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Case Report

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Improvement of the Mineralization of the Vitreous Body with Pharmacological Treatment. Report a Case

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ABSTRACT

Vitreous chamber is semisolid structure, situated between lens and retina and consisting of 99% water, rest collagen and hyaluronic acid (HA). This helps to maintain the shape of the retina. Ciliary processes produce vitreous humor which continuously but with slow rate flows to vitreous chamber. Being viscous hydrogel, movement/diffusion of dosage form/DDS within it is very slow and inconsistent. Its elimination route is through trabecular meshwork and uveoscleral route. Larger drug molecules can stay in vitreous for longer than small molecules.

Keywords: Hydrogen, Ciliary Process, Hyaluronic Acid, Hydrogel, Dissociation of Water, Oxygen, Vitreous.

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Introduction

The vitreous is a jelly-like structure, thick and viscous, that occupies the vitreous chamber in the posterior concavity of the globe. It fills the largest cavity of the eye, occupying two-thirds of its volume. It is surrounded mainly by retina. Anteriorly it forms a slight depression behind the lens and is attached to it around the circumference of this depression. Normally the vitreous body is quite transparent.

The vitreous is not simply an inert jelly. Within the body of the vitreous, fine collagen fibers crisscross in a scaffolding manner. The resulting matrix is filled with a viscous mucopolysaccharide, called hyaluronic acid. Vitreous is almost 99% water. Hyaluronic acid is a great shock absorber and can compress slowly and rebound slowly. This is important in injuries to the eye from such things as a fast-moving squash ball.

The envelope that surrounds the vitreous is primarily a condensate of the gel and is anchored to the more forward part of the retina, the ora serrata and at the head of the optic nerve along the major retinal blood vessels. If the vitreous shrinks, the resulting tension on its anchors can produce a tear in the retina. This may permit the adjacent vitreous to enter between the choroid and retina and produce a retinal detachment.

Macromolecules comprise only 2% of vitreous, yet are responsible for its gel state, transparency, and physiologic function(s) within the eye. Myopia and aging alter collagen and hyaluronan association causing concurrent gel liquefaction and fibrous degeneration. The resulting vitreous opacities and collapse of the vitreous body during posterior vitreous detachment are the most common causes for the visual phenomenon of vitreous floaters. Previously considered innocuous, the vitreous opacities that cause floaters sometimes impact vision by profound do the role(s) of vitreous in normal ocular physiology is/are poorly understood, but probably quite important, especially with respect to oxygen. The late David Beebe was a strong proponent of the importance of vitreous oxygen physiology regarding the lens and cataract formation while it has underscored the role of vitreous oxygen metabolism as related to vitreous surgery, age-related macular degeneration, and macular edema [1-4]. grading contrast sensitivity function and impairing quality-of-life.

Further evidence of a high degree of spatial organization derives from recent proteomic analyses

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of four different areas of human vitreous, specifically the anterior hyaloid, posterior vitreous cortex, central vitreous core, and vitreous base, concluding that proteins ostensibly localize to distinct vitreous substructures to variably protect intraocular tissues from infection, oxidative stress, and energy disequilibrium [5].

Asteroid Hyalosis

This generally benign condition is characterized by small yellow-white spherical opacities throughout the vitreous. The prevalence of asteroid hyalosis was previously found to be 0.042 – 0.5%, although a recent study in 801 autopsy eyes found an incidence of 1.96%; it affects all races but with a male-to-female ratio of 2:1 [6]. Curiously, asteroid hyalosis is unilateral in over 75% of cases. Asteroid bodies are associated intimately with the vitreous gel and move with typical vitreous displacement during eye movement, which suggests a relationship with collagen fibril degeneration [7]. However, PVD, either complete or partial, occurs less frequently in individuals with asteroid hyaloids than in age matched controls, which does not support age-related degeneration as a cause [8]. Histological studies demonstrate a crystalline appearance and a pattern of positive staining to fat and acid mucopolysaccharide stains traction sites, retinal effects, vitreous effects; blood vessels, retinal hemorrhages, aggravate retinal neovascularization, vitreous hemorrhage, macula, vitreomacular traction syndrome, diabetic macular edema (diff use), vitreoschisis with macular pucker; macular holes, periphery retinal tears/detachments, white without pressure. In Optic disc vitreous-papillary traction syndrome, aggravate NVD (PDVRCRVO) CRVO, central retinal vein occlusion; NVD, neovascularization of the optic disc; PDVR, proliferative diabetic vitreoretinopathy.

Electron diffraction studies showed the presence of calcium oxalate monohydrate and calcium hydroxy phosphate. Ultrastructural studies reveal intertwined ribbons of multilaminar membranes (with a 6 nm periodicity) that are characteristic of complex lipids, especially phospholipids, that lie in a homogeneous background matrix [9].

In these investigations, energy dispersive x-ray analysis showed calcium and phosphorus to be the main elements in asteroid bodies. Electron diffraction structural analysis demonstrated calcium hydroxyapatite and possibly other forms of calcium phosphate crystals. Some reports suggest an association between asteroid hyalosis and diabetes mellitus, while other investigations found no such association [10]. Asteroid hyalosis appears to be associated with certain pigmentary retinal degenerations, although it is not known whether this is related to the presence of diabetes in these patients [11, 12]. Yu and Blumenthal proposed that asteroid hyalosis results from aging collagen, whereas other studies suggested that asteroid formation is preceded by depolymerization of hyaluronan [13, 14].

Hyaluronan or hyaluronic acid contained uronic acid and an aminosugar, but no sulfoesters. The uronic acid and aminosugar in the disaccharide are D-glucuronic acid and D-N-acetylglucosamine, and that they are linked together through alternating beta-1,4 and beta-1,3 glycosidic bonds, Both sugars are spatially related to glucose which in the beta configuration allows all of its bulky groups (the hydroxyls, the carboxylate moiety and the anomeric carbon on the adjacent sugar) to be in sterically favorable equatorial positions while all of the small hydrogen atoms occupy the less sterically favorable axial positions. Thus, the structure of the disaccharide is energetically very stable [15].

Hyaluronan synthase enzymes (the suffix “ase” means that they’re not use ATP as an energy source to carry out its function) synthesize large, linear polymers of the repeating disaccharide structure of hyaluronan by alternate addition of glucuronic acid and N-acetylglucosamine to the growing chain using their activated nucleotide sugars (UDP - glucuronic acid and UDP-N-acetlyglucosamine) as substrates. The number of repeat disaccharides, n, in a completed hyaluronan molecule can reach 10,000 or more, a molecular mass of ~4 million daltons (each disaccharide is ~400 daltons) [1]. The average length of a disaccharide is ~1 nm. Thus, a hyaluronan molecule of 10,000 repeats could extend 10m if stretched from end to end, a length approximately equal to the diameter of a human erythrocyte [16].

In a physiological solution, the backbone of a hyaluronan molecule is stiffened by a combination of the chemical structure of the disaccharide, internal hydrogen bonds, and interactions with solvent. The axial hydrogen atoms form a non-polar, relatively hydrophobic face while the equatorial side chains form a more polar, hydrophilic face, thereby creating a twisting ribbon structure. Consequently, a hyaluronan molecule assumes an expanded random coil structure in physiological solutions which occupies a very large domain, The actual mass of hyaluronan within this domain is very low, ~0.1% (wt/vol) or less when the macromolecule is present at a very dilute concentration in saline [17]. This means that the domains of individual molecules would overlap each other at concentrations of 1 mg hyaluronan per ml or higher.

The domain structure of hyaluronan has interesting and important consequences. Small molecules such as water, electrolytes and nutrients can freely diffuse through the solvent within the domain. However, large molecules such as proteins will be partially excluded from the domain because of their hydrodynamic sizes in solution. The hyaluronan network in the domain allows less and less space for other molecules the larger they are. This leads both to slower diffusion of macromolecules through the network and to their lower concentration in the network compared to the surrounding hyaluronan free compartments. Interestingly, the hyaluronan chains are constantly moving in the solution, and the effective 'pores' in the network continuously change in size. Statistically, all sizes of pores can exist, but with different probabilities. This means that in principle, all molecules can pass through a hyaluronan network, but with different degrees of retardation depending on their hydrodynamic volumes.

The pK of the carboxyl groups on the glucuronic acid residues is 3-4, depending on ion conditions. At pH 7, then, these groups are predominantly ionized, and the hyaluronan molecule is a polyanion that has associated, exchangeable cation counterions to maintain charge neutrality. Directional flow of electrolyte through such a polyanionic domain can lead to sufficient charge separation to create a streaming potential.

Electrostatic repulsion between the many negative charges, which would promote dissociation of the aggregates, is countered not only by hydrophobic interactions but also by H-bonding between acetamido and carboxylate groups. These very short-range interactions demand close complementarity between the two participants, and this is best obtained when the hyaluronan interactants are antiparallel to each other. Only then do the gentle curves in their shapes mutually complement each other, and hydrophobic and H-bonding are then

optimal. E.D.T. Atkins in Bristol, U.K. observed a H-bond between acetamido and carboxylate groups on neighboring hyaluronan molecules in X-ray fiber studies.

Rotary shadowing-electron microscopy showed that honeycomb-like meshworks were formed at very low hyaluronan concentrations (1 microgram/ml). High molecular mass hyaluronan meshworks at this concentration showed no molecular ends or tails. The meshworks were essentially infinite. Every hyaluronan molecule was connected with all the rest, via the meshwork. On the contrary, although lower molecular mass hyaluronan formed meshworks at low concentrations, these meshworks were islands, separated from each other [18].

The interactions which hold meshworks together are fairly weak, so that aggregates form and dissociate, depending on conditions and temperatures. As the hyaluronan concentration increases, the meshwork contains thicker branches, until at concentrations seen, for example, in synovial fluids (>1 mg/ml) sheets and tubes of striking morphology are observed by rotary shadowing electron microscopy.

The important point is that these meshworks are ordered. The shapes of the hyaluronan secondary structures determine the shapes of the aggregates, and each branch in the meshwork of ambidexterans carries with it two clear intrinsic directions, up or down, established by the hyaluronan chains. This may have organizational consequences, for instance, in guiding morphogenesis.
Hyaluronan is a potent inhibitor of complement activated lysis of red blood cells, but only in a 'denatured' form. Hyaluronan solutions prepared and maintained at ambient temperatures were almost devoid of this activity [19].

The space occupied by the vitreous between the lens and the retina should be optically empty, and free of cells, suspended matter and blood vessels that block or scatter light. Many details of how this is achieved are not known, but the outline is clear. The vitreous is a stable gel, which in humans (and many animals) contains hyaluronan. Even high molecular mass hyaluronan does not form a gel at concentrations found in the vitreous (~2 mg/ml), and rigidity in this tissue is increased by the incorporation of a very sparse meshwork of thin collagen fibrils. The vitreous is a fiber-reinforced composite material, with the amounts of the non-aqueous components reduced to a minimum compatible with mechanical stability, thereby introducing as little solid material as possible into the light path (vitreous is ~99% water).

The thin (10 nm) collagen fibrils are held apart in bunches or sprays by bridges and ties of anionic glycosaminoglycans, probably chondroitin sulfate. These bunches run in parallel and sometimes at right angles to each other. Why don't these sprays or bundles entangle and aggregate over years of environmental stress? This seems to be a function of hyaluronan [20]. https://www.glycoforum.gr.jp/article/02A1.html.

Case Report

First Examination

NOMBRE DEL PACIENTE: R.M.O.
FECHA DE NACIMIENTO:15/Junio/1937 FECHA DE HOY: 09/Dic/2019 SEXO:Fem.

Phototype V. Left leg is too heavy to start walking. Knee, needs surgery. A lot of heaviness in the leg. He had a fall in the bathroom, and hit his spine on one side, he did not feel comfortable with the doctor. One kidney is good, and another is bad. Cataract surgery. You have lost quality of vision. Myopia and astigmatism. Somewhat uneven of view.
DM -, HAS-. Heart well.

Osteoporosis. It took a long time for Von VIVA: Nov 17 she got Prolia for 4 times. (Osteoporosis) Thyroid: Eutirox 50 ug x 24. Diosmin for varicose veins. Calcium and vitamin D3. Daily calcitriol. Vitamin D 2 times a week.
At general examination,
SpO2%: 93 %, Heartbeat: 67 x´.

First Examination

Ophthalmological examination: R.E.: -2.00 = - 2.00 x 0°. L.E.: +0.50 sph.

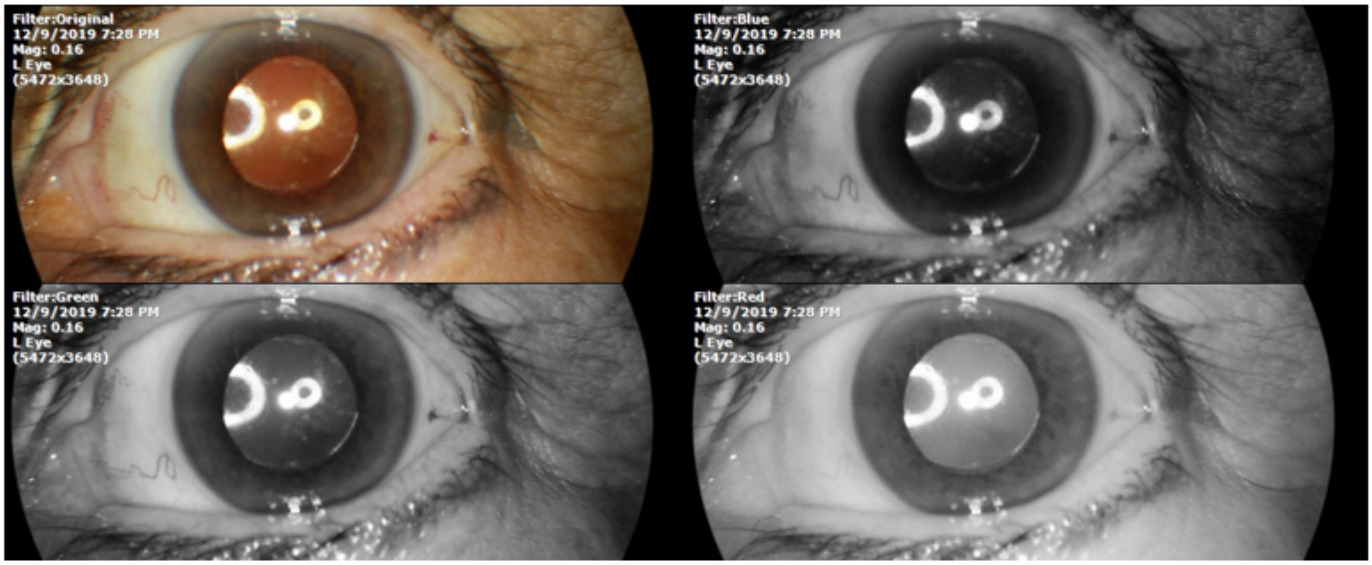


Figure 1: In the photograph of the anterior segment of the left eye, a transparent cornea can be seen, as well as the presence of a posterior chamber intraocular lens.

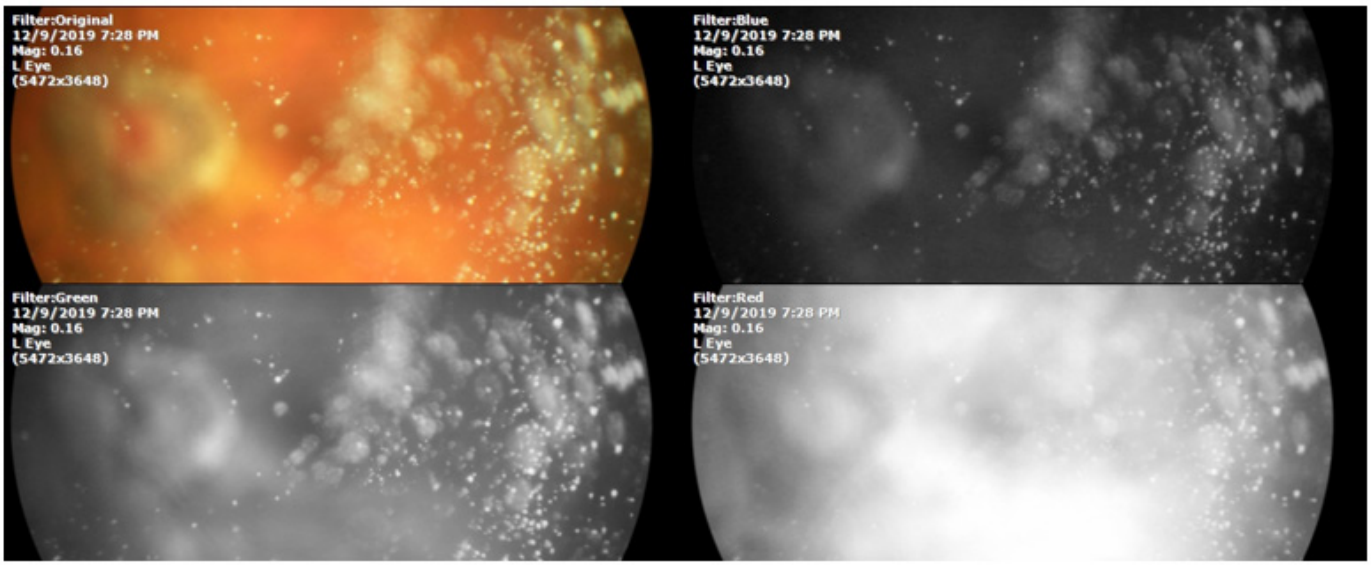


Figure 2: The left fundus photograph shows moderate mineralization of the vitreous body.

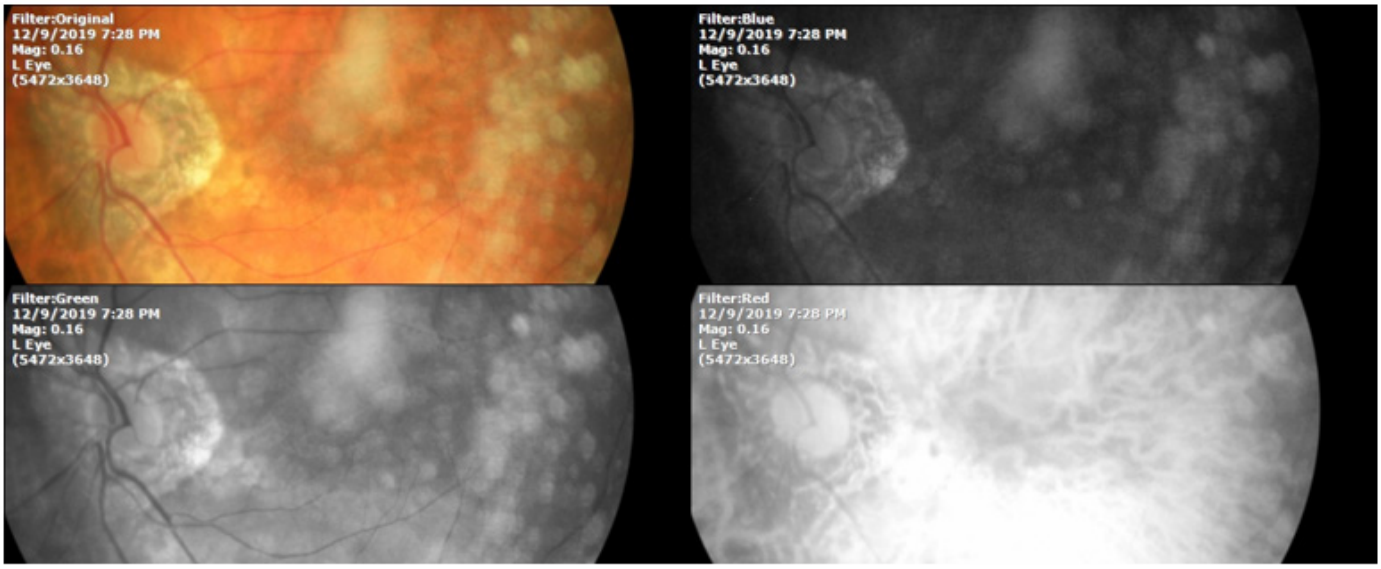


Figure 3: When focusing the instrument on the region of the left optic nerve, an extensive area of circumpapillary choroidal degeneration is observed, as well as significant vitreous condensation in the macular region.

