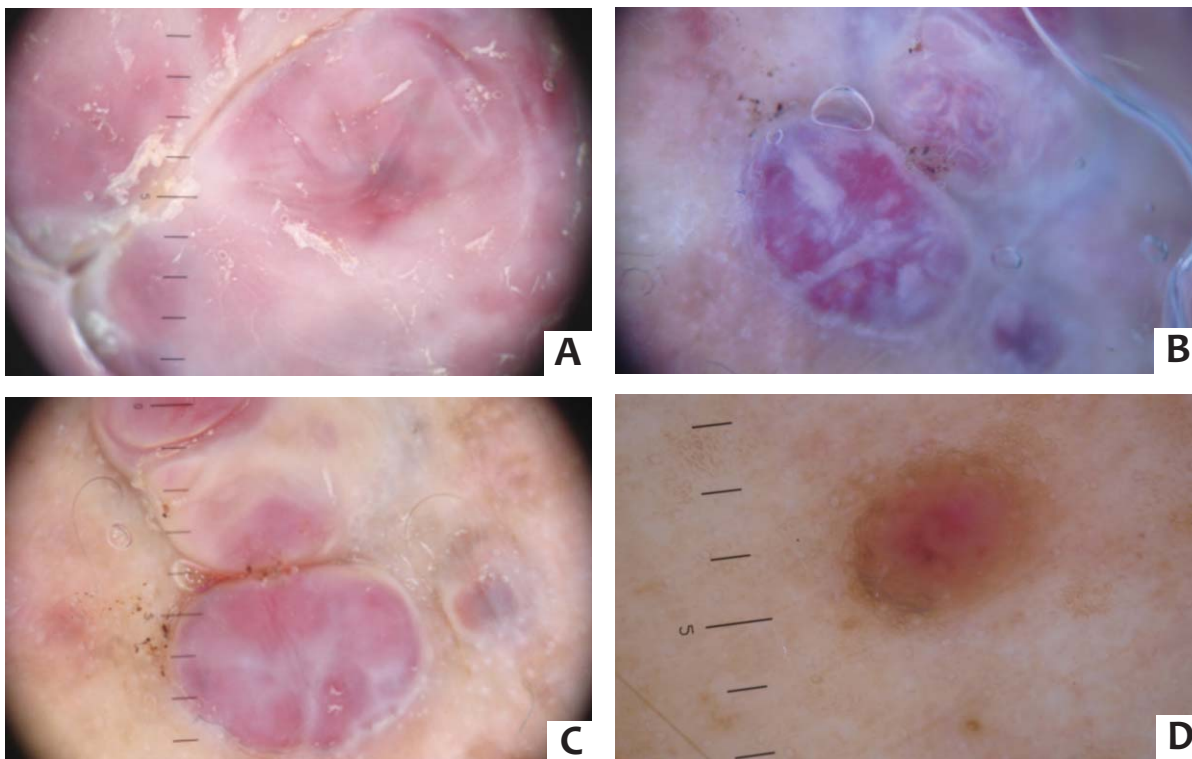
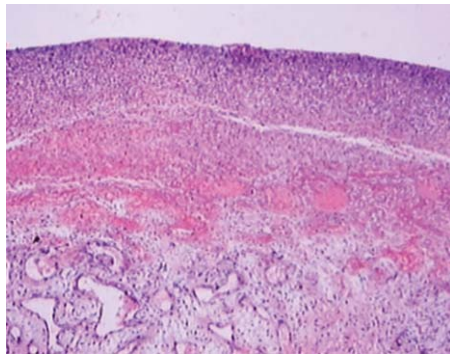


FIGURE 4: A: Dermoscopy of the lesion in Case 2; B: Dermoscopy with polarized light of the lesion in Case 2; C: Conventional dermoscopy of the lesion in Case 2 (the same lesion is shown in Figure 4B); D: Dermoscopy of the lesion in Case 2.

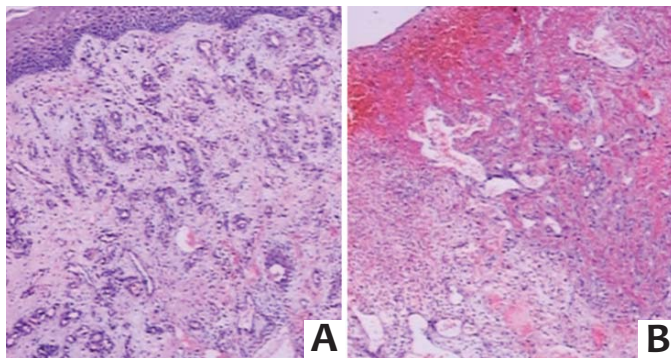


planes, however, an increase of endothelial cellularity showing elongated nuclei with fusiform aspect and mild nuclear atypia, such as hyperchromatism, was verified, without necrosis or mitosis. Despite the existence of other smaller satellite lesions (similar to the latter) on the hand of the patient, the final diagnosis was that of pyogenic granuloma (Figure 7).

