

MIRAgel

Hydrolytic Degradation and Long-term Observations

Manuela Roldán-Pallarés, MD, PhD; Julián Hernández-Montero, MD; Felipe Llanes, MD, PhD;
José E. Fernández-Rubio, BSc; Francisco Ortega, ScD, PhD

Objective: To analyze long-term complications of hydrogel (MIRAgel; MIRA Inc, Waltham, Mass) explants.

Design: Institutional clinical study of a retrospective, interventional case series of patients. We included 415 patients with complete reattachment of the retina 6 months after surgery and up-to-date follow-up. Patients underwent ophthalmological examination at each visit (mean follow-up, 187 months), and 6 underwent computed tomography and/or magnetic resonance imaging. Main outcome measures included the MIRAgel explant removal rate, clinical manifestations related to removal, interval from the start of discomfort to removal, mean time from implantation to removal, culture yield of the removed elements, results of histological examination of the capsule surrounding the removed explants (12 cases), and micro-Fourier transform infrared spectroscopic analysis results of 3 recovered explants.

Results: MIRAgel explant removal was necessary in 27 (6.5%) of 415 patients who received MIRAgel material and in 27 (7.6%) of 357 patients who had had it for 7 or more years. Clinical manifestations were related to swelling of the MIRAgel material, with a mean interval of 15 (range, 6-22) months from starting symptoms to removal. The infrared spectroscopic analysis demonstrated the presence of carboxylic groups in 3 recovered explants that had swollen considerably.

Conclusion: Prompt removal of MIRAgel explants when discomfort starts should be considered to avoid increased incidence of complications.

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Author Affiliations:
Department of Ophthalmology (Dr Roldán-Pallarés), Ultrasonography Unit, Department of Radiology (Dr Hernández-Montero), and Department of Pathology (Dr Llanes), Hospital Clínico San Carlos, and Department of Ophthalmology (Dr Roldán-Pallarés), Department of Pathology (Dr Llanes), and Spectroscopy Unit "CAI," Facultad de Ciencias Químicas (Mr Fernández-Rubio and Dr Ortega), Universidad Complutense, Madrid, Spain.

HYDROGEL IMPLANTS (ORIGINALLY MAI and then commercialized as MIRAgel [MIRA Inc, Waltham, Mass]) initially seemed to be the ideal implant material, with a soft pliable texture and low risk of infection,^{1,2} when observed 6 to 53 months after surgery.³ However, with a longer follow-up of 7 to 11 years, complications have been reported in 8.5% of patients after an intrascleral buckling procedure.⁴ Recently, several reports of removal of MIRAgel episcleral buckling material have been published.⁵⁻⁸ Clinical manifestations ranged⁵⁻⁸ from benign subconjunctival bulging, pain, strabismus, progressive limitation of ocular motility, protrusion of the buckle beneath the eyelids, and sensation of orbital fullness to pseudotumor⁹ for the episcleral buckles or to intraocular erosion and migration into the vitreous for intrascleral procedures.^{4,10} After Hwang and Lim¹¹ reported the first case of scleral buckle extrusion and fragmentation associated with a MIRAgel episcleral explant, other cases have also been published.^{12,13}

Fragmentation and peripheral degradation of hydrogel have been described in experimental models.¹⁴ The hydrogel fragments were found next to the inner limit of the surrounding fibrous capsule in human eyes undergoing reoperation; these were often found in association with mononuclear and giant cells, attesting to a foreign-body giant cell granuloma.¹⁵

Hydrolytic degradation of MAI hydrogel using micro-Fourier transform infrared spectroscopy was demonstrated by the presence of carboxylic groups in 2 recovered implant segments.⁴ The polymer implants (MAI) retrieved from these patients⁴ were made before MIRA Inc obtained the license to make MIRAgel.¹⁴ Although the MAI hydrogel is the precursor of MIRAgel and both have the same chemical composition, up-to-date hydrolysis of MIRAgel has not been demonstrated.

