The impact of implantation site on procedure success in patients with unresolved facial palsy treated with upper-eyelid gold weight loading

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Loading of the upper eyelid is a well-established procedure for the correction of incomplete eyelid closure due to unresolved facial palsy. Some incurable complications are attributed to type IV hypersensivity reaction, but there is no confirmation of this hypothesis. The aim of the study was to show the impact of gold weights on eyelid tissues depending on the implantation site. Out of 94 total patients (aged 53 ± 17 years) treated from July 2009–2021, since 2014 thirty consecutive patients were randomised into one of 3 groups: the GLE group (gold weight fixed 2 mm above the eyelash line), the GUE group (gold weight fixed at the border of the tarsus and the levator aponeurosis), and the PUE group (platinum chain fixed in the same way as in the GUE group). In the cases of complications, the explanted weights were evaluated histopathologically. The outcomes were compared between groups. Incomplete eyelid closure was corrected in all patients. Serious complications were noted in 100% of patients in the GLE group and 20% in the GUE group (p < 0.0001). A slight lymphocytic reaction was observed in the GUE group. A moderate to significant lymphocytic reaction was observed in the GLE group (p < 0.001). Adverse reactions of the upper eyelid microenvironment resulting from gold weights seem to be dependent on mechanical damage to the eyelid structures, rather than on implants themselves. The site of placement of the weight in the upper eyelid may be critical for procedure success.

Facial palsy (FP) may have many etiologies, though luckily most patients recover without any serious sequelae. However, some patients have irreversible FP which is a challenge for specialists in many fields of medicine. These are usually patients with a tumor of the cerebellopontine angle, patients who have had surgeries to remove a primary tumor, patients who have had resection of salivary gland tumors or patients with a history of trauma. Although these patients usually have a good prognosis as to their main disease, complications related to facial nerve dysfunction seem to be of the utmost importance. The inability to close the eye leads to its drying out and the development of severe corneal complications resulting in reduced visual acuity, decreased quality of life and even perforation and loss of the eye. The idea of adding weight to the non-closing upper eyelid with a gold weight was first presented by K. Illig in 1958. Smellie GD popularized this method in English-language writings and gold was introduced as the metal of choice for loading of the upper eyelid.

The following years brought a wealth of alternative surgical techniques to resolve incomplete eyelid closure. However, due to the difficulty of these surgical techniques, the cost of materials and the high percentage of complications, loading of the upper eyelid with a gold weight was resumed as it is a relatively simple, effective and safe technique. With further modifications of implants and operation techniques, gold weights have become a widely used and effective method for the correction of lagophthalmos in established FP. Complications related to implantation are relatively rare and include: weight extrusion, migration, bulging, induced astigmatism responsible for deterioration of visual acuity, under- or overcorrection and unsatisfactory cosmesis. Only a few cases of presumed allergic or other non-infectious inflammatory reaction to gold weights have been reported in the literature as a serious incurable complication, which necessitates the removal of the implant.

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Some late complications are attributed to type IV hypersensitivity reaction. However, because of the low number of patients in the study groups, uncertain accuracy of screening tests, scarce histopathological examination and limited immunohistochemical typing of the inflammatory cells, there is still no direct confirmation of this hypothesis. Gold was considered biologically inert through the late 1980s, when 0.5% sodium thiosulfate was introduced as a good screening test in the diagnosis of a contact allergy to gold. After a number of initial reports on the high frequency of allergy to gold diagnosed on the basis of patch testing with gold sodium thiosulfate, it was proven that the patch test alone is not sufficient to confirm a contact allergy. According to the study of Anhilide et al., patch testing with gold sodium thiosulfate alone has a positive predictive value of only 40%.

The mechanisms responsible for the development of symptomatic allergic contact dermatitis are still under investigation. The innate immune system can be activated by metal ions or other chemicals at the tissue/matrix interface, which causes dysfunction of the immune system and activation of the double immune response (allergen-specific effector and memory T cells mediated). However, there are many host- and biomaterial-specific factors which can modify the autologous innate stimulus, which, in turn, can influence individual susceptibility to an allergen. Except for the innate immune response, a variety of different types of proteins in the coagulation, complement, fibrinolytic and kinin-generating systems and platelets are activated in the processes of simultaneous injury and wound healing following implantation of biomaterials. Such explanations do not consider placement site as a factor. The aim of this study was to investigate the late impact of gold implants on the tissues of the upper eyelid depending on the implantation site. After conducting a case study in order to find possible causes of complications after loading of the upper eyelid with gold weights, we conclude that weight placement site in the upper eyelid, rather than a gold allergy itself, may be critical for procedure success. In the years since this initial reporting, we conducted a prospective study in order to confirm or reject this theory. This paper reports on new findings derived from follow-up research.