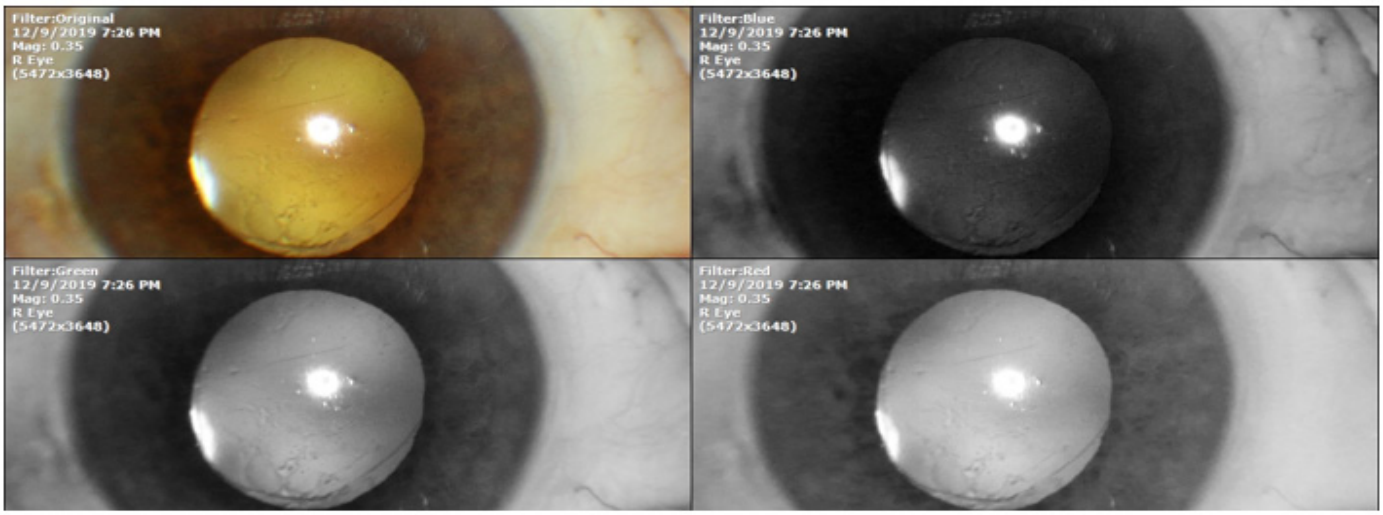


Figure 4: The photograph of the anterior segment of the right eye shows a transparent cornea, and the presence of a posterior chamber intraocular lens.

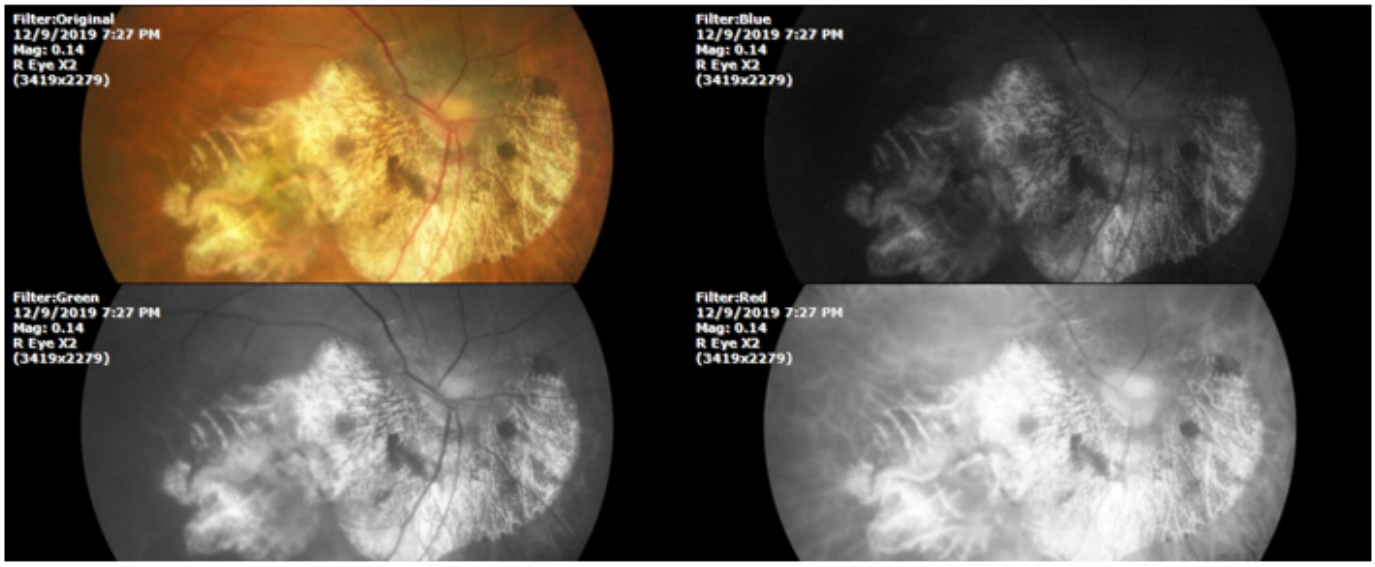
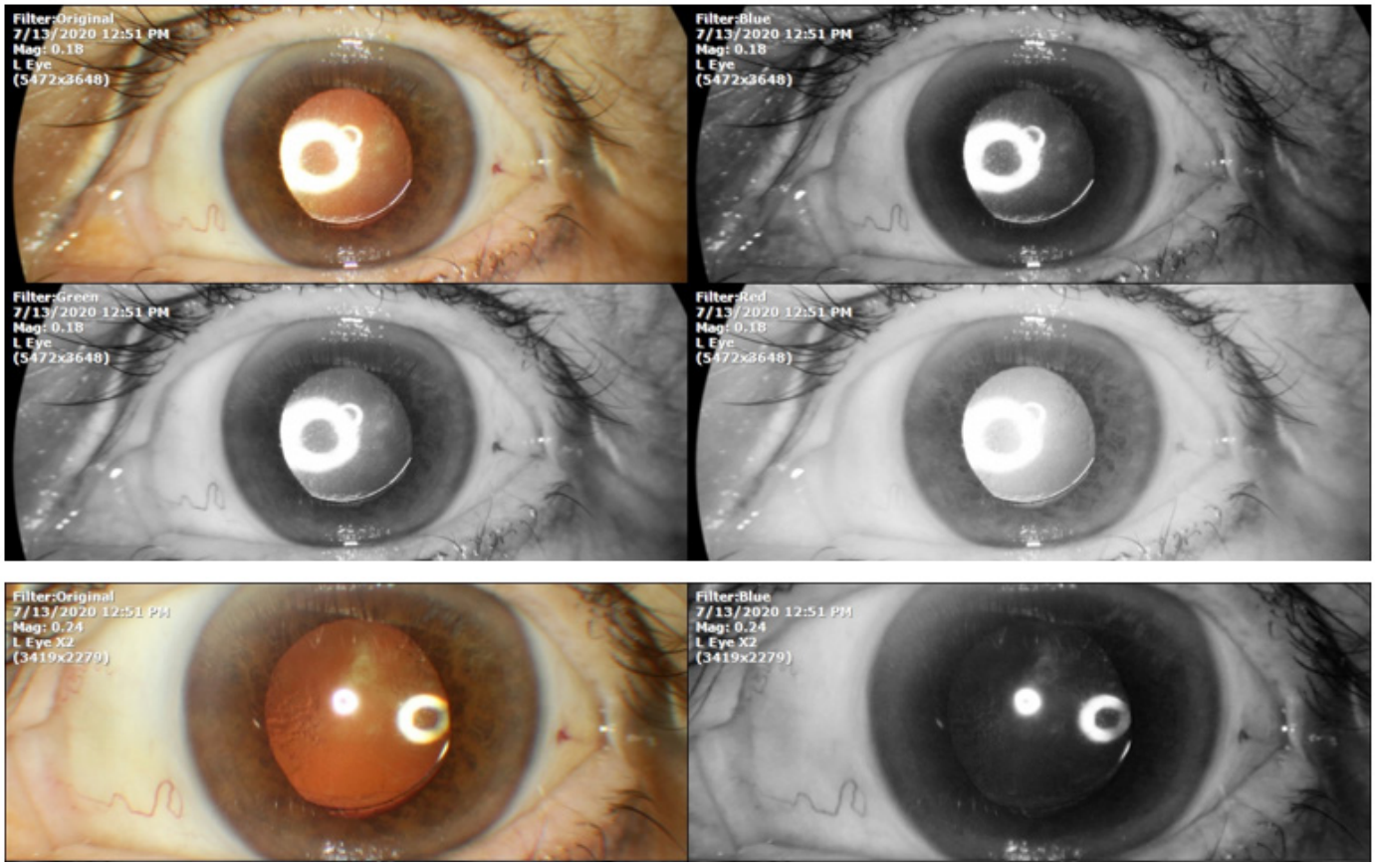


Figure 5: The photograph of the ocular fundus of the right eye shows no data of asteroid hyalosis, and an extensive area of chorio-retinal degeneration is observed that covers the macular region.

Second Examination
07 13 2020

He has taken the treatment, heaviness of the knees. The bad breath disappeared, phlegm.
General examination:
SpO2%: 97 %
Heartbeat: 67 x´.

Ocular examination:



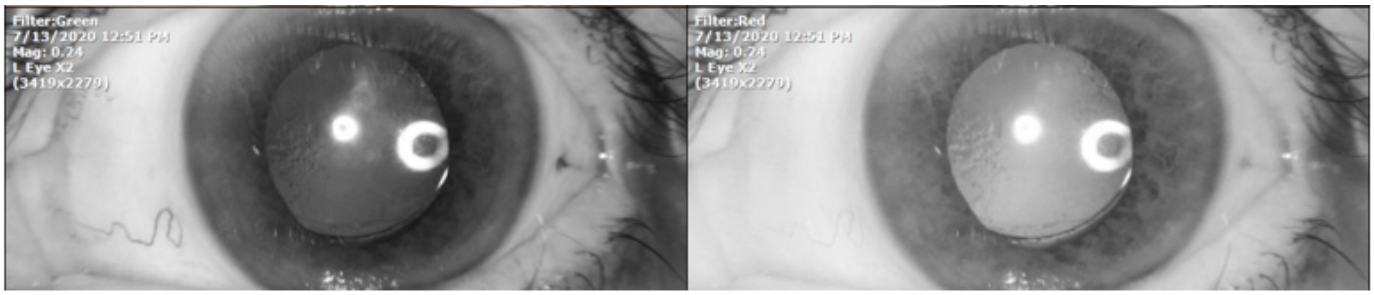


Figure 6: The anterior segment of the left eye shows the transparent cornea, and the posterior camera lens well centered.

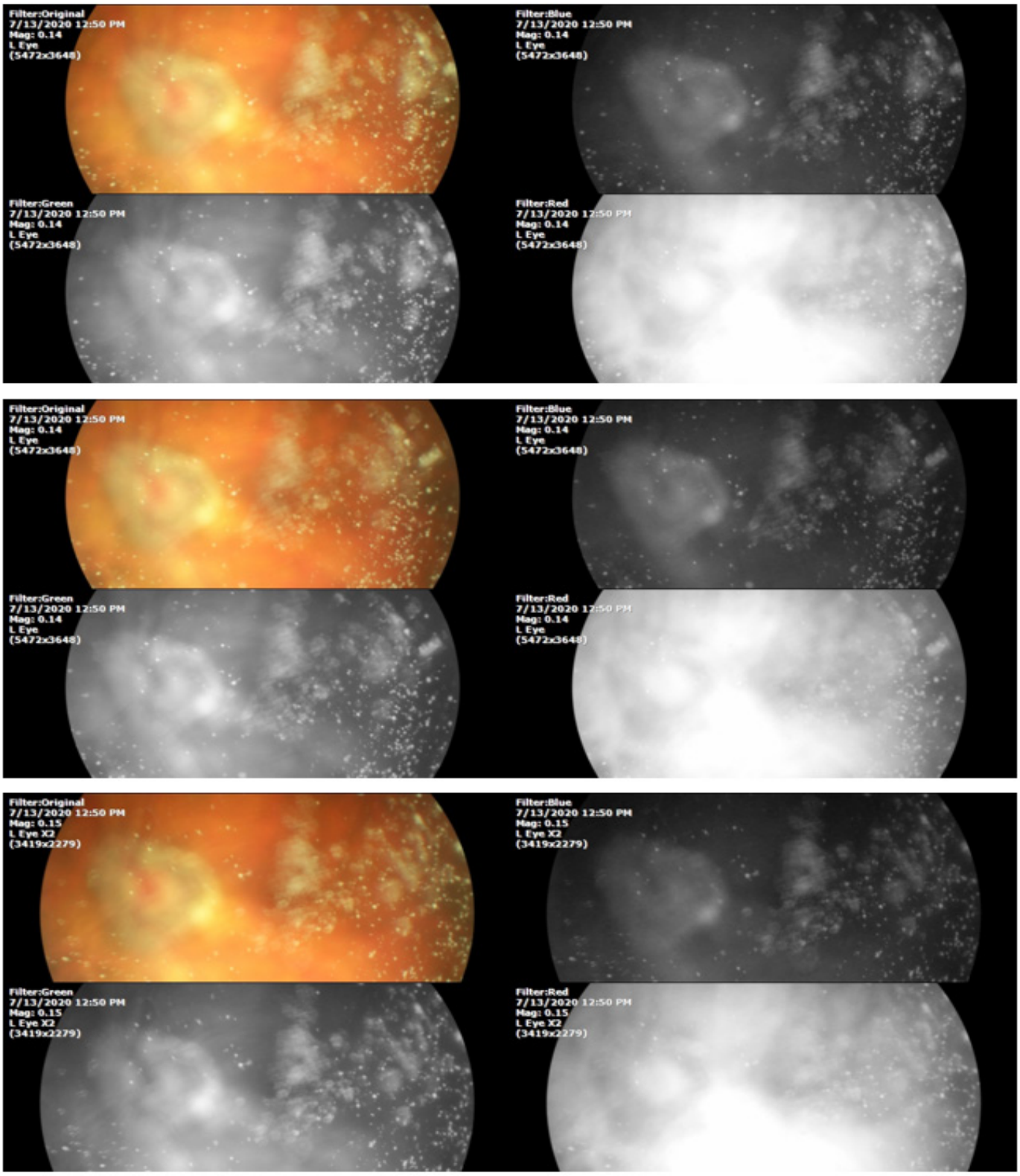


Figure 7: The photograph of the vitreous space in the left eye shows some changes in the density of the condensations of the vitreous body, especially in the macular area.

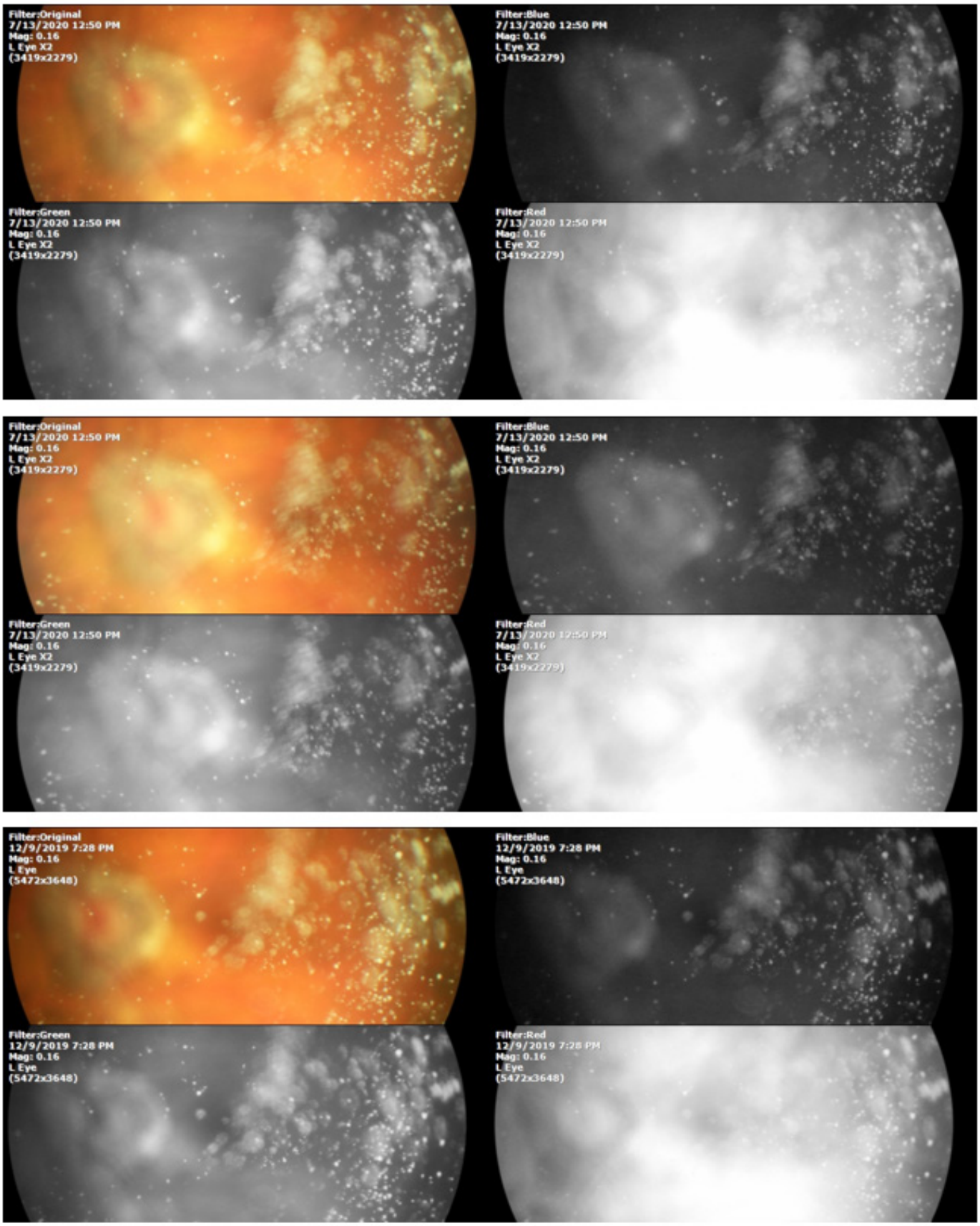


Figure 8: The areas of glassy condensation in the left eye, as well as the number and distribution of small fragments, showed some mild to moderate changes. There are several photographs to be able to focus in greater detail on different areas of the vitreous body.

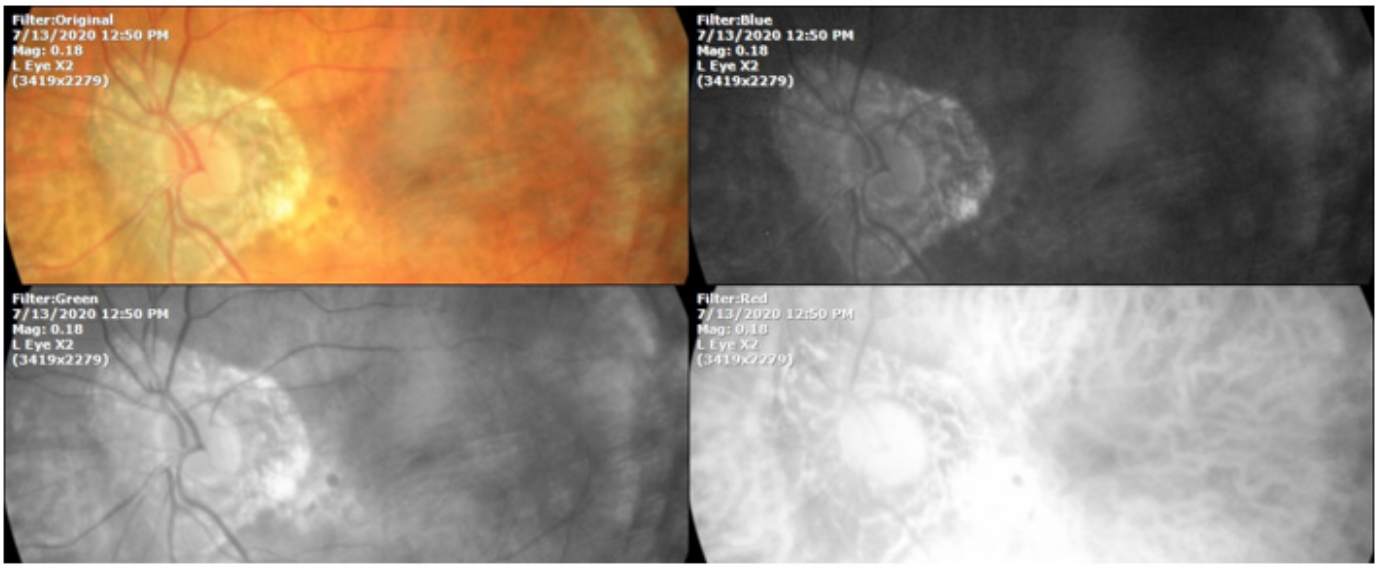


Figure 9: The photograph of the area corresponding to the optic nerve and macular region shows that the vitreous condensation is covering the macular area to a lesser extent, than in the first consultation, in which it covered it more completely.