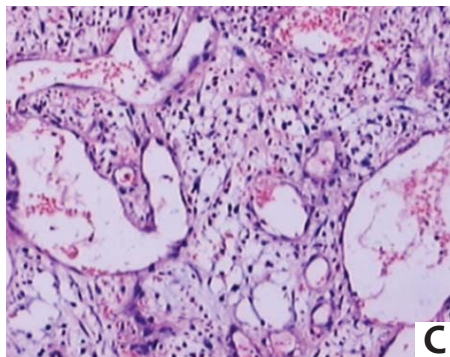
The photograph not featuring a magnified view of the biopsy taken during the histological examination of Patient 2's cutaneous lesion, shows a full view of the lesion



**FIGURE 5:** Patient 1: Ulcerated epidermis with mononuclear and polymorphonuclear inflammatory cells. Recent superficial hemorrhage, and blood capillary proliferative vascular lesion immediately beneath, are observed (photomicrography with 40X magnification in optical microscope).



**FIGURES 6: A e B** Patient 1: The radiated arrangement of proliferated capillary blood vessels in the superficial dermis are observed in Figure 6A; the proliferative microvascular lesion is seen in Figure 6B (photomicrographies with 100X magnification in optical microscope).

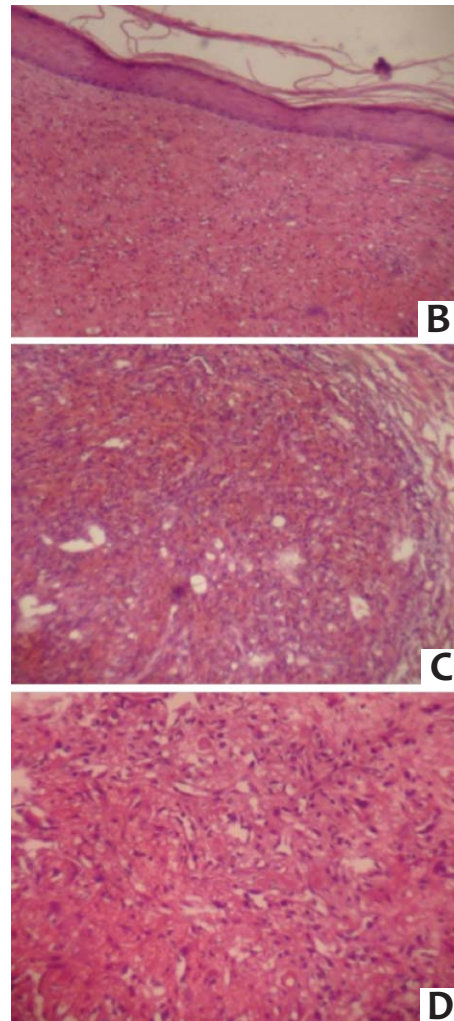


**FIGURA 6: C** Patient 1: Micro capillary blood vessels are seen in varied sizes and rounded shapes, sometimes angled, overlaid with flattened endothelial cells and containing red blood cells in the lumen. It is possible to observe dermal stroma surrounding them, with loose and edematous appearance.

with nodular area. In the photomicrography, the images show the lesion just beneath the epidermis. These areas show less cellularity and contain a more recent hemorrhage, with the most differentiated area exhibiting froth with small blood capillaries, an aspect of lobular capillary hemangioma. The deepest areas of the lesion, in the subcutaneous tissue region, are hypercellular areas composed of fusiform cells with mild to moderate atypia, rose-colored cytoplasm, and elongated and hyperchromatic nuclei. This means that these are differentiated areas—characte-



**FIGURE 7: A** Patient 2: Photograph of histological slide without magnification. Note the nodular and lobulated elevated lesion with reddish color.



**FIGURES 7: B, C e D.** – Patient 2: In the first two photomicrographies it is possible to observe the lesion overlaid with epidermal mild hyperkeratosis, with blood microvascular proliferation in the dermis, and with recent hemorrhage. Still, in Figure 7C, it is possible to note the presence of peripheral fibrous capsule conformation, corresponding to the white collarette seen in the dermoscopic examination. In photomicrography 7D, it is possible to note a proliferative vascular lesion formed by endothelial pattern cells with elongated nuclei in fusiform arrangement, more cellular than in the lesion areas in the superficial dermis, with mild cellular atypia and denser adjacent dermal stroma (photomicrographies 40X magnification in Figure 7B, 100X in Figure 7C, and 400X in Figure 7D).

ristic of hemangioendotheliomas—allowing a differential diagnosis with the low-grade angiosarcoma. The less cellular, more differentiated area is observed with greater magnification. (Figure 7)

## DISCUSSION

The cases described in the present article show pyogenic granuloma lesions with atypical and exuberant clinical presentation. Due to the fact that it was not possible to clinically exclude malignancy, patients underwent biopsy for histological analysis. First, however, a dermoscopic examination without criteria for melanocytic lesions was carried out. Homogeneous red areas, white rail lines intersecting the lesion, white collarette, ulceration, hemorrhage crusting, and isolated lesions showing pinpoint vessels, were observed. Finally, the histological examination demonstrated the presence of benign lesions.