Material and methods

Study design. This research was part of a prospective, interventional study that assessed clinical outcomes in patients after weight implantation in the upper eyelid as treatment for ocular complications of unresolved FP between July 2009 and July 2021. The study was approved by the designated ethics committee (Bioethical Commission at the Military Institute of Medicine in Warsaw; ethical approval number 57/WIM/2011, received on 17 August 2011) and adhered to the tenets of the Declaration of Helsinki. All patients provided written informed consent to participate in this study. Informed consent was obtained to publish information/images in an online open access publication.

The study groups. Out of 94 total patients (mean age 53 ± 17 years) treated at our clinic with upper eyelid loading between July 2009 and July 2021, since the year 2014 thirty consecutive patients were randomised into one of 3 groups: Patients from the first group (GLE) received a gold weight fixed to the tarsus 2 mm above the upper eyelid margin. In the second group (GUE), the gold weight was fixed at the border of the upper edge of the tarsus of the upper eyelid and the levator aponeurosis. Patients in the third group (PUE) received a platinum chain fixed in the same way as in the second group (GUE). The inclusion criteria were: (1) Unresolved FP and unchanged lagophthalmos for at least 3 months despite intensive rehabilitation, (2) ocular symptoms reported by the patient due to exposure keratopathy not responding to conservative treatment (topical treatment with moisturizers and eye patching or moist chamber), (3) at least good function (> 4 mm) of the levator muscle of the upper eyelid, and (4) condition of both the skin of the eyelid and orbicularis oculi muscle allowed for surgery. Estimation of the implant weight, the surgical technique and the evaluation process have been reported in detail elsewhere.

Detailed medical histories of previous and concomittant diseases were collected with special attention to their etiology, duration, method and efficacy of treatment. All patients were asked about symptoms, personal and family history of any allergy, wearing gold jewellery, dental restoration involving gold and the use of cosmetics containing gold. Thereafter, a full ophthalmic examination was performed. After obtaining patient consent, all findings were documented by means of standard macroscopic and microscopic pictures. All surgeries were performed by a single surgeon (IN-G) under a microscope and local anaesthesia with infiltration of a lidocaine, adrenaline and hyaluronidase mixture. Patients were washed and draped. The skin was incised in the eye crease with a surgical scalpel blade No.15. The orbicularis oculi muscle was identified and carefully separated from the skin. First, the muscle was incised transversely, parallel to the lid margin, on the level of the levator aponeurosis muscle insertion to the tarsus. Then, dissecting scissors were used to dissect it deeper and downwards to the tarsus. A sterile weight was sutured to the anterior surface of the tarsus with absorbable polyglactin sutures (Vycril 6–0) (Fig. 1). The GLE group received a gold weight fixed about 2 mm above the eyelash line. In the GUE group, the gold weight was fixed at the border of the upper tarsus and the levator aponeurosis. The PUE group received a platinum chain fixed in the same way as in the GUE group. Absorbable sutures were used to avoid inducing long term foreign body giant cell reactions, which were observed near the non-absorbable suture in our previous study. Coagulation was avoided in order not to harm the affected tissues. In concomitant retraction of the upper eyelid the anterior part of the levator aponeurosis muscle was dissected from the tarsus. In cases of extrusion or other complications which required us to remove the implant from the upper eyelid, a typical implant-size-dependent capsule that formed between the orbicularis muscle and the anterior surface of the tarsus was identified. Special care was taken to remove the whole capsule with the implant inside. The muscle was sutured with the same absorbable sutures. The skin was pieced together with silk, non-absorbable sutures (Mersilk 6–0). The wound was covered by a sterile dressing with antibiotic and steroid ointment and left for 24 h. As part of standard postoperative care, all patients received a 2-week course of topical antibiotic and steroid ointment (oxytetracycline with hydrocortisone) 4qid (4 times a day) and topical lubricants, as needed. The skin sutures
were removed on postoperative day 8. In the cases of extrusion the same sterilized implant was placed under the orbicularis muscle at the border of the upper edge of the tarsus of the upper eyelid and the levator aponeurosis.