To further understand the long-term complications of MIRAgel episcleral buckles, we report the clinical outcome of 415 patients after MIRAgel buckling implan-

Table. Characteristics of MIRAgel Buckles and Percentage of Explants Removed

Characteristics of MIRAgel Buckles*	No. of Patients	Orientation/No. of Patients	Removed Explants, No. (%)	
			All Patients	By Orientation
Segmental-localized ($\leq 180^\circ$)	90	Radial/18	5 (5.6)	1 (6)
		Circumferential/72		4 (6)
Segmental ($\leq 270^\circ$) and cerclage (240 silicone band)	135	Additional "side-by-side"/27	10 (7.4)	0
		Circumferential/108		10 (9)
Broad (360°)	190	Circumferential/95	12 (6.3)	4 (4)
		Circumferential with 240-style silicone band/95		8 (8)
Total	415		27 (6.5)	

*Indicates the removed explants by type and orientation of indentation. MIRAgel is the proprietary name for hydrogel produced by MIRA Inc, Waltham, Mass.

tation for a mean follow-up of 187 months (range, 75 months to 20 years). We evaluated the results of micro-Fourier infrared spectroscopic analysis of the explanted MIRAgel buckles from 3 patients for potential changes in the polymeric explant structure.

METHODS

DESIGN AND SETTING

Herein we describe an interventional consecutive case series of patients with rhegmatogenous retinal detachment who underwent scleral buckling surgery with the MIRAgel explant as a first surgical procedure between March 1, 1984, and December 31, 2000. The patients underwent operation at the Hospital Clínico San Carlos, Madrid, Spain, by one of us (M.R.-P.) with cryotherapy associated with the episcleral buckle.¹⁶ This is a retrospective institutional clinical study.

PATIENT POPULATION

The medical reports were reviewed for 444 patients with retinal detachment in whom MIRAgel was used as unilateral episcleral buckling material. Although only single procedures were considered, 11 patients were excluded because they needed several combined surgeries to reattach the retina (exclusion criteria). Eighteen patients were lost during follow-up. The 415 patients with complete reattachment of the retina 6 months after surgery, up-to-date follow-up information, and signed informed consent forms were included in the study, which was in adherence to the tenets of the Declaration of Helsinki and approved by our institutional research committee.

Patients made follow-up office visits 1, 3, 6, 12, 24, and 36 months after surgery and then annually or biannually. The mean follow-up was 187 months (range, 75 months to 20 years).

OBSERVATION PROCEDURES

Snellen visual acuity, ocular motility, and results of tonometry and slitlamp and fundus examinations were recorded at each visit. Computed tomography and/or magnetic resonance imaging was necessary in 6 patients.

OUTCOME MEASURES

The main outcome measures included the MIRAgel explant removal rate, clinical manifestations related to its removal, interval from the start of discomfort to removal, mean time from implantation to removal, culture yield of the removed ele-

ments, results of histological examination of the capsule surrounding the removed explants (12 cases), and results of micro-Fourier transform infrared spectroscopy analysis of 3 recovered explants. The spectrophotometer used to record spectra was a Nicolet Magna-IR 750 (Nicolet Instruments Inc, Warwick, England), with a sampling microscope (IR-Plan Advantage; Spectra-Tech Inc, Oak Ridge, Tenn). The infrared spectra were recorded by accumulation of 240 scans, with a resolution of 4 waves/cm. The postoperative outcome after MIRAgel explant removal was followed up for 6 to 156 (mean follow-up, 84) months.

RESULTS

We reviewed the medical reports of 415 patients who underwent MIRAgel episcleral buckle for rhegmatogenous retinal detachment. The mean patient age was 58 years (range, 16-82 years). MIRAgel was used in the 415 patients regularly during most of the follow-up period (March 1, 1984, through June 30, 2000) but, after June 30, 2000, only 2 of these explants were used. Postoperative follow-up for 357 (86.0%) of 415 patients was 7 years or longer. The **Table** shows the type of surgery performed in these patients.

As of this writing, 38 (9.2%) of the 415 patients reported redness and discharge from the eye that underwent operation. The criteria for buckle removal included morphological and/or functional changes related to swelling of the MIRAgel material.

Removal was necessary in 27 (6.5%) of 415 patients with MIRAgel buckle explants. Clinical manifestations, frequently multiple, in patients with removed explants included redness and discharge in 25 (93%) (cultures yielded *Staphylococcus epidermis* in only 3); extrusion in 6 (22%); subconjunctival mass and/or protrusion of the buckle beneath the eyelids in 19 (70%); strabismus, rectus palsy, limitation of ocular motility, and/or diplopia in 18 (67%); and orbital fullness and/or pseudotumor in 6 (22%).

