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TESI DI LAUREA

Diabete Mellito e Lenti a Contatto

Diabetes Mellitus and Contact Lenses

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Abstract

This work on Diabetes Mellitus and Contact Lenses had two main purposes: the first was to review a moderate part of the literature about this field of interest, preceded by a short review on cornea and its alterations as Diabetes Mellitus occurs. The second target was to conduct a small survey among Italian diabetics and healthy subjects who wore contact lenses. The aim of the survey was to find if the results would have agreed with the previous review.

The analysis based on the survey, conducted by giving the same questionnaires to healthy and diabetic subjects, was not prospective as all the interviewed were already wearing contact lenses or had worn them before. In particular, the survey was based on some parts of Efron's survey, made among diabetic patients and practitioners in the UK in 1997. In addition to this, the results of the survey were compared with other considerations, which emerged during the review. The aim of the questionnaire was to find out if RGP contacts were used in higher percentage among diabetics rather than in healthy subjects, and to see if diabetics had higher rate of drop out or interruptions in contact lenses' use due to discomfort or dry eye. The method used for the retrospective survey consisted in proposing 39 anonymous questionnaires, of which 20 were proposed to healthy contact lenses' users and 19 to diabetics; of them only 9 wore contacts. Finding diabetic contact lenses' users was pointed out as the main struggle for the success of the survey. The questionnaires were analysed with the percentage on the amounts of answers. The results showed that 45% of diabetics used RGP CLs against the 10% of the healthy subjects, meaning that RGP were preferred for diabetic corneas, even if the reasons of this choice were not asked. For what concerns interruption of contacts lenses, none of the healthy subjects interrupted CLs because of dry eye, the 10% of them interrupted because of discomfort, while among people affected by Diabetes Mellitus 11% dropped because of dry eye and another 11% dropped because of discomfort. These results are in agreement with literature, even if there are some limitations that can compromise the accuracy of the data: firstly, the samples consisted in a small amount of people, increasing the errors' rate due to comprehension of the questions and accuracy in the answers. Another limitation was the subjective nature of the data, as no objective measurements were collected during the survey. Moreover, the samples came from two Italian regions (Veneto and Friuli Venezia Giulia), which means that the survey is not representative of the Italian population. In conclusion, further analysis would be necessary to confirm the results of this survey.

The main considerations achieved by reviewing literature were that Diabetes Mellitus not only afflicts the retina (causing Diabetic Retinopathy) but also the corneal tissue. Indeed, it causes abnormalities in all corneal layers giving fragili-

ty, slower times of recovery from both epithelial and endothelial oedema, disfunctions in Na+/K+-ATPase's pump and faster aging. Furthermore, the storage of glucose and sorbitol during hyperglycaemia and chronic hyperglycaemia can lead to alterations on the tissue's transparency causing blurred vision and to refractive changes, which can sway from hyperopia to myopia very easily. Finally, diabetic eyelids are more prone to infections. If these infections become chronic then contact lenses are not to recommend to the person affected by Diabetes Mellitus.

The alterations listed above summarize why Diabetes Mellitus is a relevant but relative contra-indication to contact lenses' use: the practitioner should take in consideration the clinical picture of the diabetic cornea and decide if whether or not prescribe contact lenses, especially if the subject hardly follows the prescriptions given by the specialist.

Chapter I

What is Diabetes Mellitus?

As we introduce such a broad topic like Diabetes Mellitus, it must be clear that we are referring to a metabolic affection that can cause several damages to the entire human organism. The main effect of Diabetes is hyperglycaemia, a specific condition characterized by abnormal levels of glucose in the bloodstream, which develops in response to a deficit in secretion and action of insulin. The lack of insulin in bloodstream is directly related to the autoimmune destruction of pancreatic β-cells, while there might be a triggered resistance (in terms of tissue) to the action of insulin itself. (The American Diabetes Association, 2014)

We must clarify that a disease process might be present even if it has not still reached full-blown hyperglycaemia, anyway this condition can be responsible for unbalanced metabolism though we cannot call it properly Diabetes. Unfortunately, the normal metabolism of fat, proteins and carbohydrates becomes more difficult as the action of insulin decreases, resulting in different pathogenetic processes. (The American Diabetes Association, 2014)

Hyperglycaemia has mostly long-term consequences: the organs and tissue reaching the higher sufference from this condition are eyes, kidneys, heart and circulatory system, nerves. Some of the signs and symptoms that let us recognize marked hyperglycaemia are polyuria, thirst, polydipsia, weight loss and blurred vision, but there is also an acute sign of uncontrolled Diabetes, and it is a life-threatening one: hyperglycaemia with ketoacidosis (the American Diabetes Association, 2014).