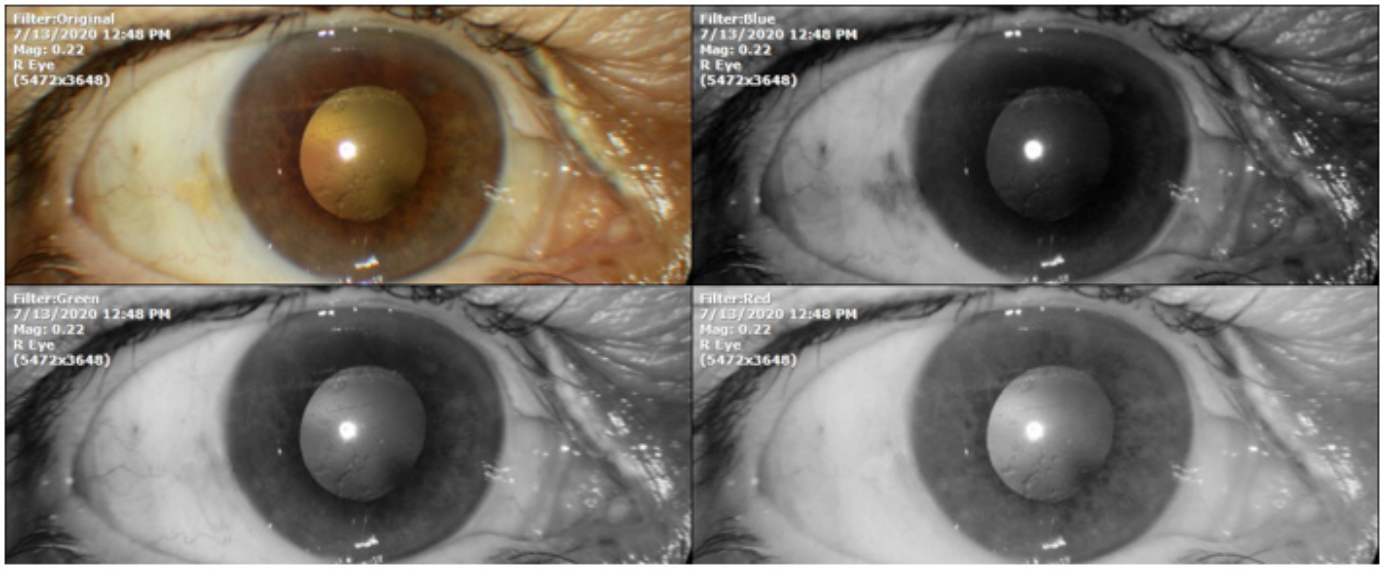


Figure 10: The photograph of the anterior segment of the right eye shows the cornea somewhat more transparent, and the posterior chamber intraocular lens is in place.

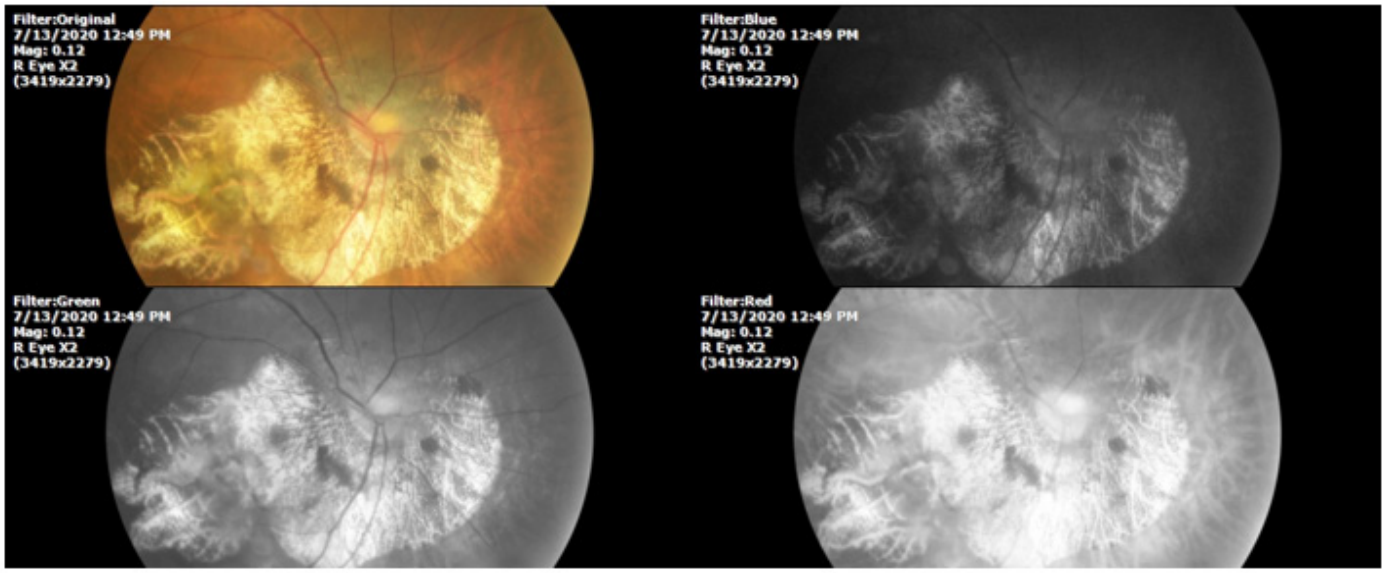


Figure 11: The photograph of the macular area and optic nerve of the right eye are more clearly observed. Allowing a better image of the chorio-retinal degeneration area around the optic nerve and macular region.

Third Consultation
July 28, 2021

The patient reports Swollen and red legs. The vision feels a little better. SpO2 %: 94 %, Heart beat: 65 x´. Sciascopy: R.E.: +/+, L.E.: +/+.

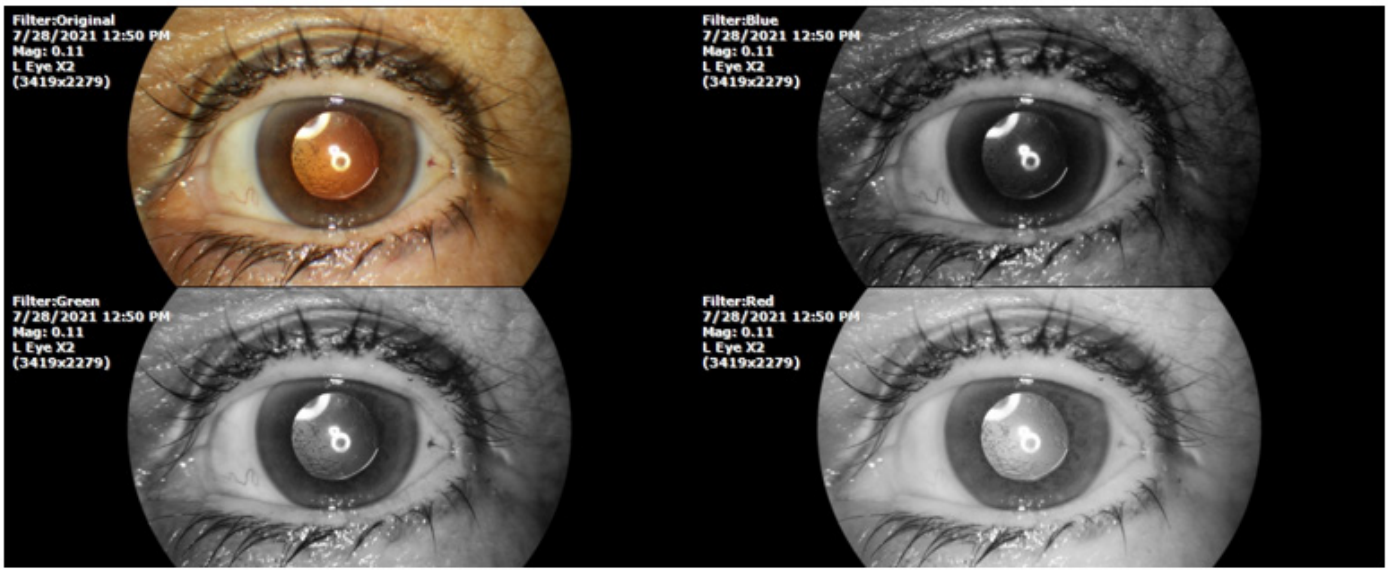
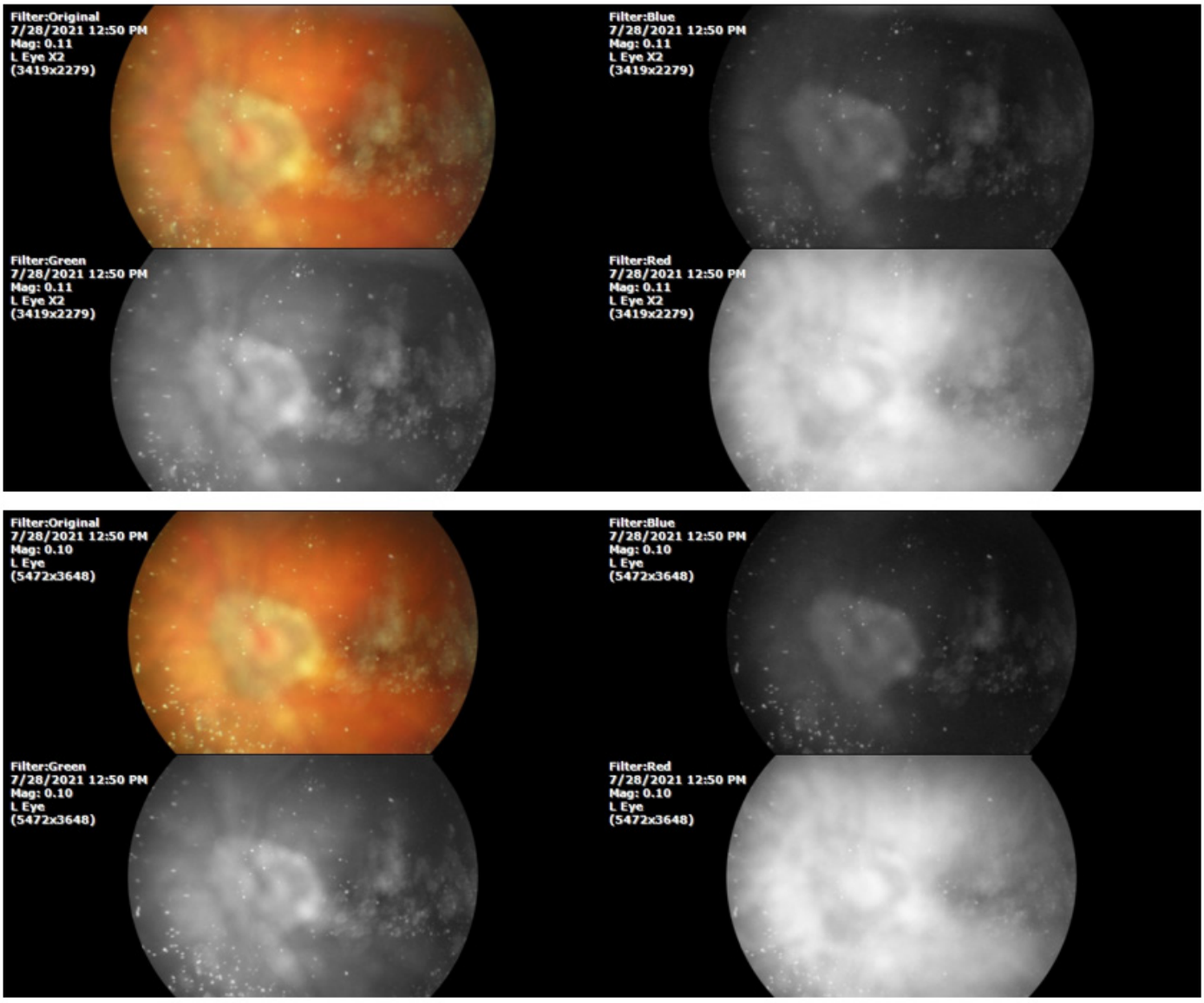


Figure 12: The anterior segment of the left eye is in good condition, transparent, shiny. The posterior chamber intraocular lens in place.



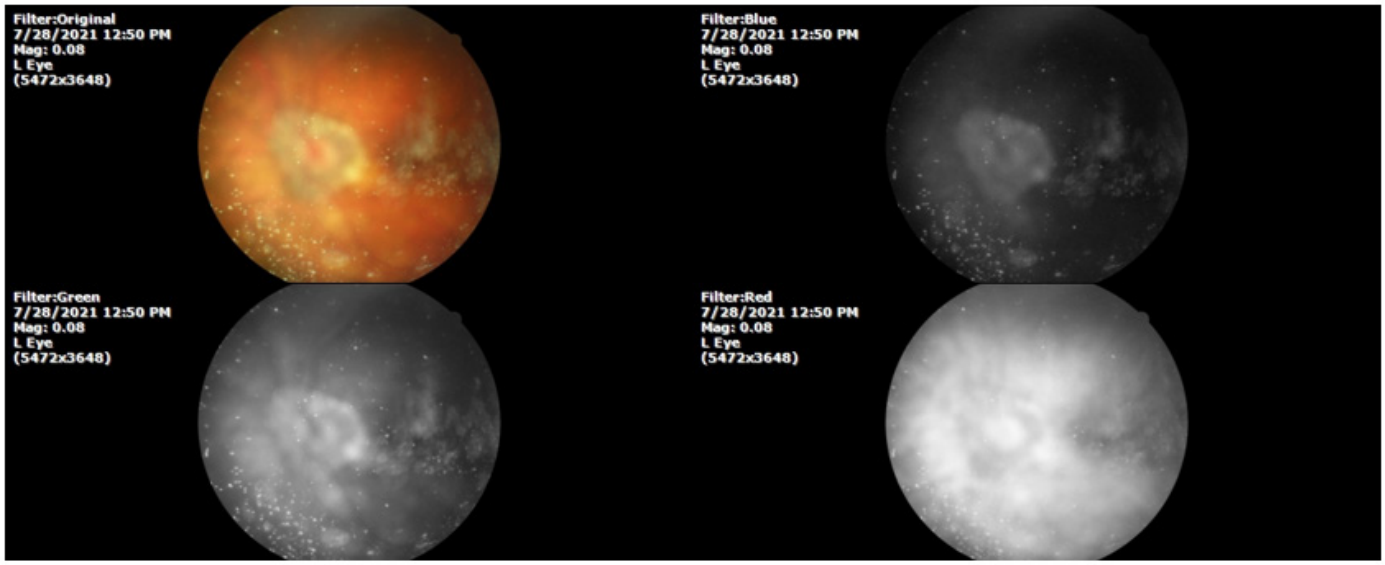


Figure 13: Photographs of the glassy space, which show changes in the glassy condensations, as well as a decrease in the number of glassy fragments. The distribution of these is now more towards the periphery.

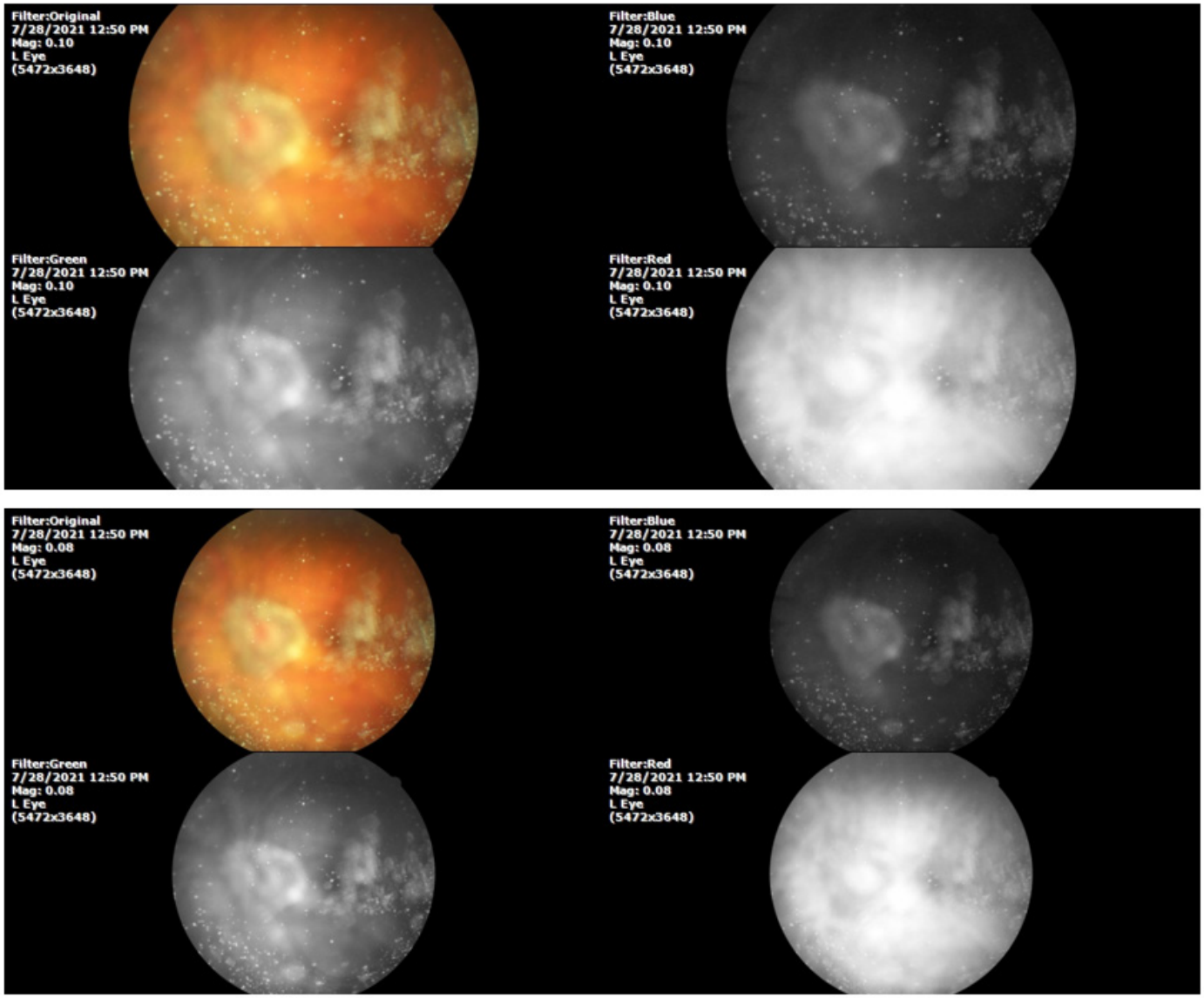


Figure 14: The condensation of the vitreous (L.E.) that almost completely affected the macular area has undergone changes because it is less dense and the macular area is now freer.