Pyogenic granulomas are benign acquired capillary lesions that affect the skin and mucous membranes, and whose pathogenesis is not yet explained. It is suggested that it might result from mechanical trauma, however the participation of hormonal factors, medications (retinoids), arteriovenous malformations, viral oncogenes and other microorganisms, as well as of angiogenic growth factors have also been proposed.

Usually solitary, painless, pyogenic granulomas may have different diameters—from a few millimeters to centimeters—and can ulcerate and bleed.<sup>1-5</sup>

Due to the fact that some nodular melanomas mimic pyogenic granulomas, biopsy is always required for anatomopathological analyses, with an aim at avoiding the delay of diagnosis and improving the prognosis.<sup>1,7</sup>

Dermoscopy is an *in vivo*, noninvasive technique, used for pigmented and vascular lesions that can help when there is suspicion of pyogenic granuloma, increasing diagnostic accuracy even in cases that are clinically atypical.<sup>1-3,5,7</sup> More recently, studies on dermoscopic patterns of pyogenic granuloma have been carried out in order to assist in the differential diagnosis with amelanotic melanoma.<sup>3</sup>

Dermoscopy should be conducted without pressure to avoid compromising vascular visualization. In the absence of criteria for melanocytic lesions, it can evidence from homogeneous red areas to well-defined vascular structures.<sup>3,5,8</sup> The main characteristics are homogeneous red areas (observed in more than 90% of cases), white collarette (80% of cases), white rail lines that intersect the lesion (30–45% of cases), ulceration (46% of cases) and vascular structures (45% of cases).<sup>1-6,8</sup> No isolated characteristic was 100% specific.<sup>3</sup> As a consequence, through observations of dermoscopic findings in pyogenic granulomas, Zaballos et al. recently defined 7 dermoscopic patterns for those lesions.<sup>1-3</sup> According to the combination of these characteristics present in the lesion, the patterns are:<sup>1-3</sup> (Figure 8):

- P1: homogeneous red area + white collarette
- P2: homogeneous red area + white rail lines
- P3: homogeneous red area + vascular structures
- P4: homogeneous red area + white rail lines + white collarette
- P5: homogeneous red area + white collarette + vascular structures
- P6: homogeneous red area + white rail lines + vascular structures
- P7: homogeneous red area + white collarette + white rail lines + vascular structures

The patients studied had had multiple lesions grouped in a single body segment. In those cases, the presence of a combination of the patterns described above could be observed, due to the presence of multiple lesions, each with a specific pattern.

The homogeneous red area corresponds to the area with absence of structure, whose color varies from red to whitish-red. It is attributed to the presence of numerous small capillaries or proliferative vessels arranged in a myxoid stroma.<sup>3,5</sup> It is quite common in pyogenic granulomas, however it is not a finding specific only to this type, for it is also common in amelanotic melanomas.

In histology, the white collarette corresponds to the attached hyperplastic epithelium that fully or partially embraces the lesion in the periphery.<sup>3,5</sup> It is the most specific structure of pyogenic granulomas. The white rail lines correspond to fibrous septa that surround the capillary tufts or lobules in the older lesions.<sup>3,5</sup> In Patient 1, on whom both conventional dermoscopy and polarized light had been performed, it could be observed that the white

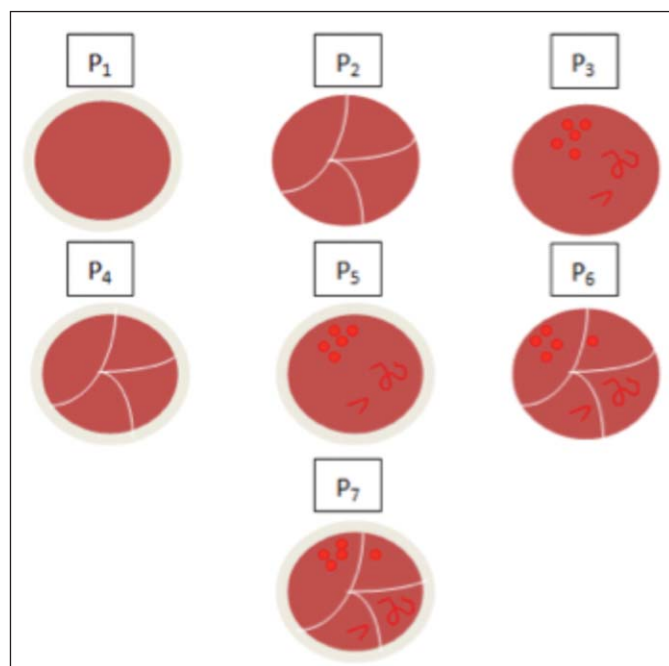


FIGURE 8: Dermoscopic patterns in pyogenic granulomas.