**Histopathology.** The surgically explanted weights with surrounding tissues were sent to the Department of Pathology, where tissues were removed and divided into four parts according to their localization (frontal upper and lower and posterior upper and lower). Each specimen was separately processed on a paraffin block, cut and stained with the hematoxylin—eosin method. Specimens were also stained with the routine Masson trichrome method to differentiate soft tissues. Immunohistochemical stains were performed using CD3, CD20, CD4, CD8 and Mac387 monoclonal antibodies (DAKO; immunoperoxidase method—DAKO autostainer). Proportion scores of CD3/CD20 and CD4/CD8 were calculated to qualify the type of lymphocytic reaction. All specimens were evaluated by the same experienced pathologist (RK).

The pathologist was not informed about the weight placement site in the upper eyelid.

The histopathology results were combined with the clinical findings.

**The statistical analysis.** Statistical analysis was performed using SPSS software (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp, USA). For measurable features, the normality of the distribution of analyzed parameters was evaluated using the Shapiro–Wilk test. The Wilcoxon pair order test was used to compare the two dependent groups. For more than two independent groups, the Kruskal–Wallis test was used. A significance level of $p < 0.05$ was considered significant.

**Results**

There was no known personal history of any metal allergy in the study group. Incomplete eyelid closure was corrected in every patient from the study group as per the primary treatment approach (Fig. 2a,b). Lagophthalmos was on average $7 \pm 3$ mm in the GLE group, $7 \pm 3$ mm the GUE group and $8 \pm 4$ mm in the PUE group prior to
surgery (p > 0.1). The average weight of the implant was 1.5 ± 0.3 g in the GLE group, 1.6 ± 0.2 g in the GUE group and 1.6 ± 0.4 mm in the PUE group (p > 0.1). Twelve patients (9 women and 3 men) aged 21–79 years (mean age 49 ± 17 years) required gold weight removal due to postsurgical complications (100% in the GLE group, 20% in the GUE group, 0% in the PUE group, p < 0.0001). Gold weights had to be removed because of: extrusion in 6 patients (60% of the GLE group), presumed allergy to gold manifested by reddened swollen eyelid in 3 patients (30% of the GLE group), unsatisfactory cosmesis in 2 cases (10% of the groups GLE and GUE) and excessive ptosis in 1 patient (10% of the GUE group). In the PUE group we observed only slight reddened eyelid in one case at a 1-month follow-up, but the patient refused to have the implant removed from the eyelid tissues.

All complications that required gold weight removal were observed at 5–84 postoperative months (in the GLE and GUE groups). The mean explanted implant weighed 1.5 ± 0.3 g.

The basic clinical data are presented in Table 1. All explanted weights were surrounded by fibrotic capsules with lymphocytic infiltrates CD3, CD4, CD8, and CD20 positive.

The intensity of the inflammatory infiltration differed between groups depending on the site of implantation (p < 0.001). A moderate lymphocytic reaction with the formation of the capsule consisted of hyalinized fibrous tissue around the implant was observed in 3 patients (30% of the GLE group). Of these patients, two also experienced dilation of the surrounding blood vessels and swelling of the eyelid stroma. (Fig. 3a) In 2 other cases a small vascular proliferation was found with edema and slight fibrosis, with only single scattered lymphocytes in the stroma (the GUE group). Significant lymphocytic reaction was noted in 7 cases (70% of the GLE group). This reaction was manifested by composition of inflammatory infiltration T and B lymphocytes (CD3+, CD20+) with the ratio of CD4/CD8 lymphocytes = 1:2 (Fig. 3c), the presence of macrophages (CD68+ in 3/7), giant multinuclear cells around a foreign body (1/7) and the presence of remnants of other structures (5/7) such as surgical sutures (1/7), glands (2/7), epithelium, epidermis—possibly eyelid epithelium or epidermis