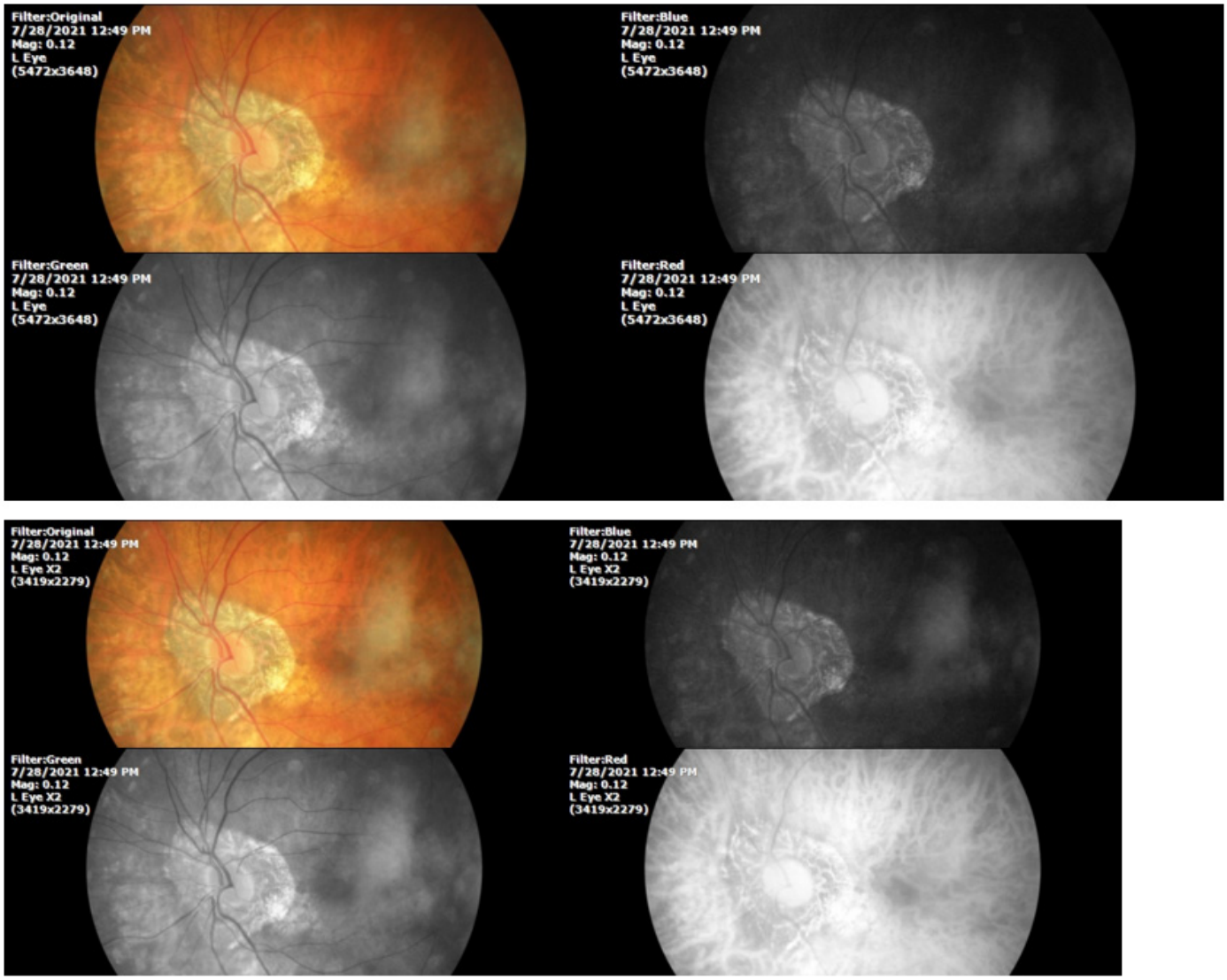


Figure 15: The image of the optic nerve and macular area of the left eye is more clearly appreciated compared to the first consultation, now the macular area can be seen in its entirety given the changes in the vitreous condensation that covered it almost completely at the beginning.

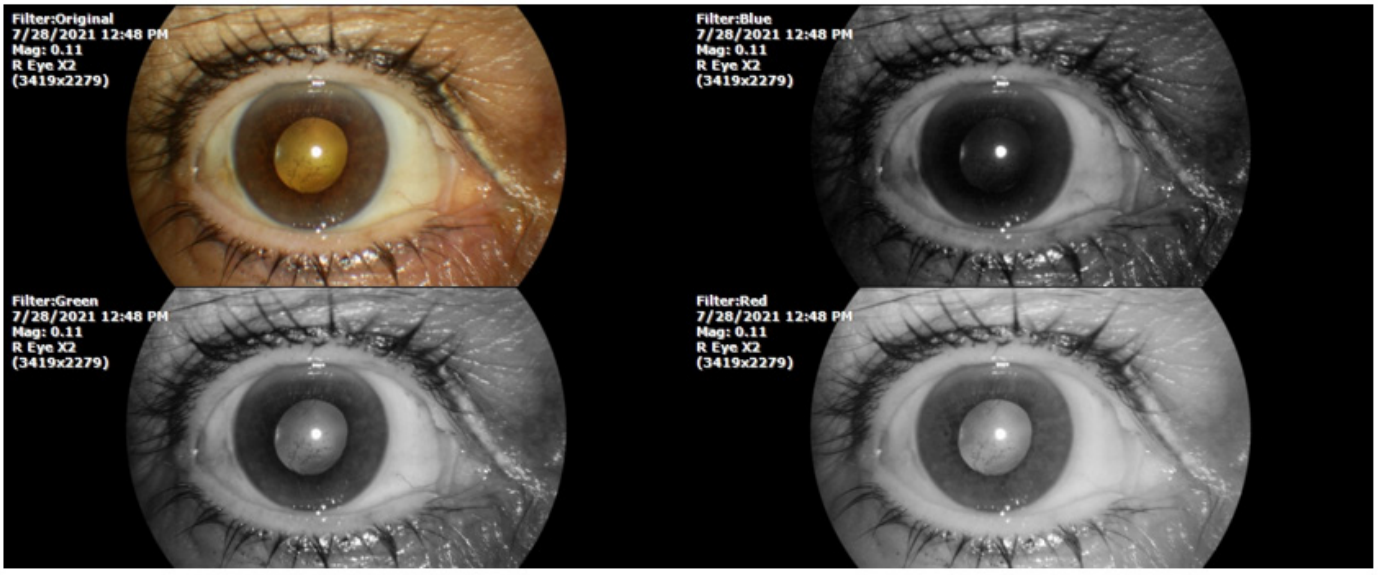


Figure 16: The photograph of the anterior segment of the right eye shows the cornea with better transparency and the intraocular lens in place in the posterior chamber.

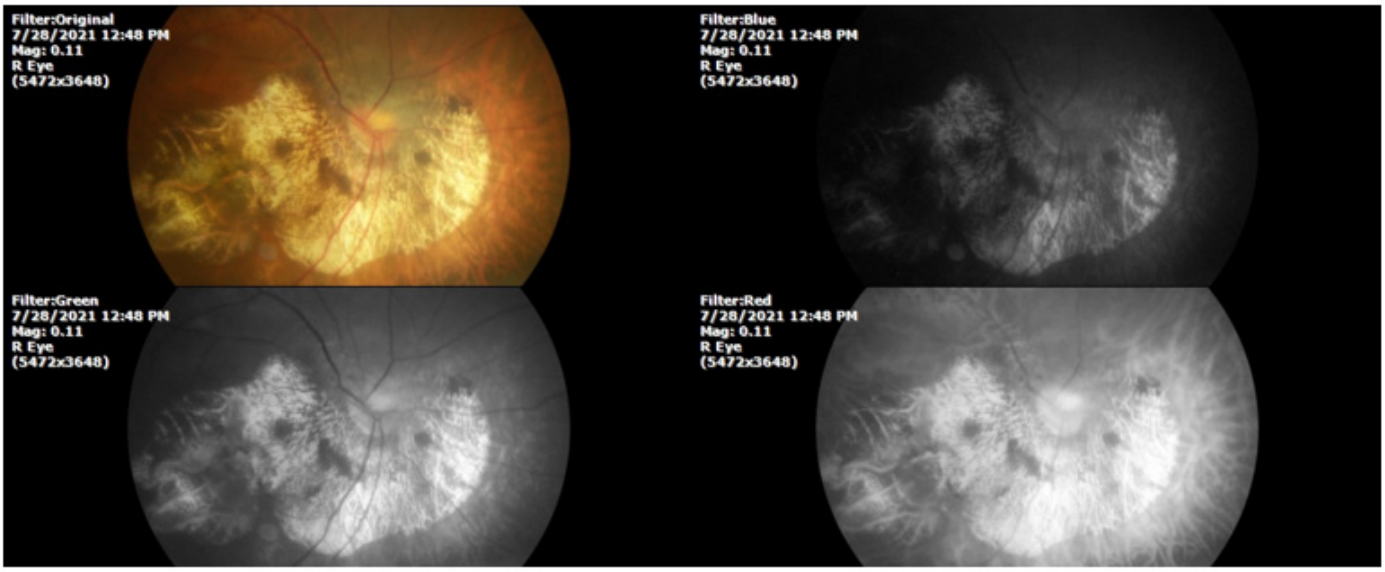


Figure 17: In the right eye, the image is sharper than at the beginning, perhaps it is the researcher's own enthusiasm, but the area of chorioretinal degeneration that covers the optic nerve, and macular area seems to have been reduced.

Fourth Consultation

February 7, 2022

Visit Every Six Months.

In the past few days he had flu symptoms, he only took the drops more often, in a week he came out, he did not get tested. She has not been vaccinated against COVID.
SpO2%: 94 %
Heartbeat: 75 FC
Sciascopy: R.E.: +/-, L.E.: +/-.

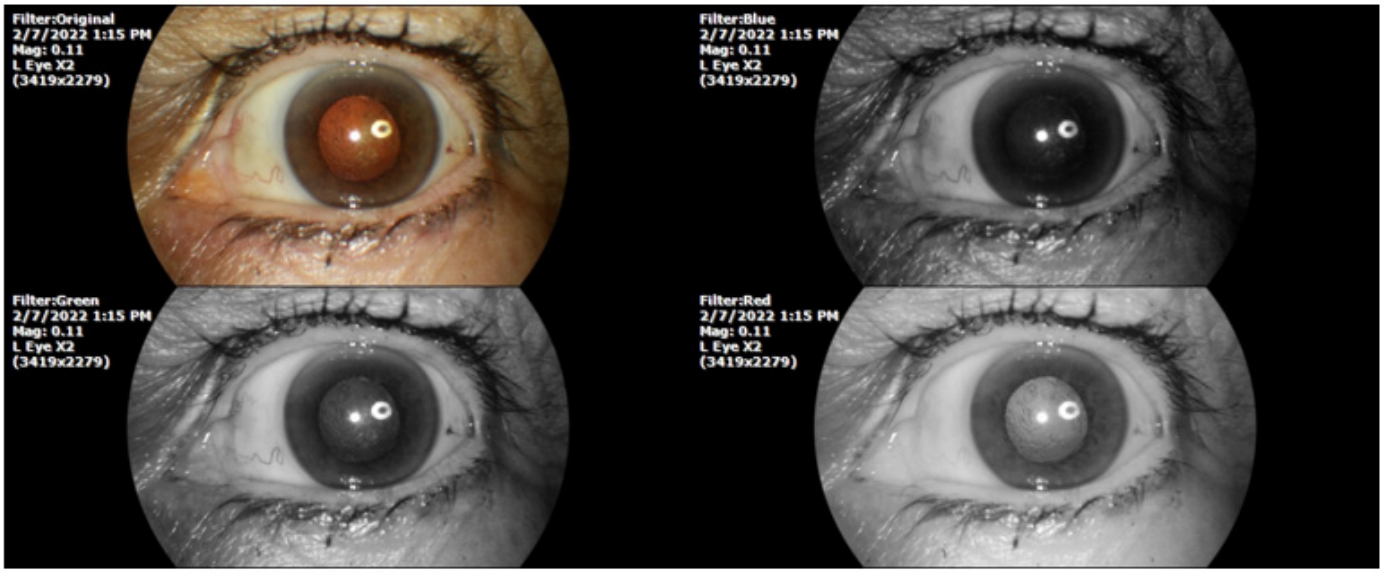


Figure 18: The anterior segment of the left eye retains its transparency and brightness. There is no evidence of vitreous mineralization in the mirror reflection.

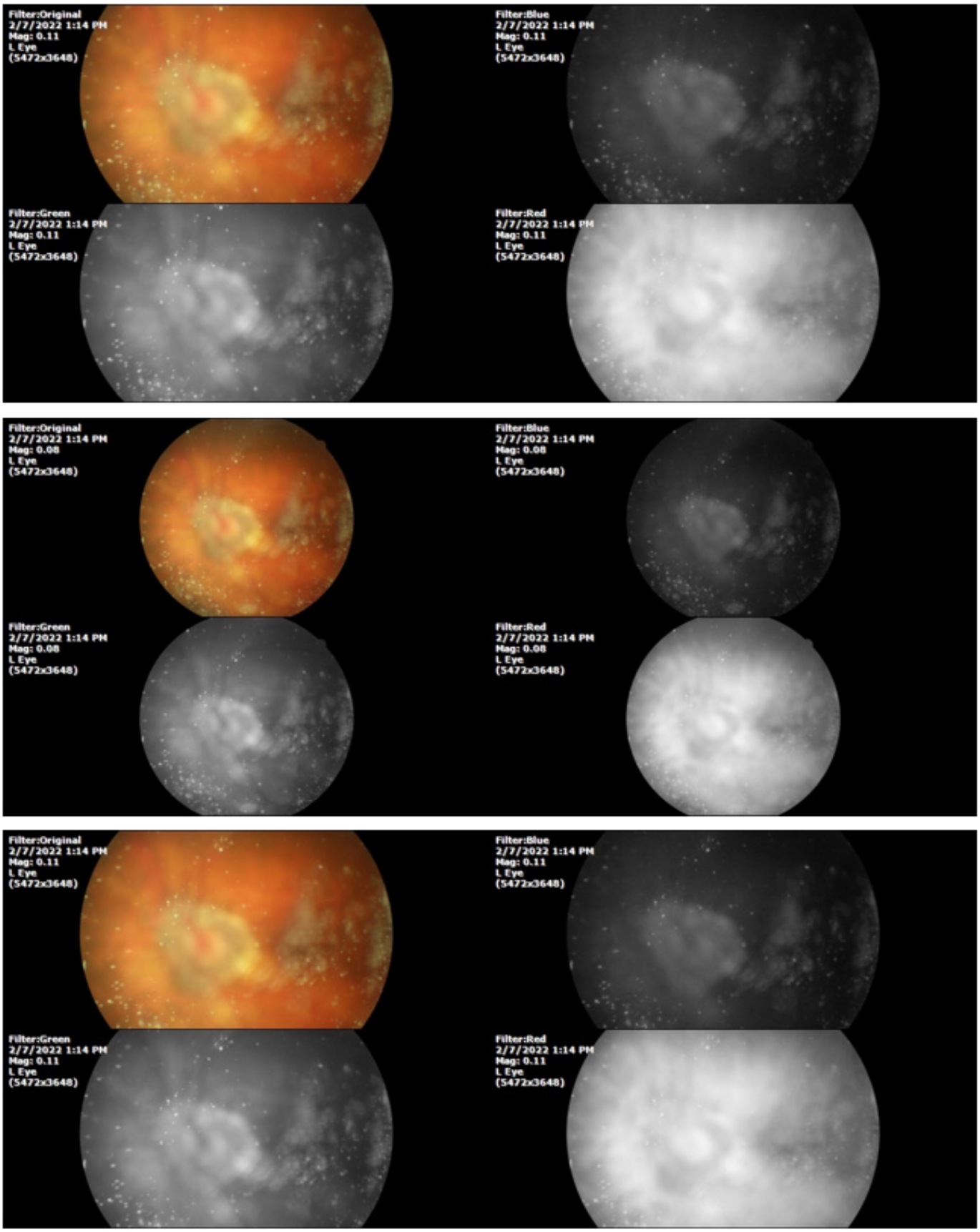


Figure 19: The photograph of the vitreous of the left eye, in different locations, shows that the density of the condensations has decreased, as well as their distribution, as they have been moving to the periphery. Their numbers have also decreased.

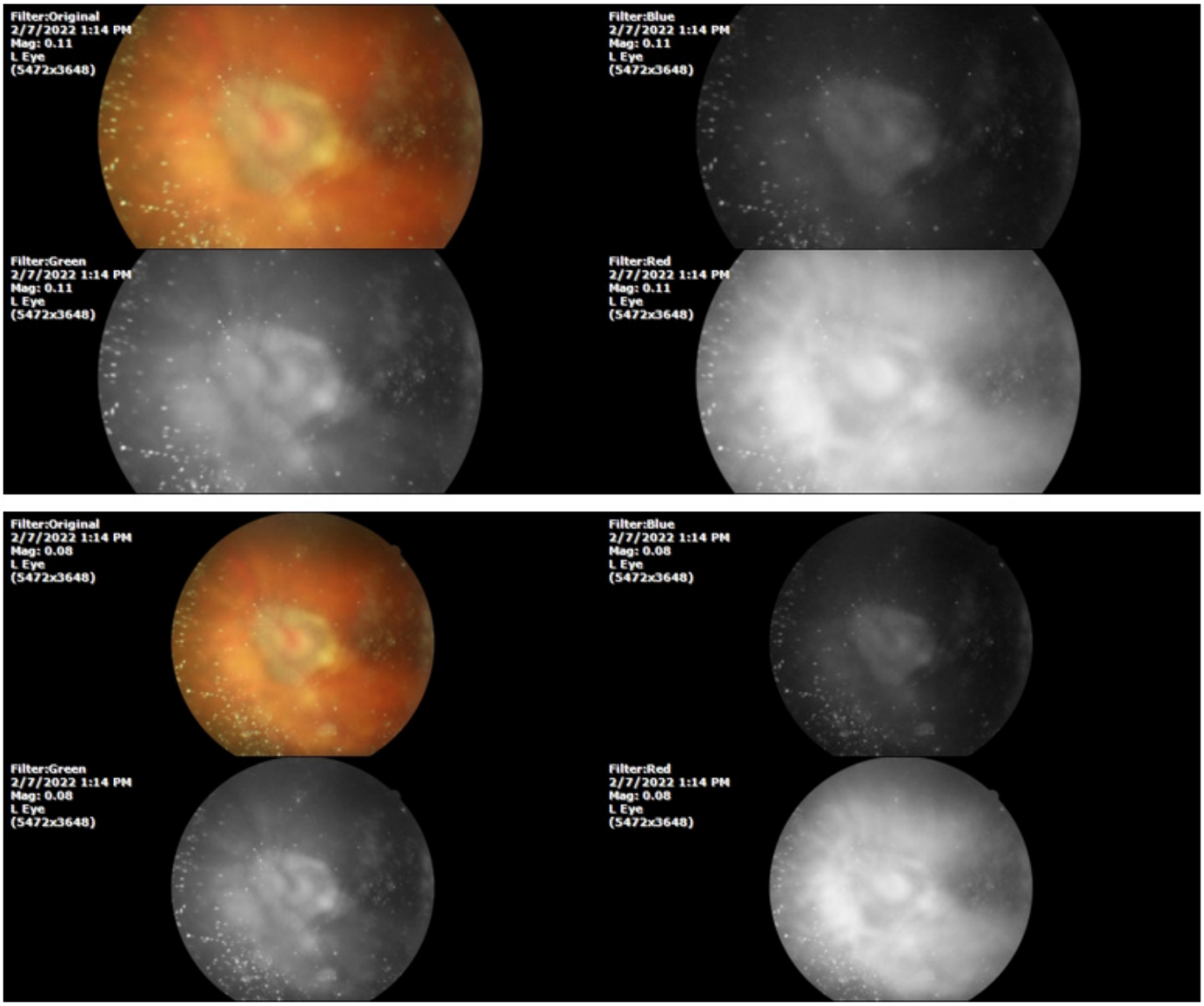
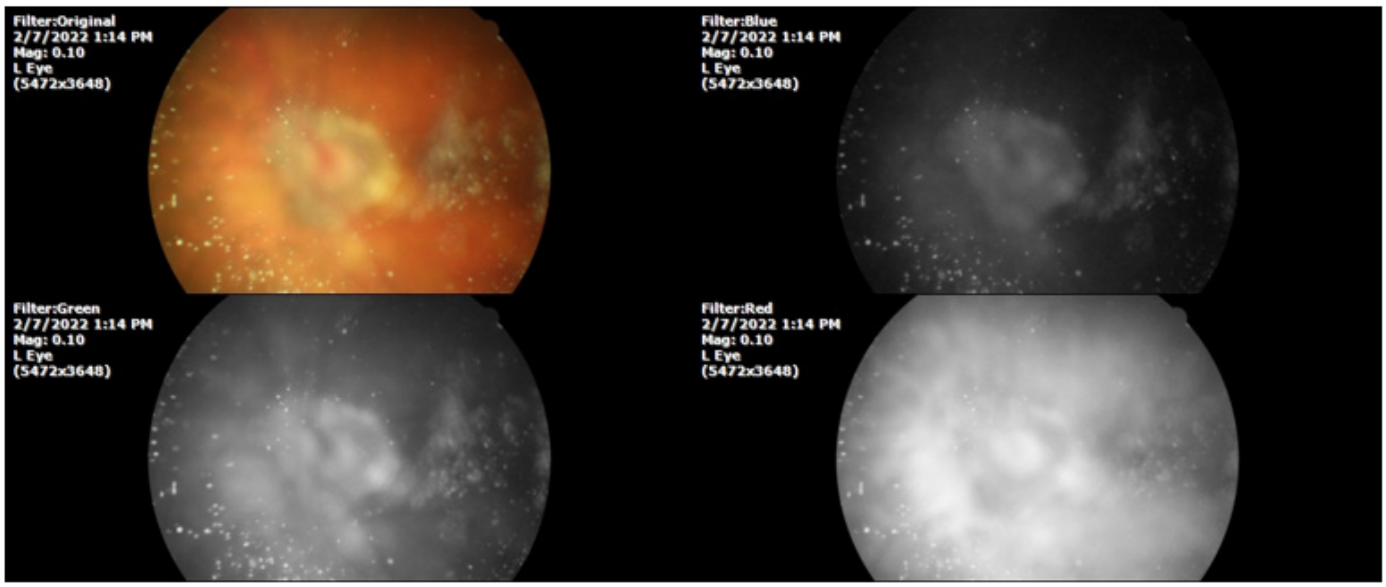


Figure 20: The region of the left eye that corresponds to the optic nerve and macular area shows that the vitreous condensations have become less dense, and the macular area is no longer obstructed.