Once a person is diagnosed with Diabetes Mellitus, we find two broad etiopathogenetic categories in which he or she could be included:

1. Insulin-Dependent Diabetes Mellitus (I.D.D.M.) or “Type 1 Diabetes”
2. Non-Insulin-Dependent Diabetes Mellitus (N.I.D.D.M.) or “Type 2 Diabetes”

These two variations of the same pathology will be discussed in the next two paragraphs. However, we could just introduce that the first results in a complete destruction of all pancreatic β-cell (islets), which means there is need of insulin for survival, while the second presents a lack in secretion and action of insulin even without clinical symptoms, it also rarely it needs insulin intake for the regular functions.

1.1 Type 1 Diabetes Mellitus

Type 1 Diabetes is the rarest form of Diabetes Mellitus as it occurs only on a 5 to 10 % of the pathological subjects. We can even call I.D.D.M "Immune-mediated" Diabetes, this is because the immunologic system stops to recognize Langerhans islets (pancreatic β-cells responsible of insulin secretion) as self-cells, thus it starts to destruct them: this event leads to absolute insulin deficiency (the American Diabetes Association, 2014). There might be one or more autoantibodies acting in this auto-immune process of β-cells' destruction: the better known, present on a rate of 85-90% when hyperglycaemia is first detected are islet cells autoantibodies, autoantibodies to insulin, autoantibodies to GAD65, autoantibodies for the tyrosine phosphatases IA-2 and IA-2β (the American Diabetes Association, 2014). How can we determine if there are no longer islets thus there is no production of insulin? The answer is to search for plasma C-peptide at a blood test: it will be undetectable (the American Diabetes Association, 2014).

Another way we can call Type 1 Diabetes is "Juvenile on-set Diabetes", this is due to the prevalence of children and teens diagnosed with I.D.D.M.; furthermore, they seem to lose Langerhans islets faster than adults: for young patients it is often present ketoacidosis combined with hyperglycaemia leading to the first diagnosis. It must be said that even if I.D.D.M. is mostly present above children it does not only affect younger people (the American Diabetes Association, 2014).

One of the peculiarities of Juvenile on-set Diabetes is that there are both genetic predisposition and environmental factors: regarding the latter it is surprising that obesity is not the most impacting factor as it is, on the opposite, for N.I.D.D.M..

1.2 Type 2 Diabetes Mellitus

Non-Insulin-Dependent Diabetes Mellitus is the more common sort of Diabetes, in fact, it occurs on a 90 to 95% of those who are diagnosed with Diabetes Mellitus. The main features of this variant are the resistance to insulin related to tissue and the deficiency in insulin secretion, which does not involve exogenous insulin at first, but in the future it probably will (the American Diabetes Association, 2014).

If we decided to check a blood test of a person affected by Type 2 Diabetes, we would find normal C-peptide levels but still high levels of glucose: this indicates that N.I.D.D.M is not immune-mediated, indeed, there is no loss of pancreatic β-cells, although the aetiology of this affection is not completely known yet. Between the environmental factors that can cause Type 2 Diabetes (eg. Lack of physical activity, age) we find obesity, and if not obesity probably it will be found an excess of fat on the abdominal region (the American Diabetes Association, 2014).

In fact, most of the subjects affected by Type 2 Diabetes are obese and obesity itself is a trigger to tissue resistance to insulin. There is a strong genetic predisposition in contracting Type 2 Diabetes, even stronger than in Type 1 Diabetes, but its mechanisms are not well defined (the American Diabetes Association, 2014).