Source: Zaballos P, et al.<sup>3</sup>

rail lines became more apparent with the use of polarization (Figures 4B and 4C).

Regarding the vessels that can be observed, the following arrangements have been described: pinpoint, irregular linear, polymorphic/atypical, telangiectasia, and hair-pin-like. In the cases described in the present study, the vessels were minimally evident, not constituting a relevant finding despite the exuberance of the lesions.

Ulcerations were found to be common to many other skin lesions and were not included in the criteria.

In the study carried out by Zaballos et al., the pattern most frequently associated with pyogenic granuloma was the P4. Fifty-two percent of pyogenic granulomas showed one of three patterns: P1, P4, and P7, with no amelanotic melanoma having presented in any of them.<sup>3</sup>

In addition to atypical vessels, other findings, such as the whitish-blue veil, blotches, and hematic crusts—all of which are common characteristics of melanomas—

were also found in some cases of pyogenic granuloma. For that reason, there is the possibility they can simulate a nodular amelanotic melanoma. As a result, surgical excision and pathological examination of pyogenic granulomas are mandatory.<sup>1-3,6,7</sup>

More recently, with the advent of new technologies such as confocal microscopy, advances in differential diagnosis have emerged. With this technique it is possible to evaluate the vascularization regarding dilatation, elongation, tortuosity, flow rate, and neovascularization. In addition, pagetoid cells and atypical melanocytes are not visualized in pyogenic granulomas. Studies are still preliminary, nevertheless there seems to be good histologic correlation.<sup>9</sup>

Due to the diversity in clinical presentations of benign tumor lesions, such as pyogenic granuloma, imaging studies linking dermoscopy and confocal microscopy, especially in atypical cases, may be useful for defining the characteristics of these tumors and their histopathologic correlation. ●

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# The use of the A-T flap for reconstructing surgical wounds on the dorsum of the hand

*A utilização do retalho A-T para reconstrução de ferida operatória no dorso da mão*

## Authors:

Rubens Pontello Júnior<sup>1</sup>  
Rogério Nabor Kondo<sup>2</sup>  
Ricardo Pontello<sup>3</sup>

<sup>1</sup> Assistant Professor of Dermatology, Hospital Universitário Regional do Norte do Paraná da Universidade Estadual de Londrina—Londrina (PR), Brazil

<sup>2</sup> Dermatology Resident Physician, Hospital Federal Bonsucesso (HFB)—Rio de Janeiro (RJ), Brazil

## Correspondence:

Dr. Rubens Pontello Júnior  
Rua Alexander Graham Bell, 433 / Casa 42  
Cep: 86063-250—Londrina—PR, Brazil  
E-mail: rubensjr@institutopontello.com.br

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## ABSTRACT

The dorsum of the hand is home to tumors that often require a surgical approach. Due to limited cutaneous mobility, wide surgical wounds become a challenge to dermatologic surgeons. The authors report the case of a patient with a tumor in the dorsal region of the left hand that, after removal with a safety margin, resulted in a wide surgical wound, and in the choice of reconstruction with an A-T flap. Six months later, the patient was cured, with total preservation of the hand's mobility and excellent aesthetic results. The concept of using flaps for closing wide surgical wounds, whenever possible, is reinforced.

**Keywords:** hand; neoplasms; surgical flaps.

## RESUMO

*O dorso das mãos é sede de tumores que muitas vezes necessitam de abordagem cirúrgica. Devido à limitada mobilidade cutânea, feridas cirúrgicas amplas tornam-se um desafio ao cirurgião dermatológico. Relatamos o caso de paciente apresentando tumor em região dorsal de mão esquerda que, após retirada com margem de segurança, apresentou ferida cirúrgica ampla, tendo sido feita a opção por reconstrução com retalho A-T. Seis meses após, o paciente apresenta-se curado, com preservação total da mobilidade da mão e ótimo resultado estético. Reforça-se o conceito da utilização de retalhos, sempre que possível, para o fechamento de feridas cirúrgicas amplas.*

**Palavras-chave:** mãos; neoplasias; retalhos cirúrgicos.

## INTRODUCTION

The dorsum of the hands often house tumors that require a surgical approach. Due to limited cutaneous mobility, wide surgical wounds become a challenge to dermatological surgeons. The present article describes the use of the A-T flap, performed in a single surgical event by a single surgeon, as an option for closing surgical wounds on the dorsum of the hand.