Considering the type of surgery, 5 (6%) of the 90 segmental-localized explants ($\leq 180^\circ$) (1 [6%] of the 18 with radial and 4 [6%] of the 72 with circumferential orientation) were removed. In addition, 10 (7%) of the 135 segmental and cerclage explants ($\leq 270^\circ$) (10 [9.3%] of the 108 under a 240-style silicone band of cerclage) were removed. Finally, of the 190 patients with a broad circumferential 360° explant, 12 (6.3%) needed removal (8 [8%] of the 95 under a 240-style silicone band and 4 [4%]

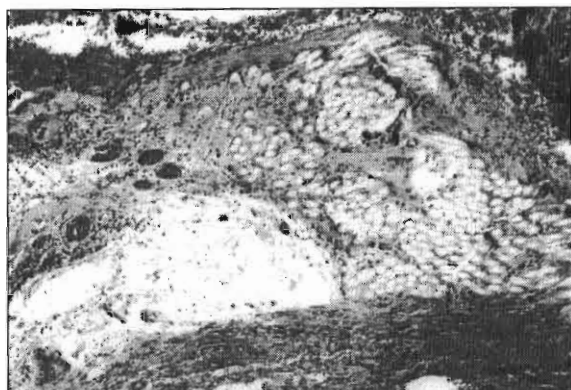


Figure 1. Histological study of the fibrous capsule surrounding hydrogel (MIRAgel; MIRA Inc, Waltham, Mass) explants in a patient with orbital pseudotumor. Giant cell granuloma is seen in relation to the sutures (Masson staining; original magnification $\times 288$).

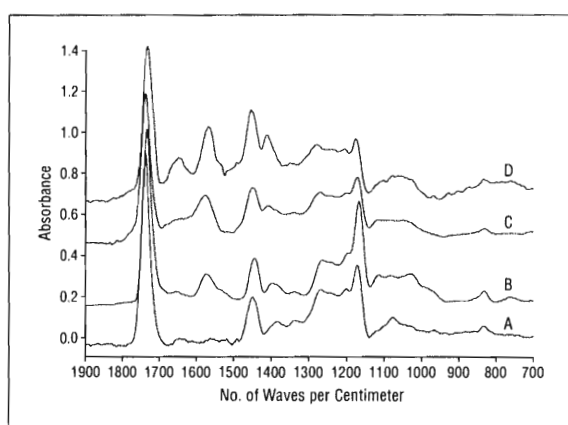


Figure 2. Micro-Fourier transform infrared spectroscopic analysis of 3 recovered hydrogel (MIRAgel; MIRA Inc, Waltham, Mass) segments (B-D) and a MIRAgel stock sample (A). An extra peak appears at about 1560 waves/cm in graphs B, C, and D (with large swelling of the MIRAgel material; C and D corresponded with clinical manifestation of orbital pseudotumor).

of the 95 without cerclage associated) (Table). The mean interval to surgical removal was 9.6 (range, 7.2-11.3) years.

We performed histologic analysis of the fibrous capsule surrounding 12 of the removed explants. Only 3 patients with orbital pseudotumor, all with broad (360°) MIRAgel indentation for more than 10 years, showed giant cell granuloma related to sutures (**Figure 1**).

We performed micro-Fourier transform infrared spectroscopy in 3 recovered MIRAgel segments (**Figure 2**). Hydrolytic degradation was associated with swelling of the material to about 4 times the width and thickness of the original and clinical manifestation of orbital pseudotumor in 2 patients in whom computed tomography (**Figure 3**) was needed for diagnosis. The gellike removed segments from these 2 patients were studied spectroscopically and compared with an original MIRAgel explant and with a less-swollen MIRAgel explant from a patient without clinical manifestation of orbital pseudotumor. Hydrolytic degradation of the material was demonstrated by the presence of the carboxylic groups (Figure 2).



Figure 3. Anteroposterior section of an orbital computed tomogram. A considerably swollen hydrogel (MIRAgel; MIRA Inc, Waltham, Mass) surrounds the eye. The scale indicates centimeters.