Doctors rarely carry out the diagnosis of "Adult on-set Diabetes" at its first stages: this is due to the slow development of hyperglycaemia. If Diabetes remains uncontrolled for a long period after its occurrence, as it happens in these cases, there will be higher risks to develop vascular or microvascular complications and other complications in genre. The subjects with the higher risk to contract Type 2 Diabetes Mellitus are women with previous Gestational Diabetes Mellitus (GDM) or people with hypertension/dyslipidemia (the American Diabetes Association, 2014).

1.3 Diabetes' care and control

On the 20TH of July 2017 Istat released some data about Diabetes in Italy: there are more than 3 million people affected by this pathology (5.3% of the population) and 16.5% of them are over 65 years (Istat, 2017). Diabetes has increased during the past twenty years, if we compare the numbers from 2000 to 2016 there is 1 more million

people who contracted Diabetes both Type 1 and 2, but besides this rise in the number it must be said that its death rate has decreased by 20% (Istat, 2017). The following tab (Tab. I) reports the crucial points of their analysis:

Tab. I: Istat data about Diabetes Mellitus referred to 2016 in Italy. This Tab shows how obesity, physical activity and socio-economic disadvantage are crucial in Diabetes' rate.

Diabetic women between 65-74 years			
With college degree	• 6.8 % • Less death rate	Without college degree / diploma	• 13.8 % • +2.3 of death rate
Northern regions	• 4%	Southern regions	• 5.8 %
Diabetic men between 65-74 years			
With college degree	• 13.2 %	Without college degree / diploma	• 16.4%
Northern regions	• 4 %	Southern regions	• 5.8%
Diabetic women between 45-64 years			
• 32.8 % are obese		• 64.2 % don't practice light physical exercise	
Diabetic men between 45-64 years			
• 28.9 % are obese		• 47.5 % don't practice light physical exercise	

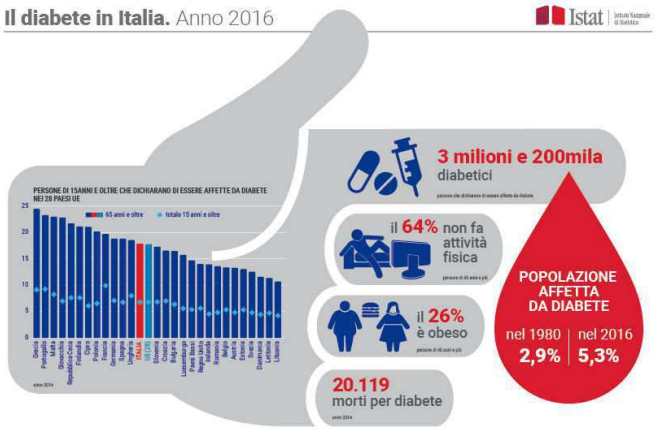


Image 1: this image sums up what said before about Diabetes in Italy, highlighting once again the importance of exercise and regular dieting to monitor Diabetes. Istat, 2017

The best way to prevent Type 2 Diabetes Mellitus consists in fighting obesity and general overweight by promoting healthy lifestyles (balanced nutrition ad regular physical activity). On the opposite, it is known that Type 1 Diabetes is triggered by an immune-mediated response: indeed, it is impossible to prevent. The best way to reduce T1 Diabetes' complications is to give a rapid diagnosis and start as soon as possible the exogenous insulin therapy combined with a restrictive diet (Ministero della Salute, 2017).

To control if people with Diabetes are following in a proper manner the guide line given by the specialist, it is possible to measure via blood test, at the Hospital, the value of HbA_{1C}, which shows the average trend of glycemia during the previous 2 to 3 months (Società Italiana Di Diabetologia, 2016). Another tool the diabetic patient can (but for I.D.D.M is a must) use to monitor glycemia is the self-measurement via glucometer. Usually, the data are taken before and after every single meal, but it depends on the medical directives and the type of Diabetes Mellitus. It could happen that HbA_{1C} values are different from self-measured glycemia (which the person must record) and that could be due to the inappropriate use of the glucometer: the specialist then should explain the right steps more clearly (Società Italiana Di Diabetologia, 2016).