## CASE REPORT

A 54-year-old male patient presented a three-month history of progressive growth of a lesion on the dorsum of the left hand. Clinical examination showed hardened tumoration with central corneum plug, 3.6 cm in diameter, suggestive of keratoacanthoma. (Figure 1)

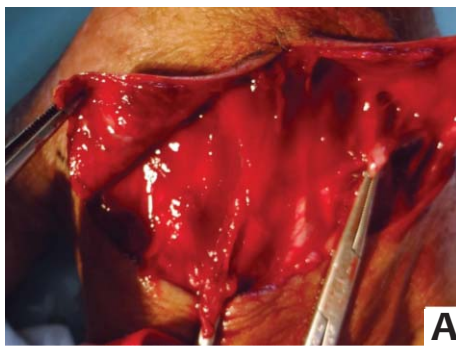
After demarcating the tumor with a 3.0 mm safety margin, plans were made for reconstruction with the A-T advance-

ment flap (Figure 1). After local infiltrative anesthesia of 2% lidocaine with vasoconstrictor, the total excision of the lesion was carried out with a minimum margin of 3.0 mm. It was followed by perilesional cutaneous divulsion, avoiding accidental cut nerves or tendons, and the preparation of the flap, with an approximation of the borders and suture with 4-0 nylon monofilament (Figure 2).

The patient returned two weeks after, showing adequate healing, which allowed for the removal of all stitches. Despite this, some limitation in the flexion of the fingers was verified. The patient was then referred for motor physical therapy, having been instructed to frequently and gradually flex and extend the fingers,



**FIGURE 1:** Tumor on the dorsum of the left hand, 3.6cm in diameter and containing a central corneum plug suggesting keratoacanthoma; delimitation of a minimum 3.0 mm surgical margin and detachment area for the preparation of the A-T flap.



**A**



**B**

**FIGURE 2:**  
**A.** Detachment of perilesional tissue.  
**B.** Immediate postoperative: simple stitch suture with 4-0 nylon monofilament.



**A**



**B**

**FIGURA 3:** Seis meses após o procedimento: cicatriz cirúrgica cosmeticamente aceitável e funções motoras completamente preservadas

immersed in water, in addition to taking oral prednisone in an anti-inflammatory dose (equivalent to 0.5 mg/kg\*day, for seven days). The one-week re-assessment of the patient showed that the movement had been completely restored. After six months, the patient showed excellent aesthetic and functional recovery, with complete patient satisfaction and no signs of tumor recurrence (Figure 3).

The histologic examination of the specimen removed surgically confirmed the initial hypothesis of keratoacanthoma.

## DISCUSSION

Extensive surgical wounds on the dorsum of the hand often create a challenge for dermatologic surgeons. When primary closure is not feasible, flaps or skin grafts are alternative techniques. Even though free grafts provide good results on the dorsum of the hands, this technique has the disadvantage of requiring a distant donor area.<sup>1,2</sup> Whenever possible, a decision is made for the use of flaps—which use adjacent tissue, following the “like-for-like” rule, leading to better esthetic results<sup>2</sup>—or the confection of rotation flaps for surgical wounds on the dorsum of the hands, recently introduced by Cardoso et al., a method that preserves functional capabilities and aesthetics.<sup>3</sup>

The A-T flap is classified as an advancement flap, and is chosen when the greater degree of sagging is located along the defect's shorter axis (as in the present case) or when the distortion of structures adjacent to the borders of the defect is undesirable (as in the case of lesions above the eyebrow). It is worth noting that extensive undermining is not recommended, for despite providing a greater amount of tissue without tension, it can give rise to the interruption of blood supply to the vertical component arising from the deep plexus, thus compromising the perfusion of the flap's distal rim.<sup>4</sup> The use of simple divulsion for detaching the

surgical margins has preserved axial vascularization, avoiding areas of necrosis in the flap even in the most distal region.

The technique has proved useful for the reconstruction of surgical wounds in the central region of the dorsum of the hands, where the flap's borders advance naturally.

## CONCLUSION

The procedure described in this paper was performed in a straightforward manner, requiring only the use of a local anesthetic. Based on the authors' literature search, it is the first report of an A-T advancement flap being used for the closure of a surgical wound on the dorsum of the hands. The conclusion is that the described technique allows for rapid reconstruction, distributing the tension of the closure over a larger surface area while preserving the functionality and aesthetic. The technique is therefore identified as a good option for large wounds that have their longest vertical axis located in the central region of the dorsum of the hand. ●

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# Siringocistoadenoma papilífero localizado na coxa

*Syringocystadenoma papilliferum located in the thigh*

## RESUMO

Siringocistadenoma papilífero é tumor benigno raro, mais comum em couro cabeludo e face. Pode apresentar-se como lesão independente ou associada ao nevo sebáceo de Jadassohn. Foram relatados na literatura raros casos desse tumor com localização na coxa. Descrevemos o caso de uma paciente com siringocistadenoma papilífero distinguido por seu componente apócrino intradérmico tubular papilífero.