| Patient | Age | Gender | Eye | Etiology of facial palsy | Weight [g] | Cause of implant removal | Clinical signs | Time from surgery to implant removal [months] | Previous eyelid surgery | Implantation site |
|---------|-----|--------|----|--------------------------|-----------|--------------------------|--------------|---------------------------------------------|-------------------------|-----------------|
| 1       | 24  | F      | L  | ANS                      | Gold [1.4]| extrusion                | reddened mildly oedematous lid with visible vessels and thin orbicularis muscle |
| 2       | 35  | M      | R  | ANS                      | Gold [1.4]| extrusion                | reddened and mildly oedematous lid with visible blood vessels |
| 3       | 42  | M      | L  | ANS                      | Gold [1.2]| extrusion                | slightly reddened with visible blood vessels |
| 4       | 37  | F      | L  | Trauma                   | Gold [1.4]| cosmesis                 | asymptomatic pale eyelid |
| 5       | 60  | F      | R  | ANS                      | Gold [1.0]| extrusion                | slightly reddened with vessels visible on the surface of the skin |
| 6       | 75  | F      | L  | HZO                      | Gold [1.8]| ptosis                   | pale eyelid with visible contour of the weight |
| 7       | 79  | F      | L  | ANS                      | Gold [1.8]| extrusion                | slightly reddened lid, parchment skin and very thin orbicularis muscle |
| 8       | 21  | M      | L  | PGT                      | Gold [1.2]| Lid oedema               | reddened and oedematous lid with visible blood vessels |
| 9       | 56  | F      | L  | congenital               | Gold [1.8]| cosmesis                 | pale eyelid with visible contour of the weight |
| 10      | 58  | F      | L  | ANS                      | Gold [1.2]| Lid oedema               | reddened and oedematous eyelid with visible blood vessels |
| 11      | 49  | F      | L  | ANS                      | Gold [1.4]| Lid oedema               | reddened and oedematous lid with visible blood vessels |
| 12      | 62  | F      | L  | Neurofibromatosis        | Gold [1.4]| extrusion                | pale cicatrcial eyelid |

Table 1. Clinical data. ANS acoustic neuroma surgery, HZO Herpes zoster ophthalmicus, PGT parotid gland tumor. GLE group = received a gold weight fixed to the tarsus 2 mm above the upper eyelid margin. GUE group = received a gold weight fixed at the border of the upper edge of the tarsus of the upper eyelid and the levator aponeurosis.
invagination (2/7) (Fig. 3b). No other inflammatory cells were identified. Histopathology results are presented in Table 2 and Fig. 3a–c.

**Discussion and literature review.** Our study confirms that the use of gold weights induces the formation of a fibrotic capsule with a limited chronic inflammatory infiltration, which has also been reported by other authors.\(^{13,17,27,28,32,41,42}\) This collagenous capsule strongly adhered to the anterior surface of the tarsal plate and by ingrowth into the fixation holes stabilized the weight in place, hence there were no muscle fibers between the implant and the tarsal plate. Serious complications which required weight removal were noted in 100% of patients in the GLE group and 20% in the GUE group during the study period (Table 1). The intensity of the inflammatory infiltration and the complication rate seem to be related to the implantation site in the upper eyelid. In all patients with extrusions and reddened swollen eyelids, the implant was sutured relatively low, about 2 mm above the eyelash line where the majority of blood vessels and apocrine ciliary glands of Moll are located,\(^{23,44}\) which may influence the intensified tissue response to the presence of the implant.\(^{41}\) In a study conducted by Bair et al., an explanted weight caused no allergic reaction after placement in the inner forearm of one patient who experienced clinical signs of eyelid inflammation.\(^{28}\) This may support the hypothesis that the site of implantation in the upper eyelid, rather than presumed allergic reaction, results in a clinical outcome that necessitates implant removal. The patient described by Iordanous and Evans, after initial ineffective treatment with oral antibiotics, was started on oral prednisone, which brought short-term improvement with a rapid

| Patient | Inflammatory cells | Masson trichrome | Accessory materials |
|---------|-------------------|-----------------|--------------------|
| 1       | Lymphocytes (+++), giant cell granuloma | Fibrosis | Suture, giant cells |
| 2       | Lymphocytes, macrophages | Fibrosis | Muscle |
| 3       | Lymphocytes, macrophages | Hyalinization | – |
| 4       | Nests of lymphocytic infiltrate | Angiogenesis | – |
| 5       | No inflammatory cells | Angiogenesis | Oedema |
| 6       | Few inflammatory cells, hyalinization | – | Pseudocyst |
| 7       | Lymphocytes in clusters, hyalinization | Angiogenesis | Hematoma |
| 8       | Lymphocytes with follicles | Focal hyalinization | – |
| 9       | Sparse lymphocytes, hyalinization | – | – |
| 10      | Lymphocytes (+++), fibrosis | – | Conjunctival epithelium |
| 11      | Lymphocytes in clusters, fibrosis | Macrophages | Glandular tubes |
| 12      | Subepidermal lymphocytic infiltrate | Hyalinization and fibrosis | Skin adnexa |