To conclude, the more the glycemia is unbalanced at HbA_{1C}, the less the therapy has been successful; we could then say that this test is one of the best tools Diabetologists have in their hands.

Chapter II

Interaction between D.M. and corneal tissue

It has already been mentioned that Diabetes Mellitus can induce many different complications at several organs and tissue of the human body, especially if the patient hardly follows the control plan given by the specialist. The lack in Diabetes' control - both for Type 1 and 2 - in addition with the long-term progression of D.M. most of the times leads to blindness. Even though blindness is almost exclusively due to a retinal complication called Diabetic Retinopathy, which we will not discuss in these pages, it is a strong indication that eyes are one of the main targets in Diabetes Mellitus. For example, there might be shifts of refraction especially between patients with poor Diabetes control and undiagnosed/newly diagnosed diabetics. These refractive changes, which are both myopic and hyperopic, could be due to variations in blood glucose. In terms of contact lenses, it could be hard if not impossible to fit these patients with their best refractive power, as it changes rapidly and often in relatively high amounts (Efron et al., 1997). At this point, the question we want to answer becomes: is it right to assume that, if Diabetes afflicts the whole eye, will there be some corneal damages? To answer this question the first thing to do is to understand how healthy corneas work and then we can see the changings as Diabetes Mellitus occurs.

2.1 The healthy cornea

The anterior surface of the eye is a composition of different tissue, one of the most important is the cornea: with its standard base curves of approximately 7.70-7.80 mm both horizontal and vertical, it gives almost 43 dioptres to the ocular system. The cornea has a total depth of 500-520 μm and a relatively high stiffness in its fibres that allows protection for the anterior section, similar to the stiffness found in sclera. (Bucci, 1993; Leonardi,2016)

The amount of power given by the cornea to the human eye is nearly 70% of the total sight power, which means that cornea is crucial for our visual performance. One of the main reasons of this enormous power is the avascular structure and transparency (Azzolini, 2010). Transparency is due to the extreme organization of all corneal layers combined with the partial dehydration of the cells. Another thing that improves transparency is the corneal avascular structure: glucose, vitamins and amino-acids are kept to the cornea by aqueous humour, while oxygen is taken from the outside thanks to the epithelium (Azzolini, 2010). The last feature of the corneal tissue is stiffness (Leonardi, 2016). This latter characteristic depends on:

A. The number of cross-links between fibrils and strips of collagen.

B. Glue-effect between keratocytes and matrix.

C. Spatial location of the fibres.

It is known that cornea has five layers with different characteristics: these layers will be discussed in the following list, keeping as example a standard healthy cornea.

1. Epithelium

   Epithelium has the main role of barrier between the inside and the outside of the cornea; it has different cellular layers: 6 to 7 layers of paving cells devoid of keratin followed by a single neat row layer of cylindrical basal cells (apical nucleated), these are connected by tight-junctions and lay on the basal membrane. After the basal layer there are 2 to 3 layers of polygonal cells, followed by flat superficial cells, which are hardly connected by desmosomes. (Leonardi, 2016)

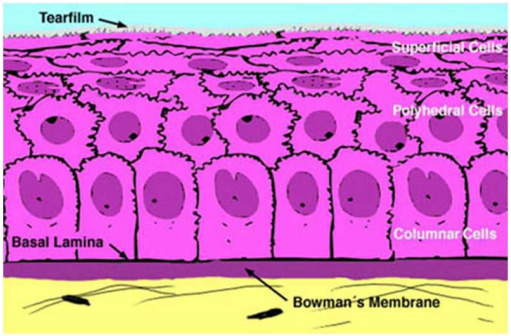


Image 2: representation of 1ST and 2ND corneal layers. Leonardi, 2016

2. Bowman's Membrane

   This membrane has a total depth of 12 μm, its main components are fibronectin, laminin and collagen IV, furthermore there is some empty space reserved to nerves. Its main feature is to separate epithelium and stroma. (Azzolini, 2010; Leonardi, 2016)