**Palavras-chave:** adenoma de glândula sudorípara; neoplasias cutâneas; neoplasias de anexos e de apêndices cutâneos.

## ABSTRACT

*Syringocystadenoma papilliferum is a rare, benign tumor, most common in the scalp and face. It can present as an independent lesion or be associated with nevus sebaceous of Jadassohn. Rare cases of this tumor located in the thigh have been reported in the literature. The present article reports the case of a patient with syringocystadenoma papilliferum, distinguished by its intradermal tubular apocrine papillary component.*

**Keywords:** adenoma, sweat gland; skin neoplasms; neoplasms, adnexal and skin appendage.

## INTRODUCTION

*Syringocystadenoma papilliferum* (SCAP) is an uncommon, benign adnexal tumor of the sweat glands. It is often located on the face, scalp, or neck, and can be present at birth, arise during childhood, or appear later on at an advanced age.<sup>1</sup> Lesions are diverse and nonspecific, and can manifest, for instance, as a solitary plate or papules and multiple nodules, usually pinkish or waxy with a verrucous erosive surface and a soft consistency.<sup>2</sup>

In most cases, the size of the SCAP increases during puberty and can be associated with other benign tumors, including the nevus sebaceous of Jadassohn, which is present in 40% of cases. Additionally, development of basal cell carcinoma (BCC) is reported in up to 10% of cases—which, in the majority of instances, presents in coexistence with nevus sebaceous.<sup>1</sup>

## Case Reports

### Authors:

Alex Panizza Jalkh<sup>1</sup>  
Anne Caroline da Silva Menezes<sup>2</sup>  
Alcidarta dos Reis Gadelha<sup>3</sup>

<sup>1</sup> Preceptor at the Medical Residency Program, Fundação de Medicina Tropical Dr. Heitor Vieira Dourado (FMT-HVD) and Hospital Universitário Getúlio Vargas—Manaus (AM), Brazil

<sup>2</sup> Scholarship Fellow of the Scientific Initiation Program of the Fundação de Medicina Tropical Dr. Heitor Vieira Dourado (FMT-HVD)

<sup>3</sup> Instructor at the Medicine Program, Universidade Estadual do Amazonas (UEA)—Manaus (AM), Brazil

### Correspondence:

Dr. Alex Panizza Jalkh  
Al. Alaska 1091 / apt. 601  
Cep: 69037-057 / Ponta Negra—Manaus—AM, Brazil  
E-mail: ajalkh@gmail.com

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SCAP was first reported by Peterson in 1892 as a tumor of the sweat glands, and since Shiefferdecker differentiated sweat glands into apocrine and eccrine (in 1917), attempts to clarify the nature of the tumor are still controversial.<sup>3</sup> Although eccrine origin has been observed in some tumors of this variety, a differentiation pattern that is predominantly apocrine is currently accepted as the norm.<sup>1</sup>

The present study is aimed at highlighting the SCAP's unusual location in this case, as a means of contributing to the differential diagnosis of atypical linear verrucous lesions in the thigh, and to the proper treatment of this rare disease.

### CASE REPORT

A 24-year-old, Caucasian, patient, born and residing in Manaus, the capital of the northern Brazilian State of Amazonas, alleged to having a lesion since birth that had increased in size, and started producing exudate and presenting pruritus after puberty. A band-shaped lesion, located in the upper third of the anterior side of the left thigh, measuring approximately 8 x 2cm was observed in the clinical examination. It was composed of exudative, pruritic, and not-painful-to-the-touch winy-erythematous papules and nodules, with a smooth surface and firm consistency (Figure 1). Histopathology revealed cystic invaginations protruding into the dermis (Figure 2). In the lumen, there were villousities overlaid by two layers of cells: the innermost, with columnar cells, showing secretion due to "decapitation"; and the outermost, with cuboidal cells. In the upper dermis, there was infiltrate that was rich in plasmocytes.

### DISCUSSION

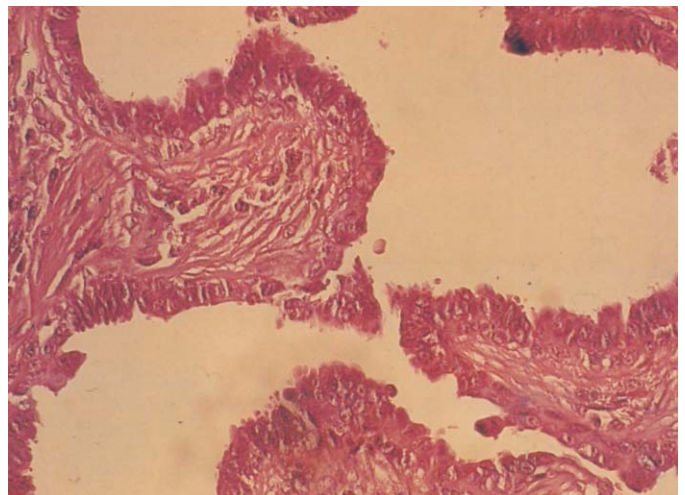
In 1917, Stokes called *nevus syringadenomatus papilliferum* a neoplasm located in the skin of the thigh of a female patient.<sup>3</sup> Since then, many cases have been published in the medical literature, mostly referring to those located on the head and neck (75%), and on the trunk (20%). In the present study, the SCAP had multiple linear lesions—similar to the eight cases reviewed by Rammeh–Rommani et al.<sup>2</sup>