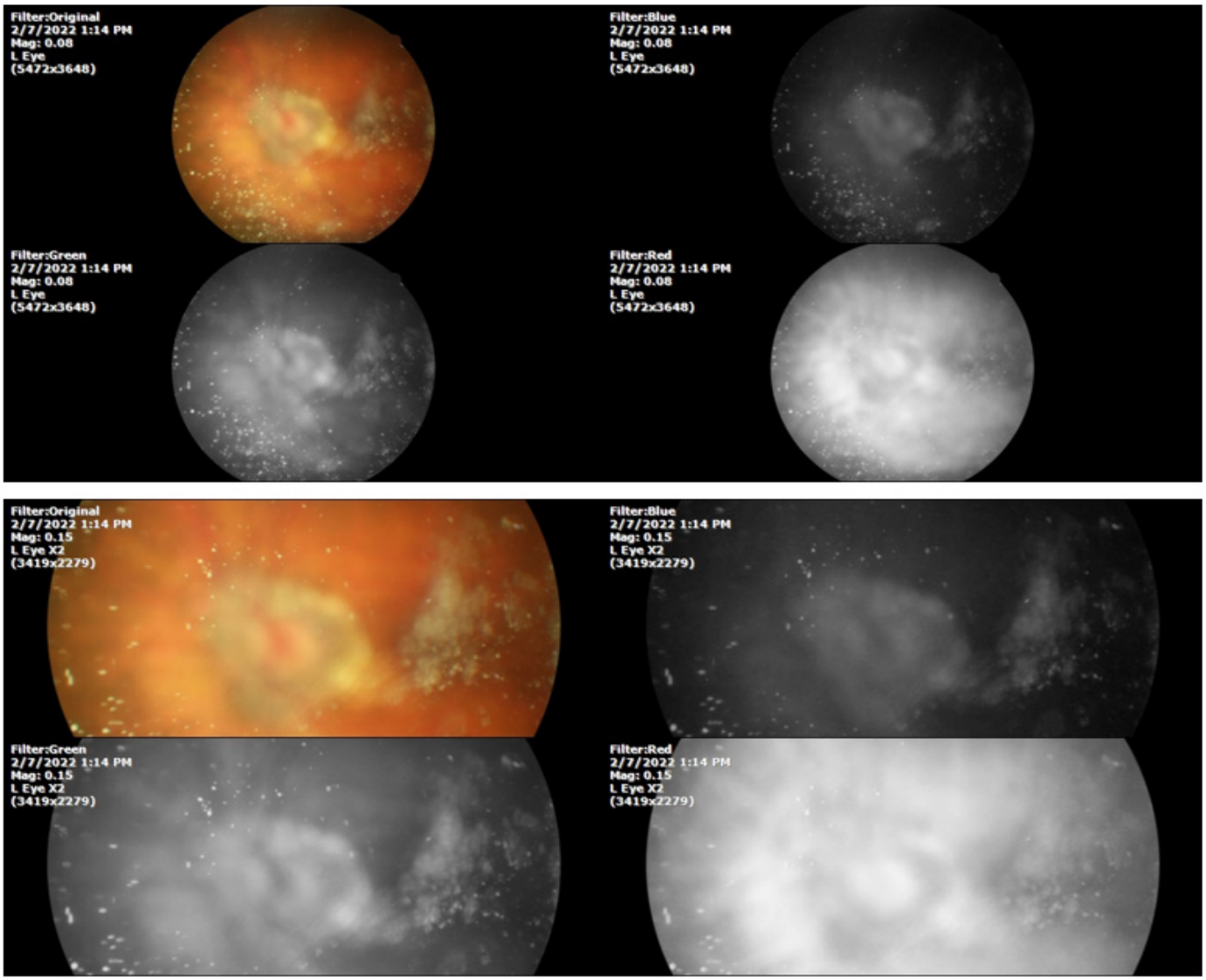
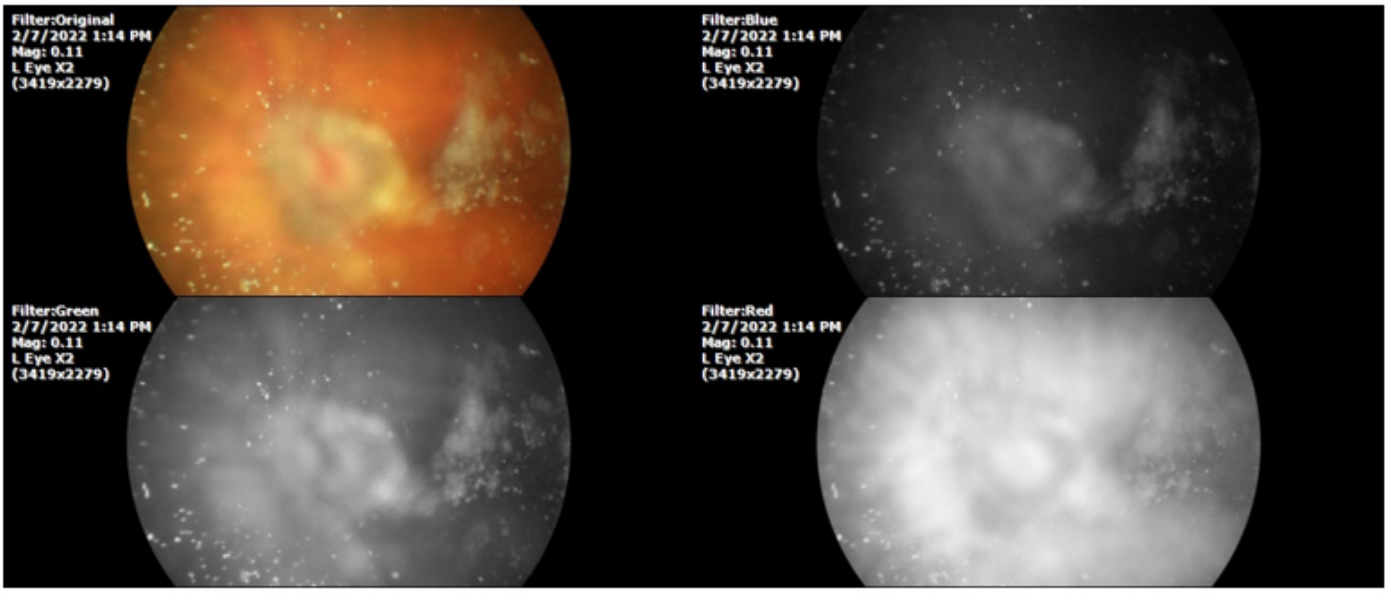


Figure 21: The macular area and left optic nerve are shown at different magnifications, which allows us to appreciate different details about the patient's evolution.



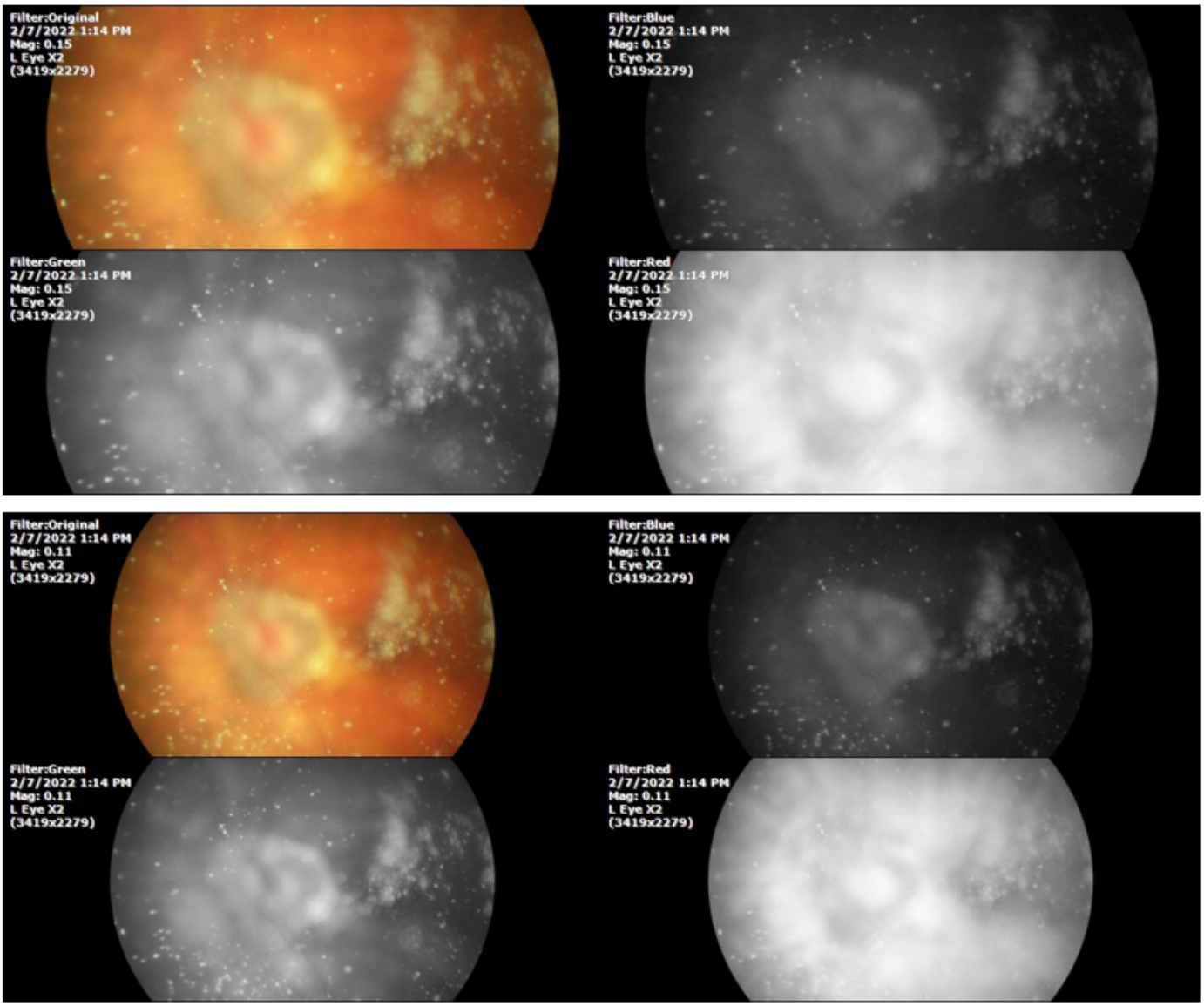
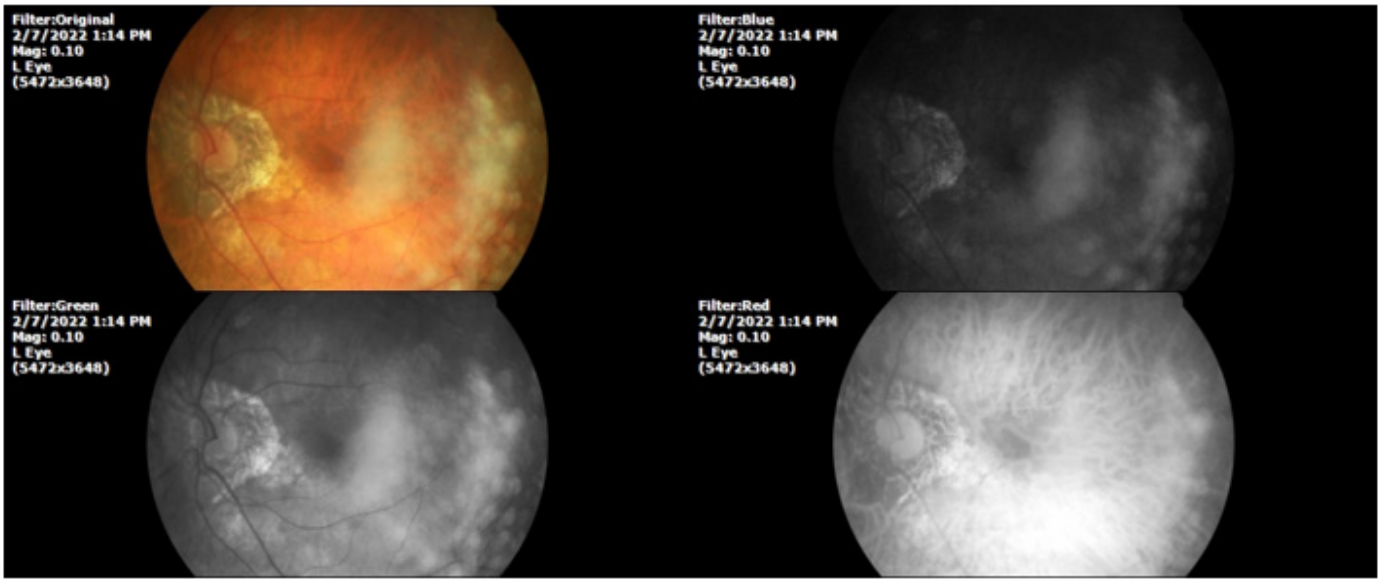


Figure 22: Photographs of the vitreous body of the left eye with different magnifications and focuses allow us to measure more completely the changes in the patient's evolution.



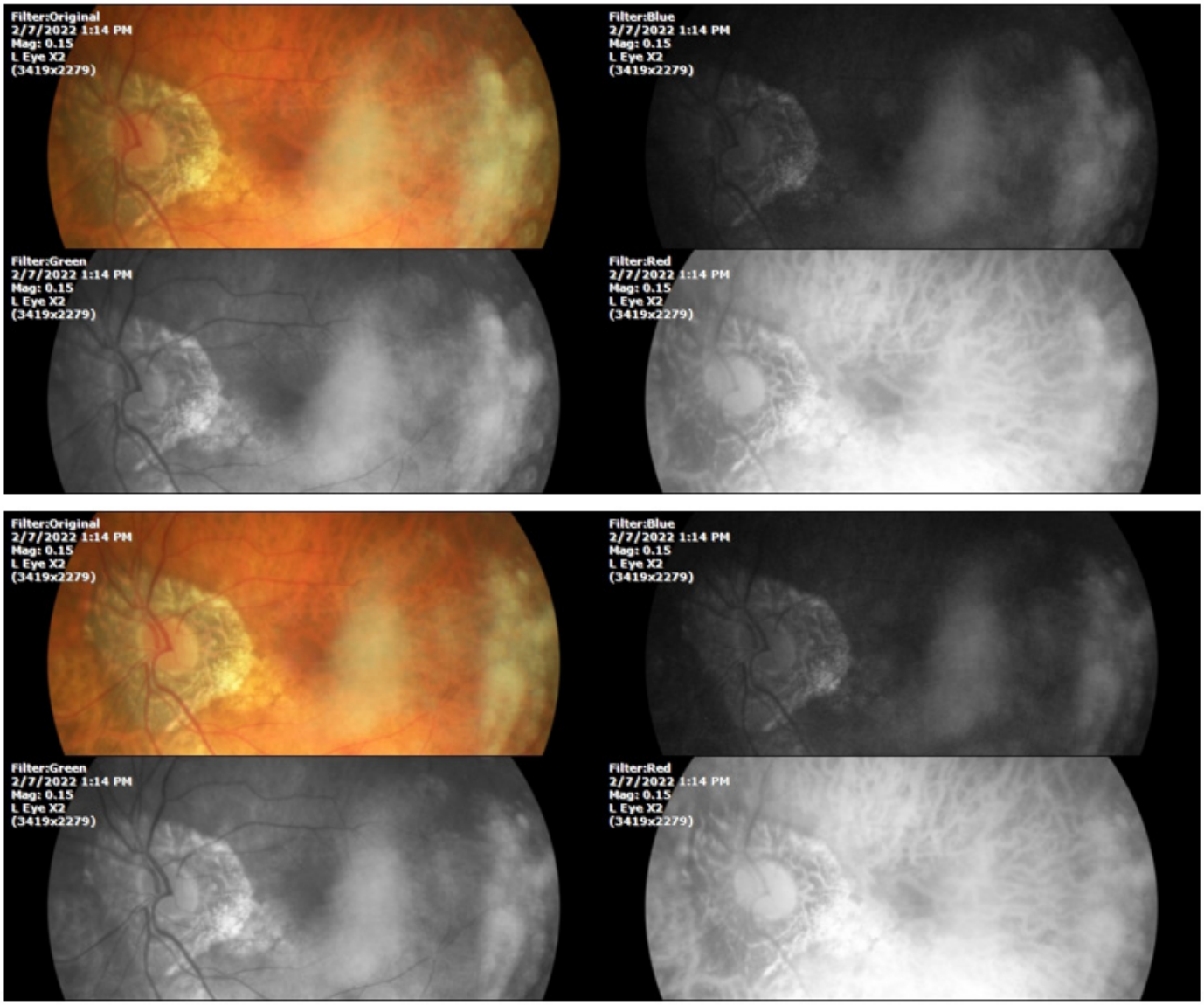


Figure 23: In the same way, by evaluating the structures of the optic nerve and macular area of the left eye, with different magnifications, they allow us to better appreciate the good evolution of the patient with regard to obstruction by vitreous condensation of the macular area.

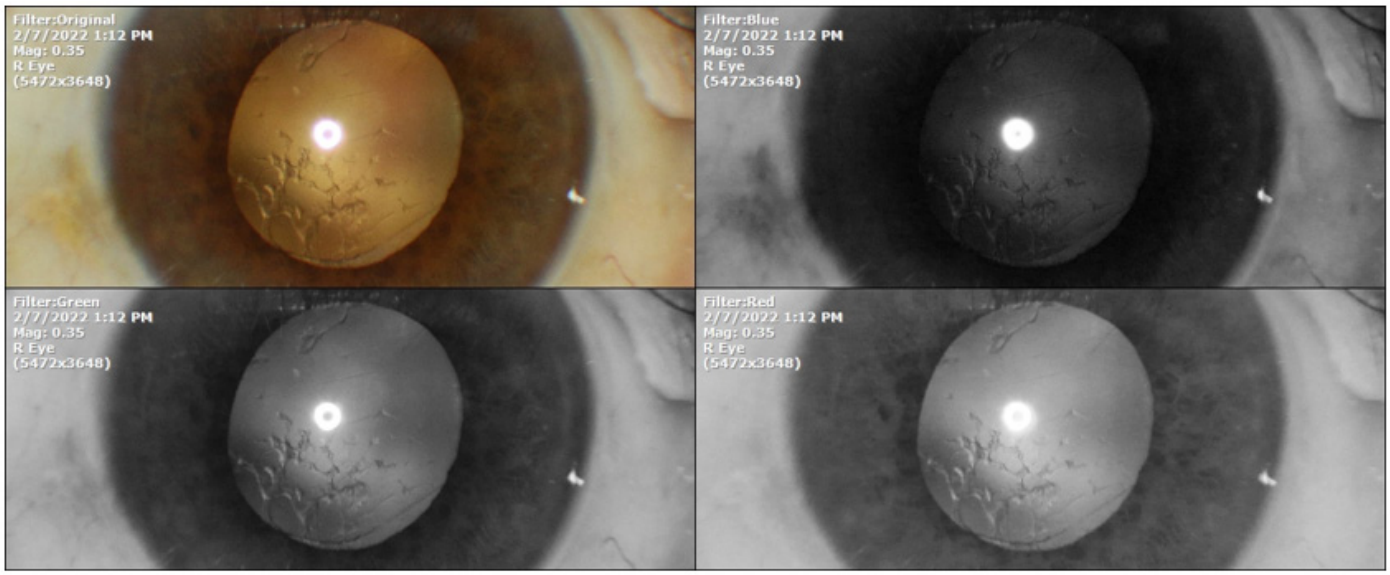


Figure 24: The anterior segment of the right eye does not show negative changes in brightness and transparency.