3. Stroma

   Stroma is the most consistent layer of the cornea (about 90%); its depth is around 500 μm and it is almost entirely made of collagen (Azzolini, 2010). The collagen present in this layer is mostly Collagen I, but there are small quantities of Collagen III, V and VI. (Leonardi, 2016)

   Stroma has three main components:

   - Lamellar layer: extracellular matrix mostly made of collagen's fibrils, placed to build up lamellar fibres. In this layer we find a total of almost 500 collagen lamellae in 2μm of thickness, these lamellae lay parallel by the surface but crossed at 90° one with the other. (Leonardi, 2016)
   - Keratocytes: fibroblastic cells with reproductive and mitotic power, this kind of cells are also responsible for collagen's production. The usual shape of keratocytes is a *stellar shape,* their side's extensions are used to connect each other. (Leonardi, 2016)

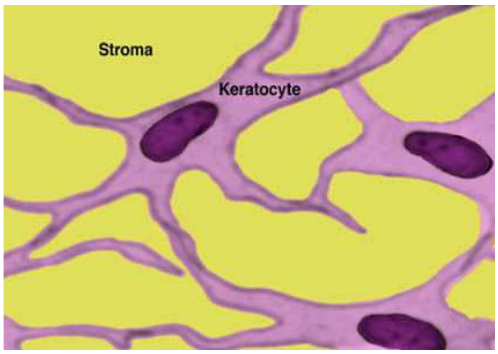


Image 3: Connections between keratocytes. Leonardi, 2016

   - Superficial cells: flat cells hardly connected by desmosomes. (Leonardi, 2016)

4. Descemet's Membrane

   Descemet's Membrane is the second membrane present in the corneal tissue. It is made of radial collagen's fibrils and has the same thickness of Bowman's Membrane, 12 μm. The aim of these fibrils is to separate stroma and endothelium. (Azzolini, 2010)

5. Endothelium

   The innermost section of the cornea is endothelium, a single layer of polygonal flat cells with an important role in corneal transparency and tissue trophism. Regarding the latter, the normal intake of nutrients is possible thanks to the leaky barrier: this consists of gaps between the cells (Leonardi, 2016). Within endothelium we find *Zonula Occludens*, a complex net of actin's strands used to increase adhesion between the polygonal cells. Another feature of endothelium is that, as the tissue gets older, cells reduce their density but their diameter increases. (Leonardi, 2016)

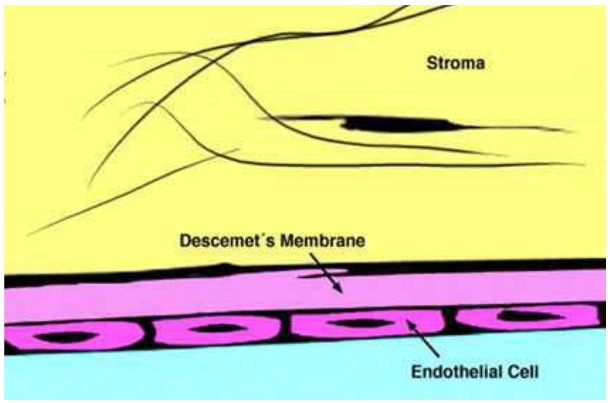


Image 4: Representation of 4TH and 5TH corneal layers. Leonardi, 2016

2.1.1 Corneal innervation

Cornea has a complex net of sensitive nerves whose role is to inform the organism of foreign bodies or wounds: this is made possible by inducing pain sensations. Concerning the sensitive innervation, it has been seen that cell's membranes of epithelium are directly connected with nerve's terminals: this connection means that

cornea has high sensitivity. Indeed, it is possible to induce pain sensations by stimulating (touching) one single epithelial cell. (Leonardi, 2016)

Tab. II shows the three main branches of corneal innervation:

Tab. II shows the main branches of corneal innervation with their principal features. Leonardi, 2016

Innervation	**Characteristics**	**Other**
Sensitive	Long ciliary nerves from the fifth cranial nerve, which form the limbal plexus. 1 mm before these nerves cross the limbus to enter the cornea, they lose all their myelin sheaths.	The nerves run parallel by the surface with radial paths. The cornea has lot of tactile-sensitive nerves which means intense feeling of pain when injured.
Sympathetic	The function of this innervation is not well defined yet, but we know there is a few fibres of cervical ganglion.	
Parasympathetic	Unknown.	