More recently, two cases have described instances in which multiple tumors have arisen simultaneously, originating from sebaceous nevi.<sup>1</sup> As with Stokes' initial case, the lesion in the patient described in the present study, was located on the thigh, tumors on the body's extremities being a less common occurrence. This patient's lesion was present at birth, as is the case in 51% of these tumors. The authors emphasize the unusually exuberant growth of the lesion, its dimensions being reported at 8 x 2cm.

This kind of tumor has been described as asymptomatic, although sometimes it presents pain and pruritus.<sup>7,8</sup> As with other case reports, the patient in the present study had pruritus and discomfort due to the lesion's exudative and pruritic character,



**FIGURE 1:** Band-shaped lesion located in the anterior portion of the upper third of the thigh, showing winy-erythematous papules and nodules with ulcerated areas.



**FIGURE 2:** Microvillousities overlaid by a double layer of cells, invaginating into the cystic cavity. There is a presence of plasma cells.

in addition to the obvious compromise of the aesthetic appearance. Present in 40% of cases, the association of SCAP with *nevus sebaceus* was not detected in the referred patient.

Due to the rare nature of the neoplasm, the authors highlight the importance of the histological examination to establish the differential diagnosis.<sup>1</sup> The surgical excision of the lesion resulted in its cure.

The authors warn about the very rare possibility of cases of *syringocystadenocarcinoma papilliferum* arising from SCAP, which can be recognized due to a nuclear atypia and increased mitotic activity combined with an invasive character.<sup>10</sup> ●



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# The usefulness of Karapandzic flap in the reconstruction of large defects of the lower lip

*Utilidade do retalho de Karapandzic na reconstrução de grandes defeitos do lábio inferior*

## ABSTRACT

The reconstruction of defects resulting from tumor resection is a challenge for the surgeon, who should get good results both functional and aesthetic. The objective of the present study is to describe the surgical technique used in a 78-year-old male patient with the diagnosis of squamous cell carcinoma in the lower lip and who underwent excision of the lesion and reconstruction with the Karapandzic technique. This flap is employed in the reconstruction of surgical defects that cover 40–75% of the lip's extension.

**Keywords:** carcinoma, squamous cell; surgical flaps; lip neoplasms.

## RESUMO

*A reconstrução dos defeitos resultantes das ressecções tumorais constitui um desafio para o cirurgião, que deve buscar bom resultado tanto funcional quanto estético. O objetivo deste trabalho é descrever a técnica cirúrgica usada em homem de 78 anos com diagnóstico de carcinoma de células escamosas no lábio inferior e que foi submetido à excisão da lesão e reconstrução com a técnica de Karapandzic. Esse retalho é usado na reconstrução de defeitos cirúrgicos que ocupam de 40 a 75% de extensão do lábio.*

**Palavras-chave:** carcinoma de células escamosas; retalhos cirúrgicos; neoplasias labiais.

## INTRODUCTION

Squamous cell carcinoma is the most common malignant neoplasm of the lips. It is an aggressive and invasive tumor, which can metastasize if not treated early and radically. Only 5% of the neoplasms of the lip occur in the upper lip, and the vast majority are basal cell carcinomas. The other 95% affect the lower lip, where the squamous cell carcinoma is predominant due to greater exposure to ultraviolet radiation. This anatomical area is of great interest due to the high frequency of the condition, which involves the buccal cavity's natural sphincter.<sup>1-6</sup>

The reconstruction of defects resulting from tumor excision poses a challenge to the surgeon, who must aim for good functional and aesthetic results. For that reason, numerous techniques are described for the reconstruction of this anatomic region.<sup>1-6</sup>

## Case Reports

### Authors:

Paula Luz Stocco<sup>1</sup>  
Guilherme Fonseca<sup>2</sup>  
Lucas Emanuel de Lima Azevedo<sup>1</sup>  
Thais Bittencourt Gonçalves Teles<sup>1</sup>  
Carmélia Matos Santiago Reis<sup>3</sup>

<sup>1</sup> Resident Physician in Dermatology, Hospital Regional da Asa Norte (HRAN/SES)—Brasília (DF), Brazil

<sup>2</sup> Dermatologist Physician, Hospital Regional da Asa Norte

<sup>3</sup> Medical Resident in Dermatology Supervisor, Hospital Regional da Asa Norte