Table 2. Histopathology.
recurrence of the symptoms after discontinuation of the steroids. Topical steroids (0.5 cc of triamcinolone, 40 mg/cc) injected into the tissue of the upper eyelid resulted in complete resolution of symptoms in one of Bair’s patients who developed a sterile inflammatory reaction 1 week after gold weight implantation. The same authors report antibiotic-corticosteroid ointment applied 3 weeks after surgery in the second of 3 cases of non-infectious inflammatory response to eyelid implants as totally ineffective. We also injected topical steroids into the oedematous tissue of the eyelids in patients: 8, 10, 11 at a 1-month-follow-up, but there was only partial and not long-lasting clinical improvement observed (Table 1). This may suggest that the steroid concentration might be too low to inhibit an advanced immune reaction in the upper eyelid and perhaps might have been effective at the co-existence of many modifying factors which vary among individuals. We acknowledge the fact that our data described. He suggests that it is impossible to foresee the exact tissue reaction to the implant because of the PUE group the patient with reddened eyelid refused to have the implant removed from the eyelid tissues, thus no platinum chain was examined histopathologically. Nevertheless, from the cases we have observed, apart from obvious individual variability, a certain pattern of undesirable reactions to gold implants emerges. These reactions can be divided into two distinct types depending on the implantation site:

1. Slight to moderate lymphocytic reaction with the formation of the capsule consisted of hyalinized fibrous tissue around the implant—characteristic and observed in other parts of the body when implanting biologically inert materials. We observed this type of moderate lymphocytic reaction in 3 cases, 2 of which were accompanied by dilation of the surrounding blood vessels and swelling of the eyelid stroma (30% explanted weights in the GLE group).

In 2 other cases only small vascular proliferation was found with edema and slight fibrosis, with only single scattered lymphocytes in the stroma (100% explanted weights in the GUE group) (Fig 3A).

2. Significant lymphocytic reaction (7 cases, 70% explanted weights in the GLE group, 70% of the GLE group), composed of inflammatory infiltration T and B lymphocytes (CD3 +, CD20 +) with the ratio of CD4/CD8 lymphocytes = 1:2 (Fig. 3C), the presence of macrophages (CD68 + in 3/7), giant multinuclear cells around a foreign body (1/7) and the presence of remnants of other structures (5/7) such as surgical sutures (1/7), glands (2/7), epithelium, epidermis—possibly eyelid epithelium or epidermis invagination (2/7) (Fig. 3B).

This study confirms that weight placement site in the upper eyelid may be critical for procedure success. We strongly believe that by providing detailed information about past medical histories, conducted examinations, weights used, surgical technique, postoperative care plan and histopathological findings in every case, our study may constitute a step further in the process of comprehending the possible impact of gold weights on the upper eyelid microenviroment in patients with unresolved FP.

Conclusion
Placement of gold weight in the upper eyelid induces a limited chronic inflammatory response of varied intensity and local fibrosis which helps to stabilize the implant in place and may reduce its biological activity. Gold weights produce only a slight reaction while remaining biologically inert. Fibrosis and single scattered lymphocytes seem to indicate a reaction to the mechanical irritation of the eyelid tissues, which may be accompanied by the widening of small blood vessels and swelling of the stroma. The severe reactions we observed after placement of weights close to the lid margin are instead caused either by the type of auxiliary materials used (sutures) or by dragging other tissues into the area around the implant (the observed inflammatory reactions are largely consistent with those observed in chronic inflammation of the eyelid glands [composed of inflammatory infiltrate, macrophages, giant cells]). It seems, therefore, that the decisive factor in such reactions to gold implants is mechanical damage to the eyelid structures, and not the material of the weight, itself. The site of weight placement in the upper eyelid may be critical for procedure success. Upper implantation of weights seems to cause less damage to the eyelid tissues. Placement of the gold weights about 2 millimeters above the eyelash line with absorbable sutures should be avoided due to the high risk of complications.

Data availability
The datasets used and/or analysed during the current study are available from the corresponding author upon request.

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**Author contributions**
I.N.-G. contributed to the conception and design of the work, acquisition, analysis and interpretation of data for the work, drafting the work and preparation of the final version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. R.K. contributed to the conception and design of the work, the analysis and interpretation of data for the work, critical revision of the work for important intellectual content and approved the final version to be published and agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. M.R. contributed to the conception and design of the work, the analysis and interpretation of data for the work, critical revision of the work for important intellectual content and approved the final version to be published and agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

**Competing interests**
The authors declare no competing interests.

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