.

2.2 The diabetic Cornea

When Diabetes Mellitus occurs, there are noticeable changings in all cornea's layers. Each of them will be discussed in the following schedule.

1. Epithelium

Within the diabetic corneal epithelium there is less density of cells, but also the number of cellular layers decreases; furthermore, there could be variations in O.C.V. (Osmotic Coefficient of Variation), formation of superficial debris, intracellular integration of mucous materials, formation of granular areas around the nuclear zone (Saini J.S. et al., 1996). A specific disease called diabetic epithelial Keratopathy is present among diabetic patients and it causes slower wound repair, increased permeability, striate keratitis, blebs, microcystic oedema and storage of glucose (Efron et al., 1997).

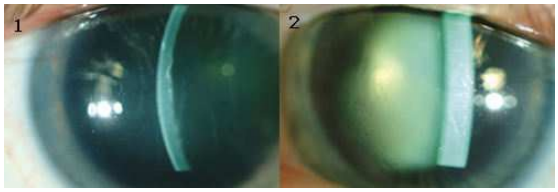


Image 5: bilateral stromal and microcystic oedema, with the left eye (2) worse than the right (1). Galor et al., 2007

Erosions on epithelial surface are not a rare consequence of Diabetes Mellitus effects on the anterior section, these scratches are mostly due to poor adhesion of epithelium and anterior stroma (Efron et al., 1997). Concerning the role of epithelium as a barrier, it has been found that corneal permeability is as much altered as the HbA_{1C} increases; this complication may be linked to Diabetes' control. (Gekka M.et al., 2004)

2. Epithelial Basal Membrane

The E.B.M. of the diabetic subject seems to be fragile and has faster aging than the normal Basal Membrane. It is therefore possible to find storage of bioproducts like glycogen that in some cases can cause the breakup of Basal Membrane. (Sanchez J.C. et al, 1998)

3. Stroma

The stroma is affected by an excess of glycosylation, found in plasmatic proteins, nervous proteins, collagen and erythrocytes' membrane. When hyperglycaemia occurs, an increase in cross-linking between collagen's fibres and fibrils may be present. The high number of cross-linked fibres leads to a loss of transparency, which brings to blurred vision. (Kyung-Chul Yoon et al., 2004)

4. Endothelium

Within the endothelium of subjects affected by Type 2 Diabetes, there is a smaller percentage of hexagonal cells with higher Area's C.V. than in healthy subjects. Similar results have been found among Type 1 Diabetic patients: the only difference is that this complication occurs in a shorter period of time (Schultz R., 1984). It is known that Diabetes reduces the action of ATPase-pump within corneal endothelium, which leads to changes in endothelial permeability; the first effect is the production of damages as Intraocular Pressure (IOP) compensation occurs (Lee et al., 2006). Moreover, it seems

to be present a faster compensation to the action of Na^+/K^+- ATPase among diabetics with the less duration of I.D.D.M. (Zaidi et al., 2002).

The diabetic endothelium seems to have a structural disorder rather than a functional disorder; in fact, the fluorescens permeability is similar between both healthy subjects and diabetics (Keoleian et al., 1992).

For those affected by Diabetes Mellitus the amount of time for injuries' recovery is greater than for normal subjects, this means that the structural disorder induced by D.M. may lead to a functional disorder, exacerbated by stressing or not giving enough oxygen to the tissue. This information should be considered when contact lenses are given to the diabetic person (Zaidi et al., 2002). The diabetic endothelium, to conclude, is a vulnerable layer, often prone to pleomorphism and polymegathism. (Schultz R., 1984)

2.2.1 Other changings taking place in diabetic corneas

The first thing detected is the lower corneal sensitivity among diabetic subjects than healthy. This condition leads to some relative contra-indication for contact lenses use, as we will see in the next chapter. The casuistry of this loss of sensitivity is not clear but for some researchers it could be due to the alteration in glucose's metabolism, related once again with Diabetes' control. Surprisingly, this feature is not connected with the duration of Diabetes Mellitus (Kyung-Chul Yoon et. al., 2004).