After explant removal, the retina remained attached in 23 (85%) of the 27 patients, with no significant changes in visual acuity (mean, 20/60). Usually after removal, diplopia disappeared and the eyes became orthophoric. Redness and discomfort persisted in 6 (22%) of the 27 patients, even after cultures yielded negative results, probably related to residual MIRAgel fragments. Two patients developed vitreous hemorrhage and a new retinal detachment after removal of a meridional MIRAgel explant under a 240-style cerclage silicone band. Two other patients, both with broad indentation (360°) under a 240-style cerclage silicone band, experienced scleral rupture during surgical maneuvers to clean the MIRAgel fragments embedded in the scleral wall, making it thicker and rigid. Finally, 3 of these complicated cases became phthisical. No other complications were found to be related to removal.

COMMENT

For the first time, to our knowledge, considerably swollen MIRAgel explants and clinical manifestations of orbital pseudotumor have been related to hydrolytic degradation of episcleral MIRAgel demonstrated by infrared spectroscopy. Removal of these buckles is a consequence of the explant's progressive degradation and swelling.

At present, removal has been necessary in 27 (6.5%) of 415 patients who received MIRAgel explants, and in 27 (7.6%) of 357 patients who received MIRAgel explants 7 or more years earlier. Eight of these 27 cases have already been reported.^{5,17}

It has been suggested in the literature⁶⁻⁸ that a greater quantity of material used will increase the possibility of removal. In our patients, there was a trend toward a higher removal rate (Table) with an increased quantity of buckling material, and any of the cases with MIRAgel used as an additional and small side-by-side indentation to resolve a fishmouth phenomenon required removal. The association of MIRAgel with a silicone band of cerclage also increased the removal rate in our patients. As first suggested by Marin et al,⁴ the sutures may play a role in the physical or functional breakdown of the surrounding fibrous capsule, allowing hydration and swelling of the MIRAgel explant.

In our cases, swelling of the MIRAgel explant combined with progressive limitation of ocular motility and protrusion of the buckle beneath the eyelids frequently indicates the need for MIRAgel removal, as reported by other authors.⁶⁻⁸ The symptoms usually started with redness and discomfort, and it took a mean of 15 (range, 6-22) months to slowly develop those symptoms related to swelling of the material. Six of our patients had orbital pseudotumor at the initial examination and required computed tomography and/or magnetic resonance imaging for diagnosis. Two of these cases with orbital pseudotumor (the interval from the start of redness and discomfort to removal was 20 and 22 months; the time from implantation to removal of the MIRAgel material, 11.1 and 11.2 years) showed great swelling of the MIRAgel explant related to its hydrolytic degradation.

To our knowledge, this is the first report demonstrating hydrolytic degradation of MIRAgel by the presence of carboxylic groups using micro-Fourier transform infrared spectroscopy. Until now, chemical changes in the polymer were only confirmed spectrographically for the MAI hydrogel intrascleral implants.⁴ The presence of carboxylic groups found in our removed explants implies ester hydrolysis. The ionized carboxylic groups result in water absorption and, consequently, the MIRAgel material swelled and became gel-like and friable. These characteristics explain the difficulty in grasping and removing MIRAgel fragments—sometimes embedding in the scleral wall, which then became thicker and rigid—and complications related to surgical removal. Persistence of discomfort after MIRAgel retrieval may likely be associated with residual MIRAgel fragments.

After MIRAgel removal, the retina remained attached in 23 (85%) of 27 patients with stabilized visual acuity. In 2 of the cases of pseudotumor and considerable swelling of the MIRAgel material, scleral perforation occurred during removal with intraocular hemorrhage and final retinal redetachment. Retinal redetachment was found in 4 (15%) of 27 patients after MIRAgel material removal. The eyes usually became orthophoric and diplopia disappeared, but redness, discomfort, and ocular motility disturbance persisted in 6 (22%) of the 27 removal cases. We agree with Le Rouic et al⁶ that patients should be informed of the possibility of complications related to the surgical removal of episcleral MIRAgel buckles.

Cultures in only 4 of our 27 removed MIRAgel explants yielded positive results. Negative culture findings may be owing to long-term antibiotic and/or corticosteroid therapy that was used to treat redness and discharge, or owing to the particular characteristics of the MIRAgel material. MIRAgel was reported to be an ideal buckling element that was considered less prone to infection because it lacked dead spaces and could absorb and gradually release antibiotic drugs.^{3,18}

Hence, MIRAgel buckles resulted in delayed, late complications owing to buckle swelling from hydrolytic degradation and required removal in 6.5% of patients, with a mean follow-up of 187 months. Patients with MIRAgel buckles require long-term follow-up, and removal should be considered once symptoms develop.

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