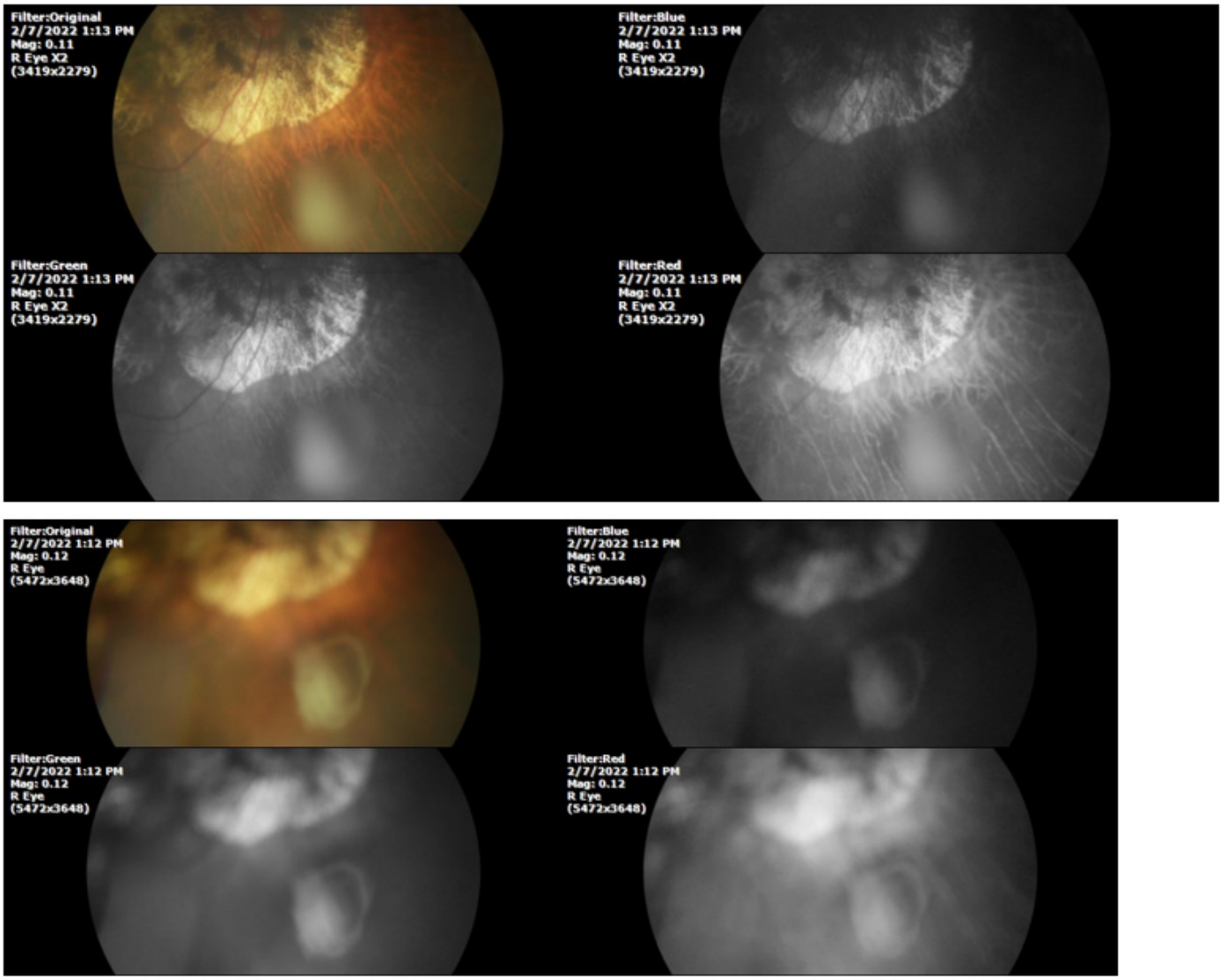


Figure 25: Floating operculum in the vitreous body of the right eye in the lower periphery, in the nasal region. The retina is in place.

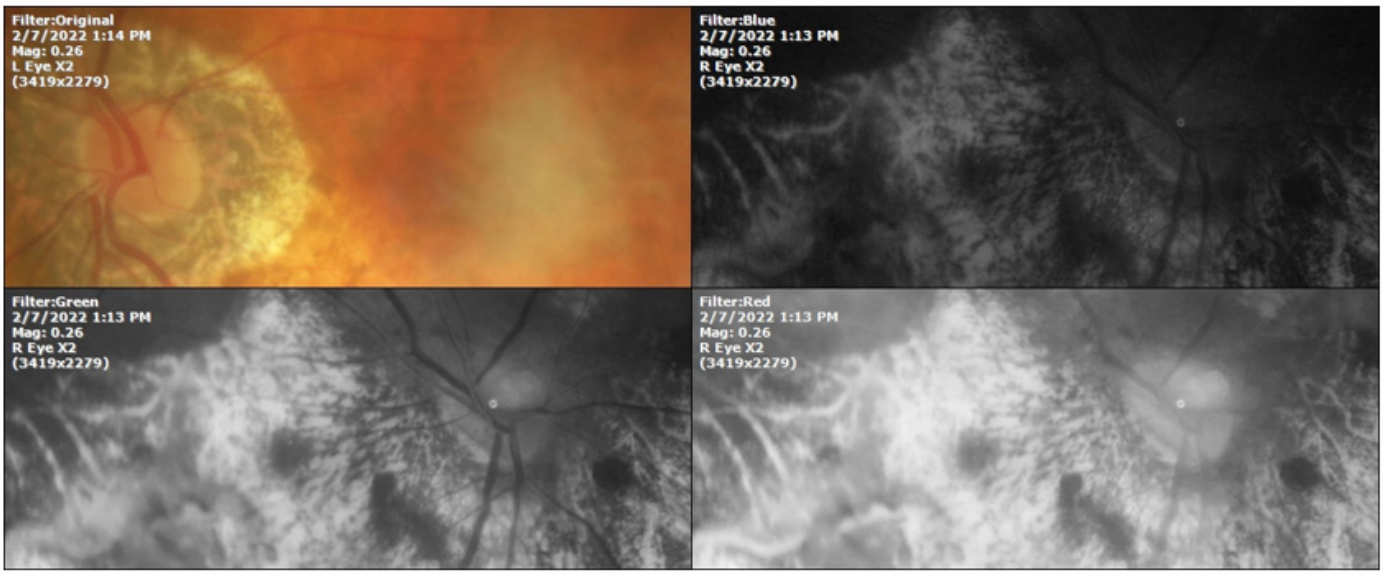


Figure 26: In the center of the optic disc of the right eye, a hyper-refractive point can be seen at the confluence of the blood vessels of the optic nerve (right).

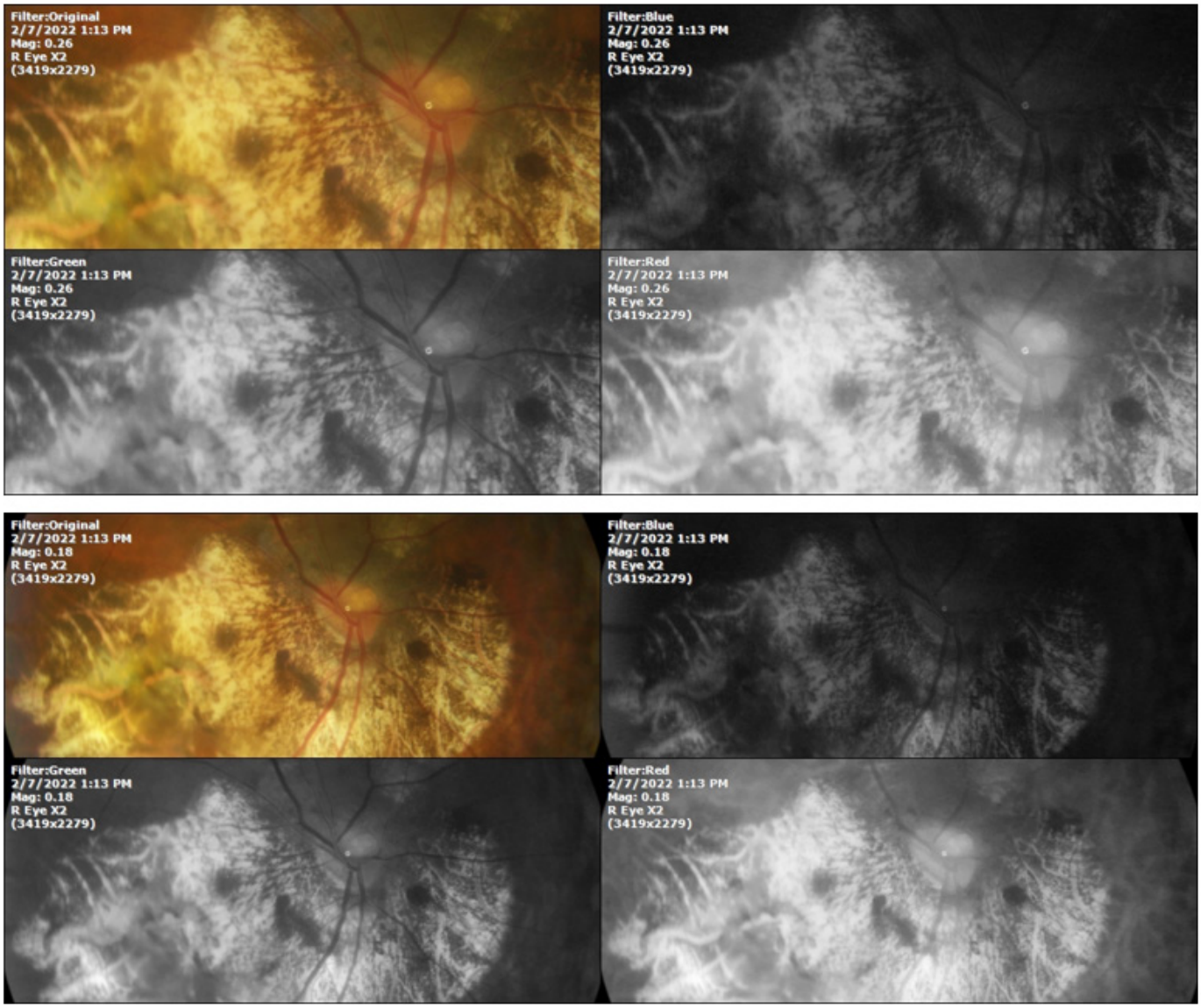
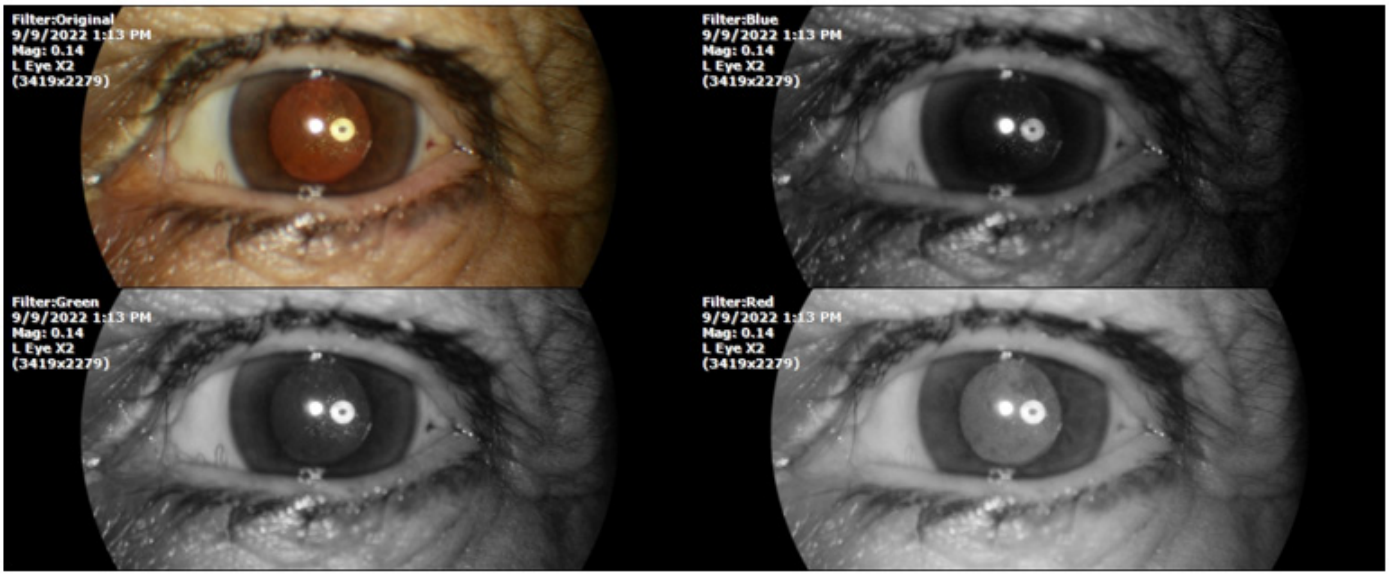


Figure 27: In different sockets and with different magnifications, the hyper refractive point at the confluence of the vessels of the right optic nerve persists.

Fifth Consultation

September 9, 2022

Sometimes the patient sees cloudy, tinnitus occasionally. SpO2%: 93 %; Heartbeat: 62 x´; Sciascopy: R.E.: +/+, L-E.: +/+



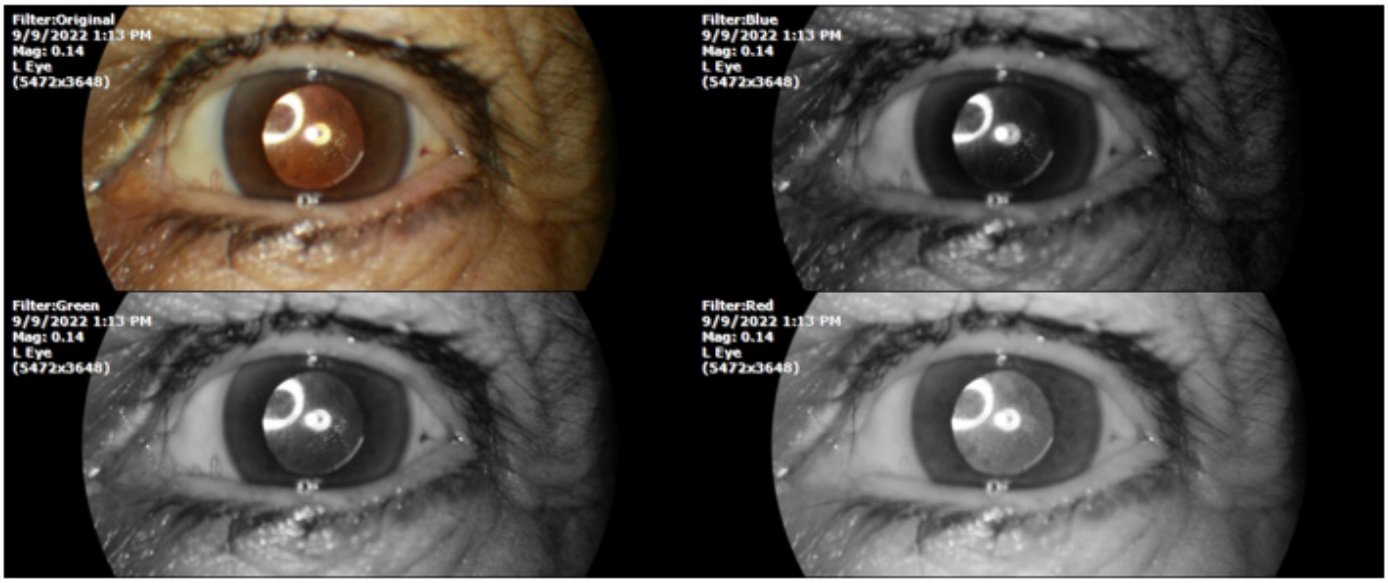
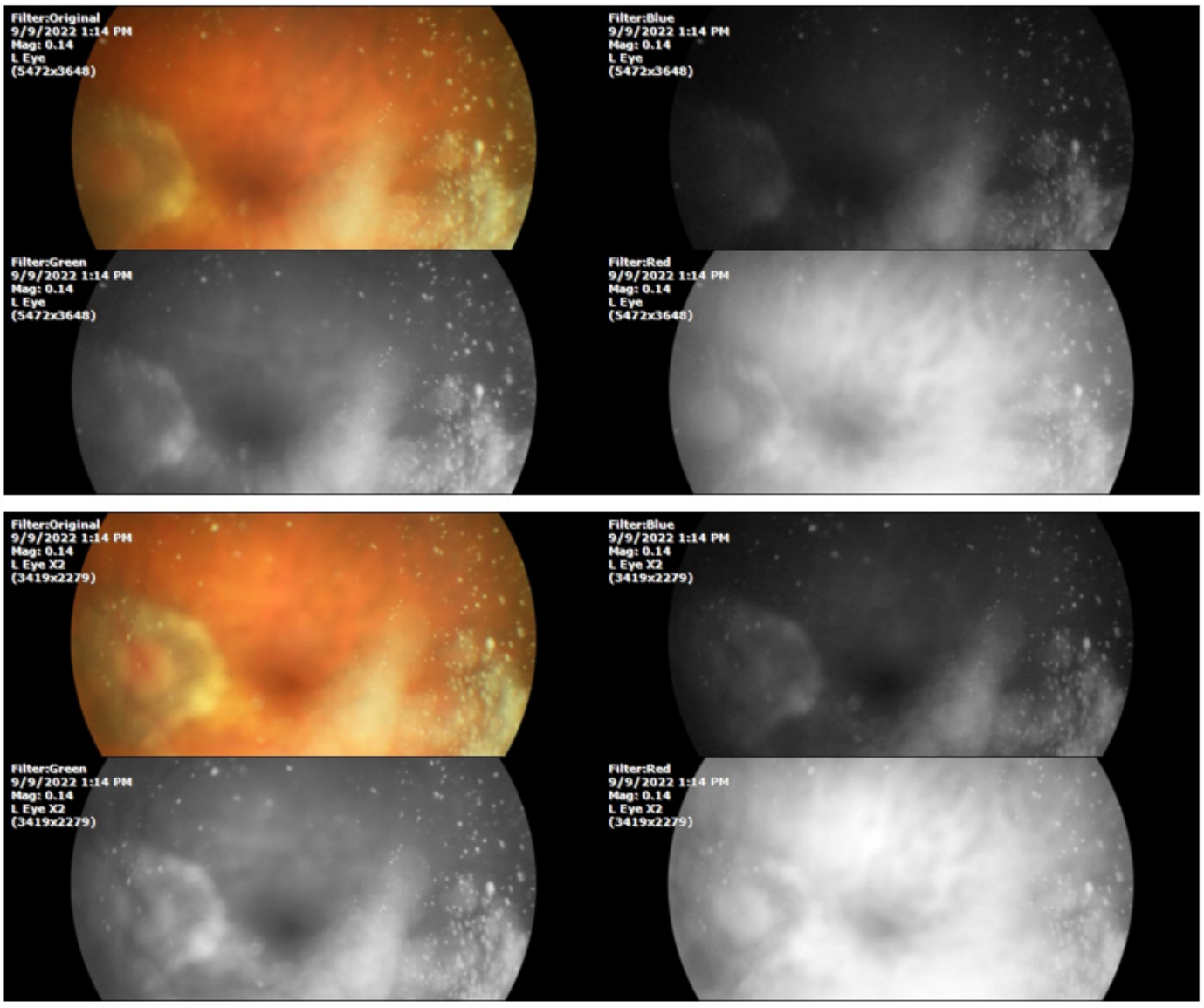


Figure 28: The image of the anterior segment of the left eye, with good brightness and transparency. Specular reflection does not detect mineralization of the vitreous body.