Corneal thickness is another struggle for those affected with Diabetes Mellitus: it indeed increases if DR both proliferative and non-proliferative is present (Efron et al., 2012). This complication above is almost certainly due to enhanced corneal hydration plus alteration in endothelial functions as the underlying cause, which might be a consequence of glucose sorbitol storage (Efron et al, 2012). If diabetic subjects falling within this clinical presentation wish to wear contact lenses for extended periods, their endothelium may have less capacity to cope with endothelial stress (Efron et al., 2012). Corneal hydration is mostly affected during hyperglycaemia: this may be an indicator of enhanced glucose in both tear film and aqueous humour, causing abnormal corneal swelling, which also becomes slower (Efron et al., 2012).

Regarding some connections between damages and duration of Diabetes Mellitus there is one study that can be mentioned. By analysing quantitative parameters such as corneal thickness and corneal endothelium morphology with the ANCOVA method, it has been possible to affirm that the diabetic group (200 patients with I.D.D.M) had increased corneal thickness and, regarding endothelium, both less regularity and density of hexagonal cells than the healthy control group (100 patients). Furthermore, it has been highlighted how Diabetes' duration influenced the central corneal thickness ($p < .05$) while there was no correlation between duration of Type 1 Diabetes and endothelial morphology ($p > .0,5$). (Lee JS et al., 2006)

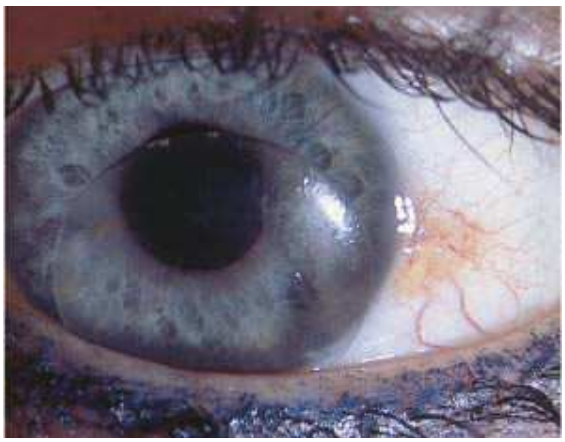


Image 6: Dry eye, hard contact lens, hydrophobic lens surface, mucin deficiency.
https://entokey.com/primary-fitting-and-wearing-problems/

Another possible complication for diabetic patients is the lower tear film parameters than in healthy people. The main consequence is the increased risk in contracting Dry Eye Syndrome, which is a relative contra-indication to contact lenses' use. In presence of both loss of sensitivity and less production of tear film we might then observe higher rates of epithelial injuries (Kyung-Chul Yoon et al., 2004). The main factor that brings to D.E.S. is the lack of goblet's cells seen in diabetic subjects, which means there is a deficit in mucous tear film layer (Kyung-Chul Yoon et al., 2004). The less production of tear film might occur in response to a lacrimal gland's neuropathy, although the entire process is still unclear. The drop in basal tear film production is the first change noticed and it is also used as an indicator of Diabetic Retinopathy' s progression, while the decrease in reflex tear production probably is the result of corneal loss of sensitivity. (Kyung-Chul Yoon et al., 2004).

The answer to our first question has come by literature: the diabetic cornea is more vulnerable than the healthy one so D.M. clearly affects the whole eye. This evidence brings to light the complexity in applying contact lenses on diabetic corneas.

Chapter III

Diabetes Mellitus and contact lenses

The last chapter introduced how Diabetes Mellitus can compromise some functions of human corneal tissue: we made a question about these damages and literature answered that yes, Diabetes afflicts the whole eye including the cornea. It is known that contact lenses are medical devices directly applied on the anterior section of the eye (cornea or sclera), this means existence of interactions between corneal tissue and contact lenses. The next topic under discussion will be the role of Diabetes Mellitus when contact lenses are worn, to understand the processes taking place in those cases it is good to re-cap how soft contact lenses (SCL) and rigid gas-permeable contact lenses (RGP) work.