### Correspondence:

Dra. Paula Luz Stocco  
SQS 103, Bloco K, apt. 103, Asa Sul  
Cep: 70342—Brasília—DF, Brazil  
E-mail: paula\_stocco@hotmail.com

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The following techniques are available among surgical procedures for the treatment of lesions in the lower lip: shaving, “V” excision, with or without the leveling of the vermilion; Karapandzic flap; Estlander flap; and reconstruction with Bernard–Burrow–Webster flap.<sup>1-6</sup>

The shave or leveling technique is used in cases of superficial lesions affecting the mucosa and submucosa, but which do not infiltrate the musculature. The “V” technique excision, with or without leveling of the vermilion, is indicated for cases where a large lesion covers a part of the vermilion, requiring that it be excised in a wedge shape. Resections of up to 30% of the lip allow for a primary suture without tension. Resections leading to defects of between 30–40% are best addressed through resections in “W” or using labial flaps.<sup>1-6</sup>

The Karapandzic technique is suitable for repairing central defects of the lower lip through rotation and advancement of up to  $\frac{3}{4}$  of the lip, preserving the sphincter function, innervation, and irrigation. The Estlander technique (pedicled lip transfer flap) is used when 30% of the lip must be resected and may be substituted with a flap made from the upper lip. That flap’s maximum length must be greater than 1.5 cm or 2.0 cm, which corresponds to about  $\frac{1}{4}$  of the length of the lip. The reconstruction technique using a Bernard–Burrow–Webster flap is preferable for use with defects of up to 65%, when the resection results in a major defect that needs to be reconstructed with vascularized flaps.<sup>1-6</sup>

The Karapandzic and Bernard–Burrow–Webster flaps are among the more frequently used options for reconstructing large lip defects. The Karapandzic flap is suitable for defects covering  $\frac{2}{3}$  of the length of the lower lip. In cases of larger defects the resulting microstomia contraindicates this procedure. In total or subtotal labial defects, the Bernard–Burrow–Webster flap remains a good reconstructive option.<sup>1-6</sup>

The factors influencing the selection of the treatment type and technique to be employed are related to the tumor and patient.<sup>1-6</sup>

## CASE REPORT

The case involves a seventy-eight-year-old male patient with an ulcerated lesion in the lower lip that had developed for six months, with progressive growth (Figure 1) and absence of regional lymphadenopathy on palpation. The clinical diagnosis of squamous cell carcinoma was confirmed through biopsy.

Under ambulatorial regimen and local anesthesia, the patient underwent an uneventful excision of the lesion and reconstruction with the Karapandzic myocutaneous flap technique. The preparation of the flaps consisted of bilateral perioral incisions, originating in the lower borders of the surgical defect and extended along the mentolabial and nasolabial grooves (Figure 2).

The orbicularis oris muscle and oral mucosa were incised up until the point of the labial commissures. A delicate dissection of planes was carried out so that the incisions did not reach the oral mucosa laterally. Advanced myocutaneous flaps were then prepared to cover the defect. The neurovascular structures



**FIGURE 1:**  
Ulcerated lesion  
on the lower lip



**FIGURE 2:**  
Preoperative  
marking for  
carrying out  
perioral incisions

were spared, thus preserving the lip’s sensitivity and motility (Figures 3 and 4).

The flaps were medially oriented, with the suturing of the mucosa, orbicularis oris muscle, and skin in three successive planes, allowing the restoration of the oral sphincter’s continence (Figure 5).

The aesthetic and functional result was satisfactory, given that the sutures coincided with the natural grooves. The oral continence, the sensitivity, and mobility of the lip were preserved. Nevertheless, there was a slight microstomia with no functional impact that can be mitigated with commissurotomy (Figure 6).

One year after the procedure, the patient had no signs of local recurrence or local–regional metastasis.

## DISCUSSION AND CONCLUSION

The flap described by Karapandzic in 1974 is one of the options for reconstruction of large defects of the lip. It is based on the anatomical preservation of the facial nerve’s vascular pedicles, which maintain the lip’s future irrigation and functionality, with the advantage of being carried out in a single surgi-



**FIGURE 3:**  
Advancement of the myocutaneous flaps



**FIGURE 4:**  
Advancement of the myocutaneous flaps



**FIGURE 5:**  
Suturing of the myocutaneous flaps



**FIGURE 6:** Final aesthetic and functional results

cal event and possibly under local-regional anesthesia. 1-5 It is the appropriate flap to correct defects affecting 40-75% of the length of the lower lip, and can be applied in reverse in the reconstruction of the upper lip. The Karapandzic flap has as its main virtue the preservation of the mobility of the lower lip and its sensitivity, as well as the oral continence. Its greatest drawback is microstomia, which also occurs—to a greater or lesser degree—with other flap techniques used in the reconstruction of full thickness surgical defects. 1-6 ●

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