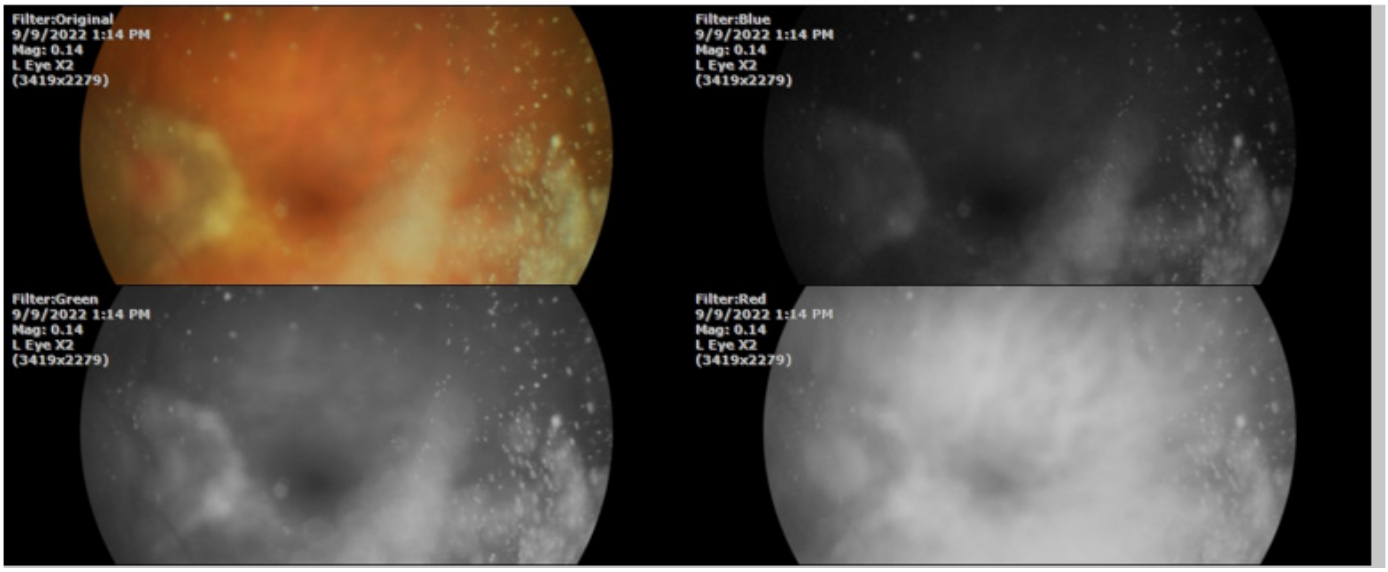


Figure 29: The photograph of the vitreous body of the left eye with different approaches and locations shows that the vitreous condensation that covered the macula has been completely displaced and has tended to go to the periphery, as well as the fragments of mineralization of the vitreous.

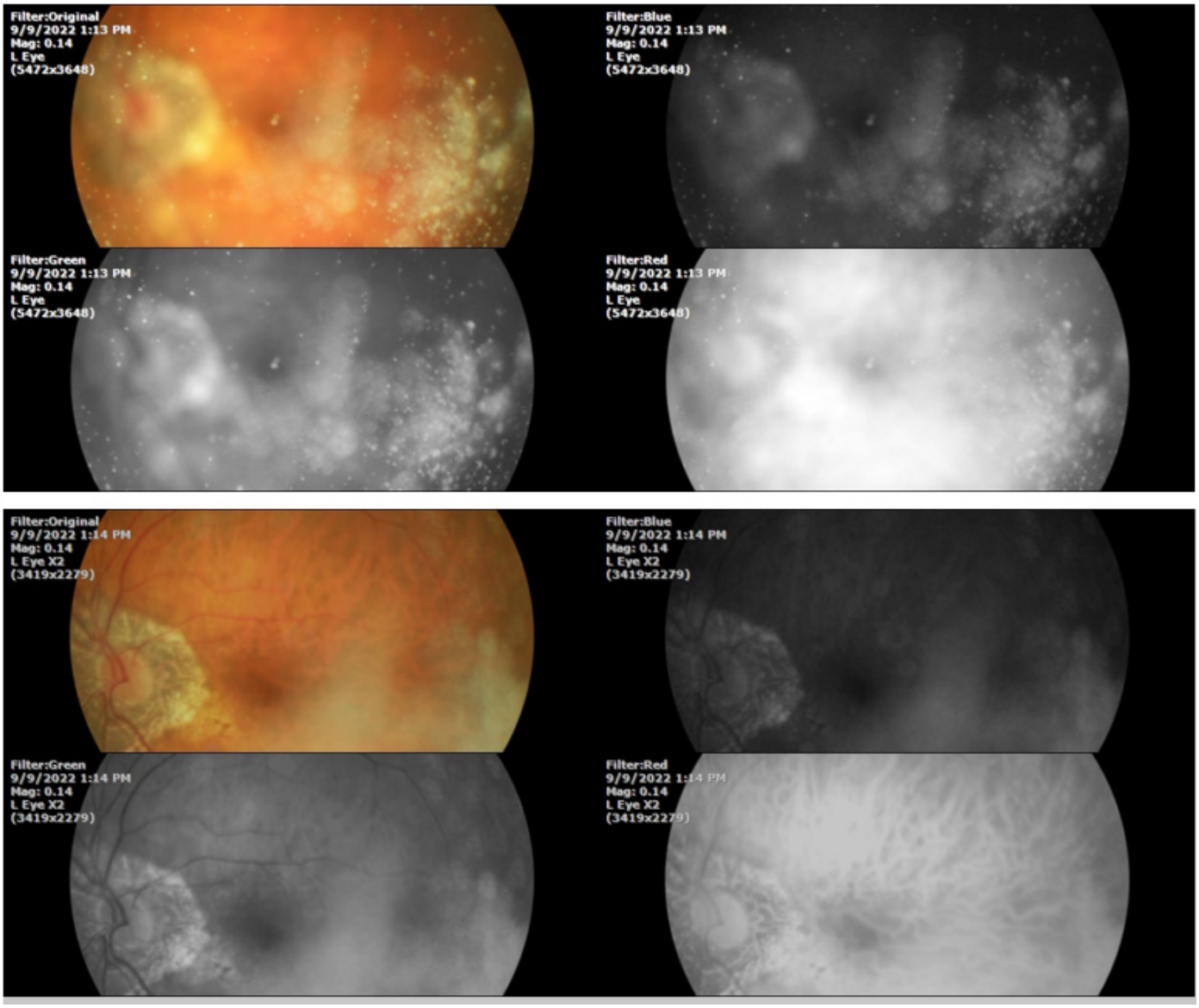


Figure 30: The image focused on the vitreous and then on the retina of the left eye, corresponding to the optic nerve and macular area, allows us to appreciate a clear decrease in changes, and the best thing is that the macular area is completely free.

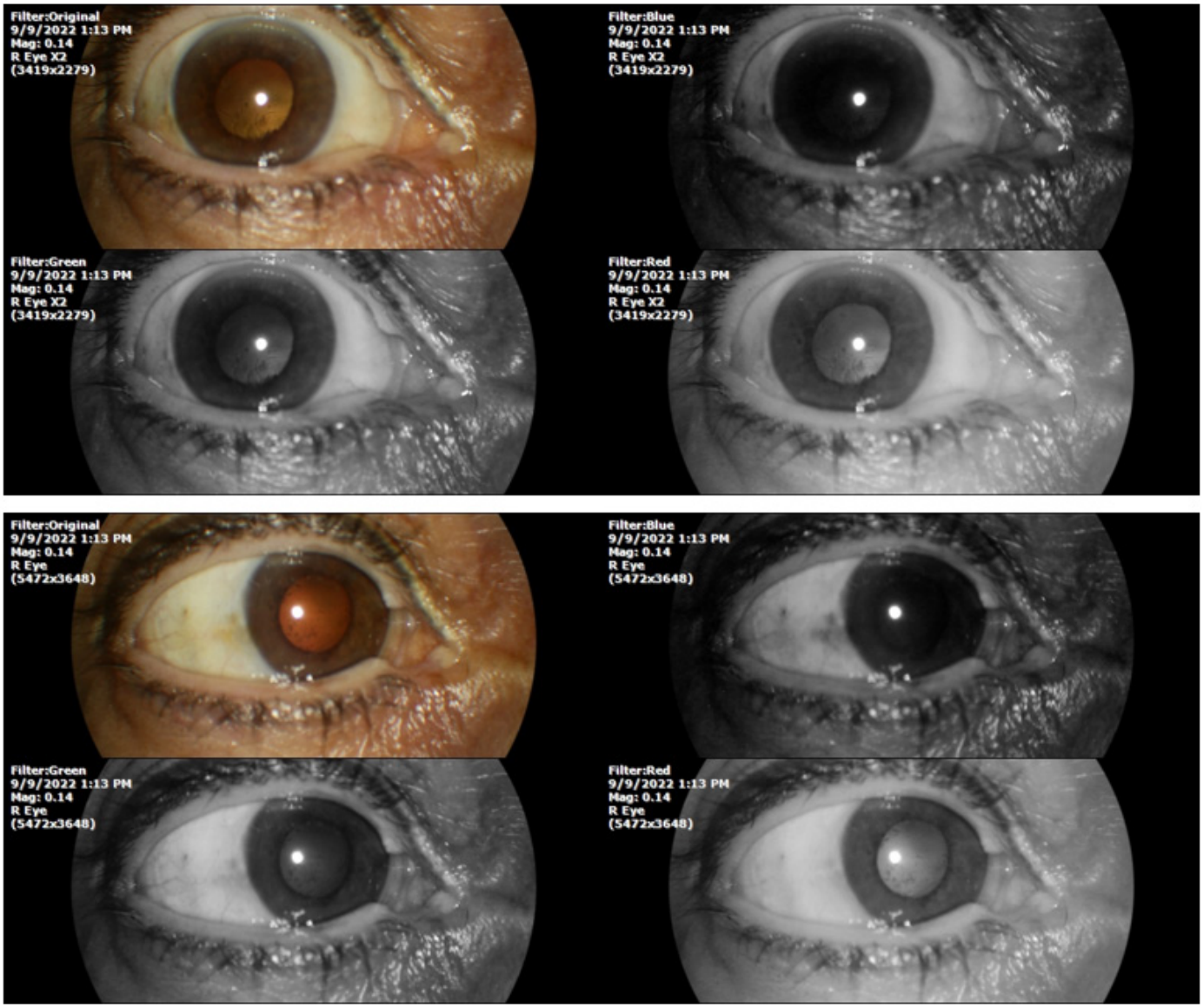
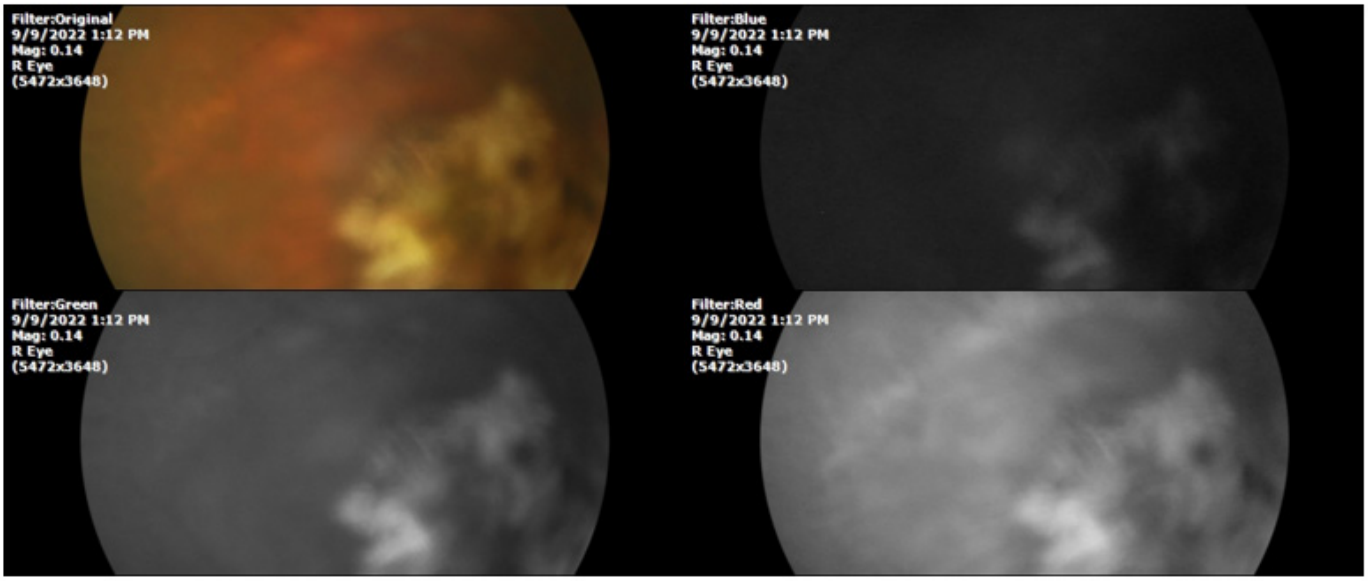


Figure 31: The specular reflection of the right eye does not show data compatible with pathology.



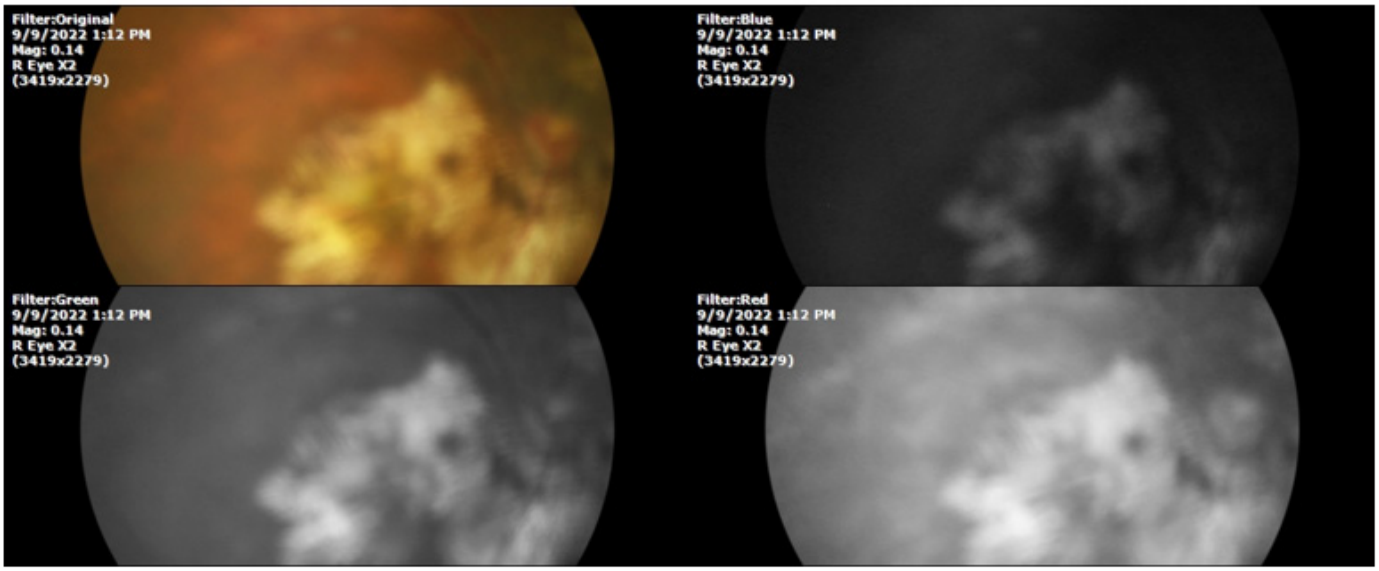
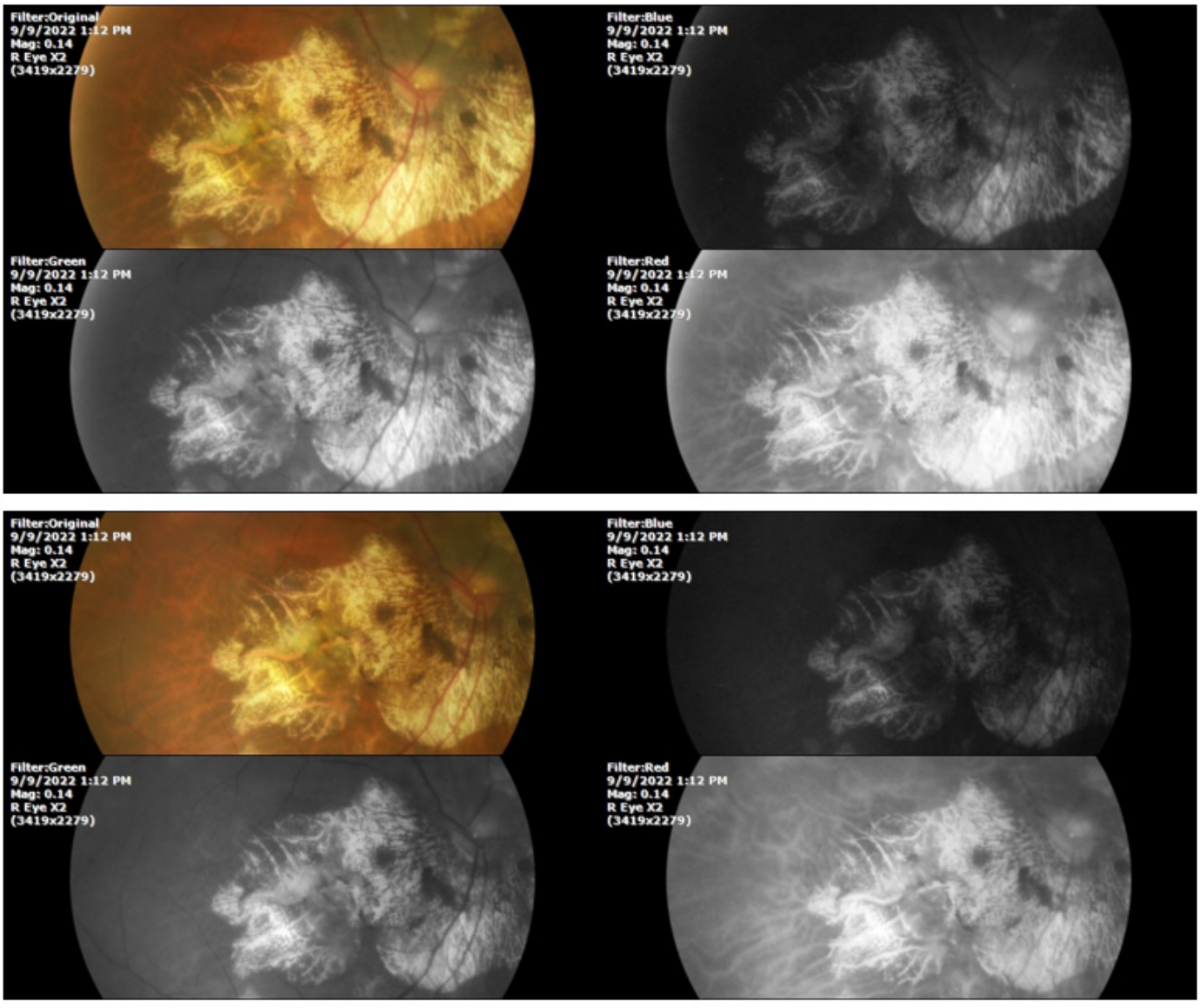


Figure 32: The photograph of the vitreous space of the right eye appears to be out of focus, but this is due to the different approaches of the vitreous and retina. It does not show pathological data.



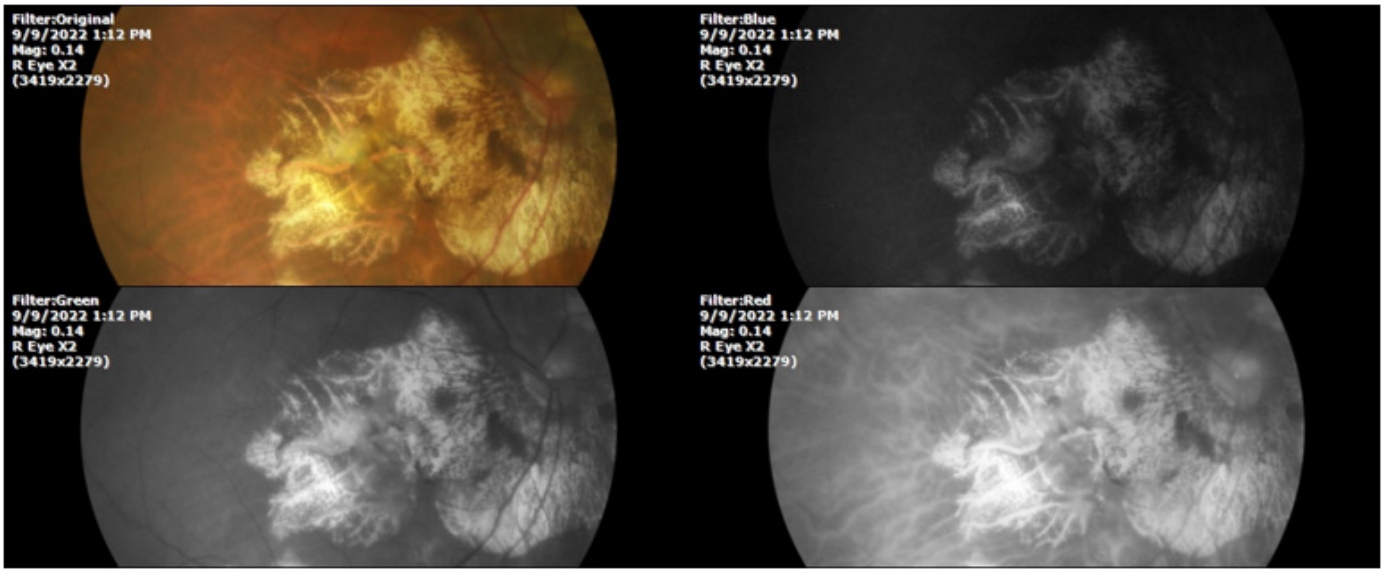


Figure 33: The photograph of the right eye, of the area of chorioretinal degeneration, with different magnifications, allows us to appreciate some details about the fact that there has been no deterioration, but on the other hand, it seems to have been reduced.

Comment

Many cells carry receptors for hyaluronan. Hyaluronan is an ancient molecule, evolutionarily speaking, Hyaluronan molecules are straight chains containing hundreds or thousands of sugar units, which are of only two kinds: N-acetylglucosamine and glucuronate, in alternation as disaccharides. Only one kind of hyaluronan exists. It is the archetypal glycosaminoglycan. Similar anionic glycosaminoglycans include chondroitin, keratan and heparan sulfates which, by contrast, can exist in astronomical numbers of possible isomers, because their sulfate groups can be distributed along the polymer in many ways. Since each glucuronate unit carries an anionic charge at physiological pH, associated with its carboxylate group, there are often hundreds of negative charges fixed to each chain. These charges are balanced by mobile cations such as Na+, K+, Ca++ and Mg++. An hyaluronan molecule is a little chunk of soluble cation exchanger. The charges are important in determining solubility in water, since hyaluronan, converted into an uncharged polymer by fully esterifying with methyl, is insoluble [22].

The improvement in the clinical picture of the vitreous in this patient was to be expected, since the enzymes that synthesize hyaluronan do not use ATP as an energy source, so they use hydrogen which comes from the dissociation and reforming of intracellular water that occurs in each one of the cells of our body. On the other hand, both pH and the balance of ions and cations also involve energy expenditure, which comes from the intense dissociation of water that occurs especially in the human eye, given its high melanin content, which on average is 40% more than in the skin.

So, when the turnover rate of water dissociation inside the cells is not in balance with the metabolic requirements of the cells, due to contamination of water, air, and food; Both the hydrogen and oxygen available, which have been the cornerstone of cellular functioning since the beginning of time, the organism, or the tissues show changes compatible with pathology, as is the case of the patient, who had been out of balance for decades, and therefore developed pathological myopia, and as the imbalance of oxygen and hydrogen continues, then it presented vitreous mineralization and joint problems, since hyaluronan is present in multiple tissues and with various functions.

Sometimes its role is mechanical or structural; grossly obvious, as in the synovial fluid, the vitreous humor, or Wharton's Jelly in the umbilical cord. On the other hand, it interacts at vanishingly small concentrations with some cells, showing very high specificity and triggering off important responses. Keep in mind that many cells carry receptors for hyaluronan, because Hyaluronan is an ancient molecule.

The key lies in the shapes that hyaluronan can take up, because, the more random a system, the less information there is in that system. The achievements of living material were gained by reducing entropy, increasing information and making use of permanent and reproducible shapes.

Hyaluronan chains contain two kinds of links. One kind, the sugar rings, are relatively fixed in their shapes. Between these rigid units are the glycosidic links, which consist of single oxygen atoms joining one sugar to the next. These oxygen atoms contribute two bonds that are directed like the arms of the letter V. Refined computer simulations suggested that water played an important part in stabilizing the structure.

The tapelike structure shows gentle curves both in plan and elevation projections, and these are important in determining how hyaluronan molecules can form duplexes with each other. Interestingly, chondroitin, keratan and dermatan sulfates also prefer to take up a similar two-fold helix in water.

Hyaluronan has the properties of a highly hydrophilic (polyhydroxylic) material simultaneously with hydrophobic patches characteristic of lipids, i.e. it is amphiphilic. Hydrophobic molecules clump together in water, thus reducing their interface with the solvent. This mechanism drives the formation of membranes

and contributes to the stability of e.g. the double helix in DNA. It is called hydrophobic bonding, although no chemical bond is formed.

The hydrophobic patch accounts for very interesting properties of hyaluronan. Phospholipids (important components of membranes) can form complexes with hyaluronan. Thereby, the lipidic inflammatory mediator, platelet activating factor, could bind similarly and that by sequestering this and other noxious substances hyaluronan might exert a beneficial action in inflamed joints. As is the case of this same patient who experienced joint problems, especially in the lower limbs and whose photographs taken during the Second Consultation (13/07/2020) we show below: (Figures 34-39)

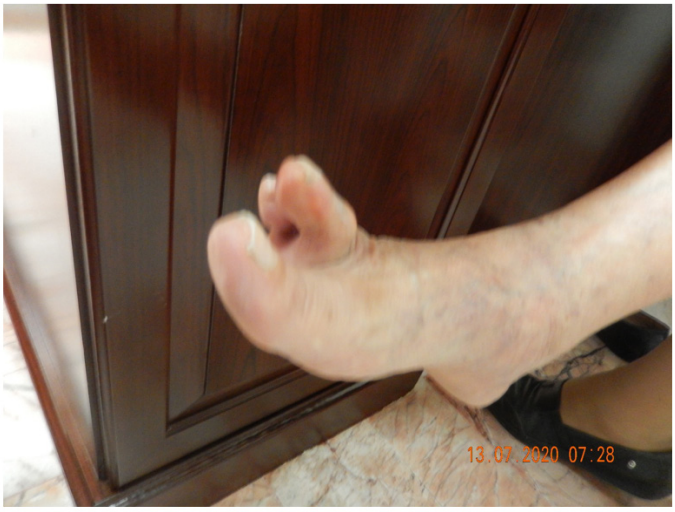


Figure 34: Deformation of the foot on the right side, the photograph was taken during the second consultation, when the patient began to report changes in body discomfort.

Figure 35: Another aspect of deformation.

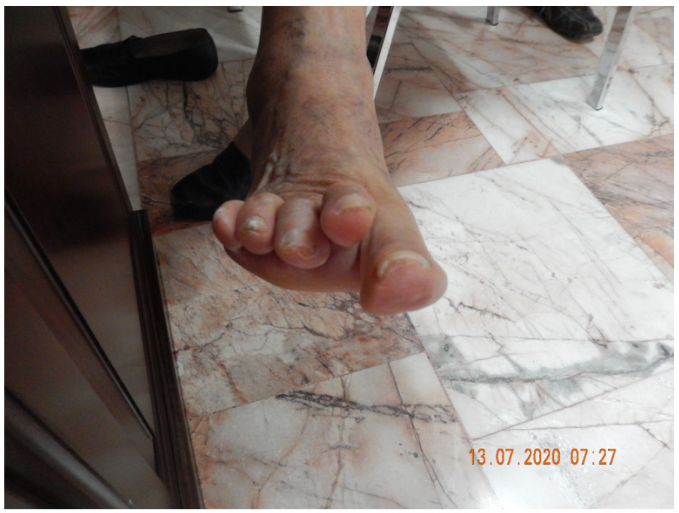


Figure 36: Another view of the right foot deformation.

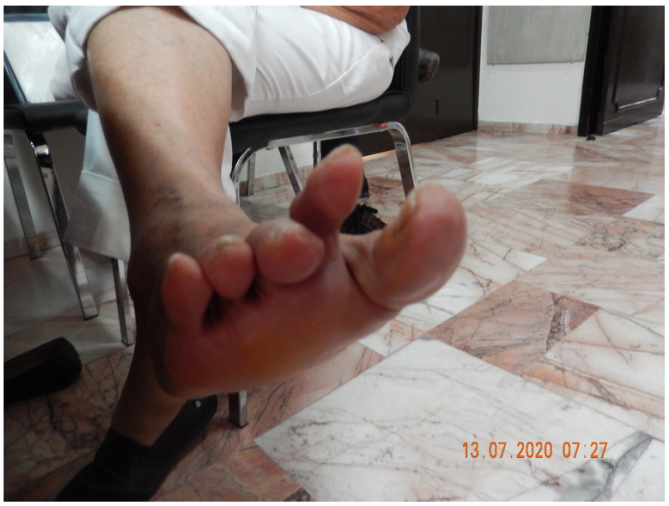


Figure 37: The discomfort of the deformation in the anatomy of the right foot also improved, which was to be expected, since the dissociation and reformation of water constitutes the very first reaction of life and therefore of any process that shapes it.

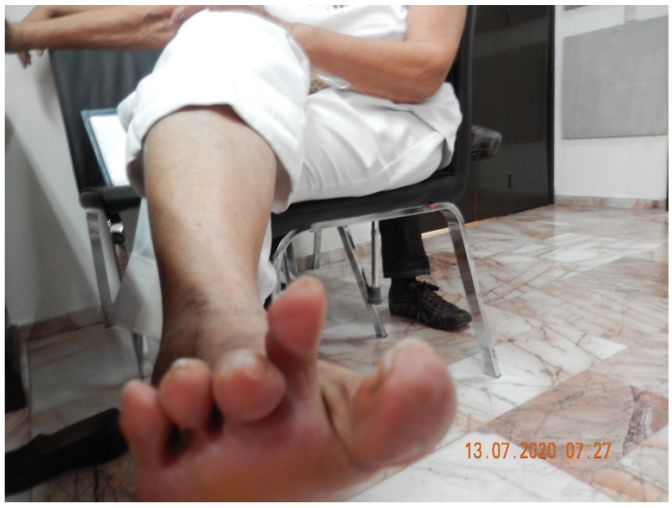


Figure 38: Another aspect of the deformation of the anatomy of the right foot.

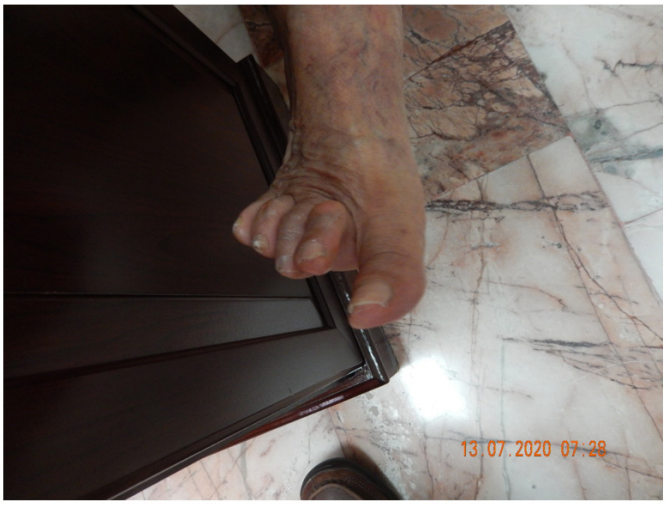


Figure 39: The patient reported that the discomfort in her feet had also decreased with the QIAPI 1 ™ sublingual treatment every hour.

The following photographs were taken six months later, during the third consultation. (Figures 40-46)

July 28, 2021

The patient mentioned something about Swollen and red legs.

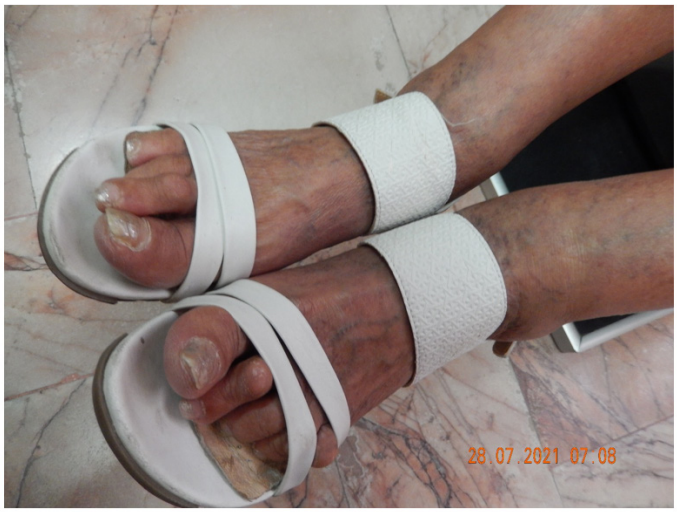


Figure 40: Despite the somewhat discreet discomfort, the photograph shows positive changes.

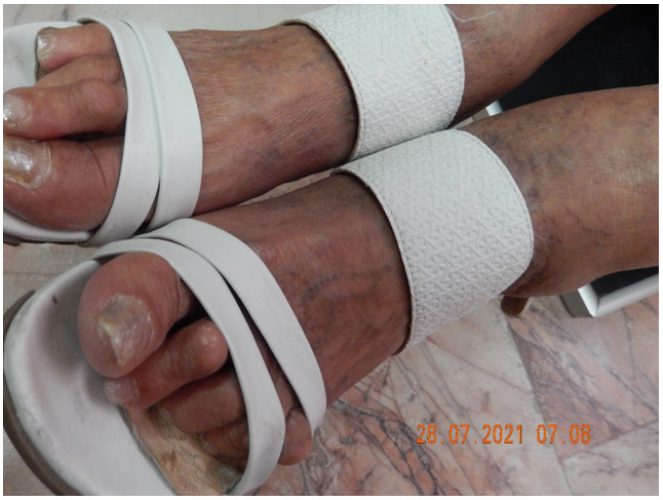


Figure 41: The appearance of the toes is almost normal.

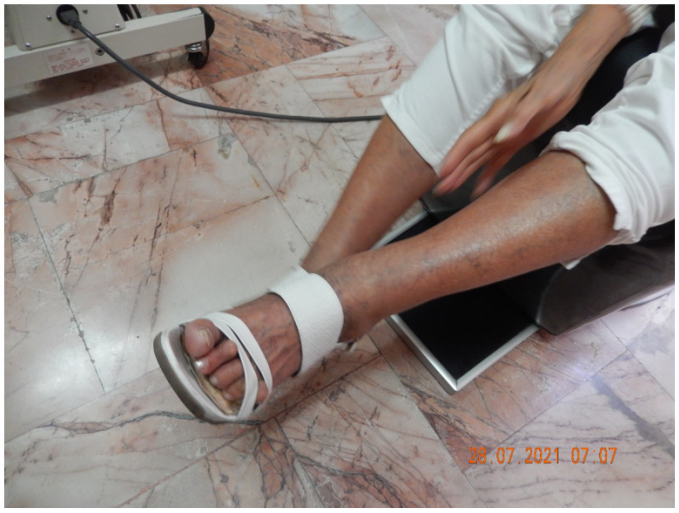


Figure 42: Some edema of the left lower limb is observed.

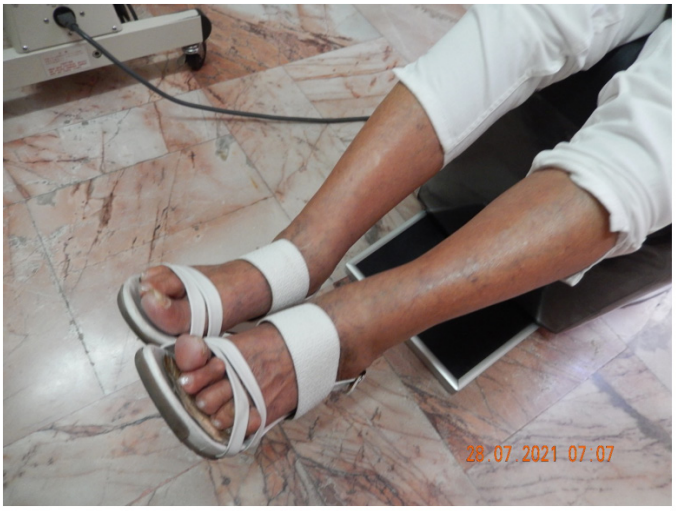


Figure 43: The comparative photograph shows some edema on the left side, which incidentally disappeared when the drug was applied topically.

Figure 44: Although there is some edema and hyperemia, the discomfort is minimal.

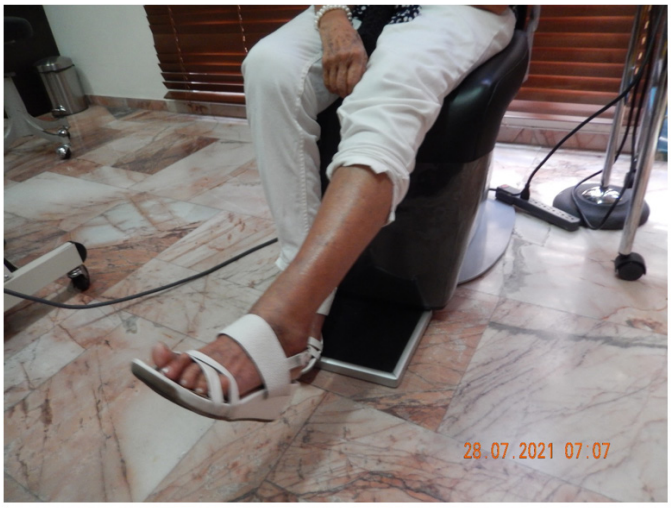


Figure 45: The moderate edema is in the distal part of the lower limb, in this case left.

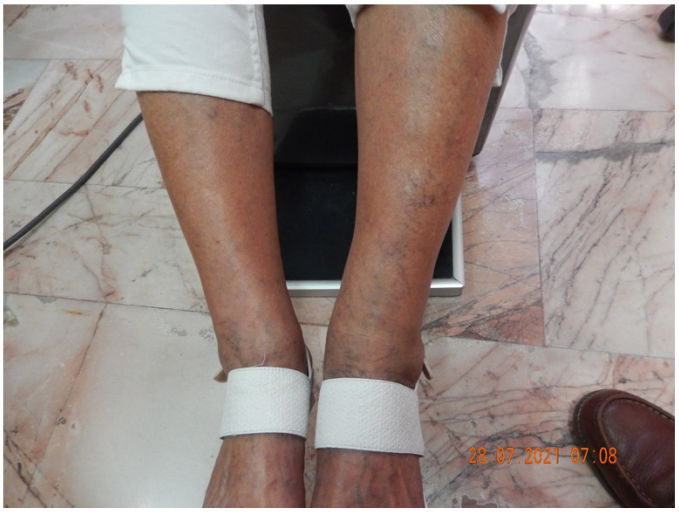


Figure 46: The edema is not pronounced and improved with local application of the medication, in addition to sublingual application every hour.

Relationships of hyaluronan with lipid membranes start very early, since hyaluronan is biosynthesized in the outer cell membranes, which underlines the importance of these compounds in biology. Also, hyaluronan increases in lymph flow during absorption of fats from the small intestine.

Conclusion

Perhaps many of the biological roles of hyaluronan always depended on its ability to work with membranes, carrying something in or out of a cell. Hyaluronan also aggregates with itself, partly helped by bonding between the hydrophobic patches. The flat and tape-like secondary structure has fascinating properties; both sides are identical, but one side of the tape runs in the opposite sense to the obverse side, i.e. they are antiparallel, like DNA and RNA. Because of this, what is possible on one side of the tape is also possible on the other. Aggregates can grow from both sides. The word “ambidexteran” is used to describe such polymers, from ambidextrous; "able to use both hands equally well".

And in the vitreous, as in any tissue of the body, the balance between attractive and repulsive charges largely determines the formation, conservation, and aging of the tissue, organ or even system. So, the unsuspected capacity of human cells and eukaryotes and prokaryotes in general plays a fundamental role, because as long as the process of dissociation and reforming of water works well, the body works optimally because it is very well done.

But when this process, which is the foundation of life, is unbalanced by environmental factors (pollution), then the body begins to manifest multiple failures, but the origin of them can be traced back to the levels of oxygen and hydrogen from the dissociation and reforming of water that occurs incessantly, day and night, in each of our cells throughout life.

Acknowledgement

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Conflict of Interest

The finding of the unsuspected capacity of human cells to oxygenate themselves and the development of QIAPI 1®, was done at our facilities.

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