3.1 Soft contact lenses

Contact lenses are medical devices used for a wide range of purposes like physical activities, cosmetic reasons, visual needs and others. The aim of soft contact lenses, released after RGP contact lenses, is to increase comfort and correct low to high refractive errors such myopia, hyperopia and astigmatism with a smaller financial outlay. Today we know that the main difference between RGP and SCL is in terms of materials: SCL have most likely standard parameters but a wide choice of materials, while RGP contact lenses have great options for their parameters but a smaller range of materials.

Soft contact lenses divide in two main families:

1. Non-hydrophilic or “hydrophobic” SCL
2. Hydrophilic SCL

Hydrophobic SCL are made of oxygen and silicon, their best hallmark is to be extremely flexible, but there is a weak spot: silicon tends to attract bioproducts released by tear film, which means formation of debris between the epithelium and the backside of the lens; to achieve more hydrophilicity chunks of HEMA or PVP could be added (Gheller, 1993).

Hydrophilic SCL, on the opposite, are made of hydrogel: this material is made of combined polymers able to hold high percentages of H_2O molecules between their fibres (up to 80%) and to remain hydrated for a specific amount of time. These features make hydrophilic soft contact lenses comfortable, flexible and with a great ability in tear film turnover under their backsides (Gheller,1993). The weak point of these contact lenses is the evaporation rate: the time of hydration becomes shorter as the amount of water kept between the fibres becomes higher (Gheller, 1993).

Among hydrophilic SCL we find five main groups of hydrogel materials with different evaporation rates plus one other material: bio-mimetics. The next tab (Tab III) summarises these polymeric textures.

Tab. III: soft contact lenses materials. Gheller, 1993

Materials	**Features**
low hydrophilicity non-ionic materials I group	High levels of -OH functional groups prone to resist dehydration without bonding with protein debris (GMA, HEMA). The Oxygen Transmissibility (Dk) has low to medium rates.
High hydrophilicity non-ionic materials II group	More empty space to link with H_2O molecules and consequently higher Dk. After about 8 hours of usage the water content declines by 40% (HEMA, NVP).
Low hydrophilicity ionic materials III group	High levels of acid functional groups, which separates when dipped in water, releasing O_2. These materials have low to

	medium Dk (HEMA, MA).
High hydrophilicity ionic materials IV group	High polarity and high Dk exactly as high hydrophilicity non-ionic materials (NVP, MA).
Bio-mimetic materials	Group f materials physiologically matched with corneal tissue. These polymers come from researches among implants: one relevant molecule is Phosphorylcholine, a phospholipid like those present in vasal membranes. Phosphorylcholine has strong hydrophilicity and a limited predisposition to attract protein debris.
Silicone-hydrogel V group	Similar to high hydrophilicity non-ionic materials, these polymers have high gas-permeability and great comfort. The main struggle is to put in place these kinds of SCL as they are, in terms of stiffness, more closely related to RGP contact lenses.

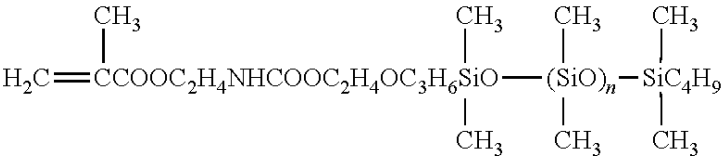


Image 7: example of Silicone-hydrogel. Back et al., 2011

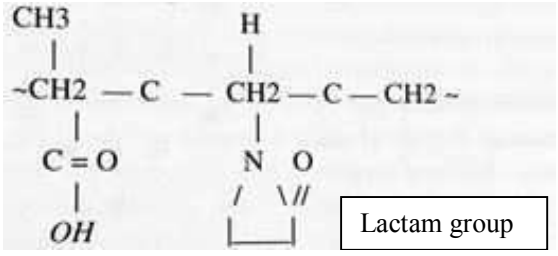


Image 8: example of IV group; Gheller, 1993

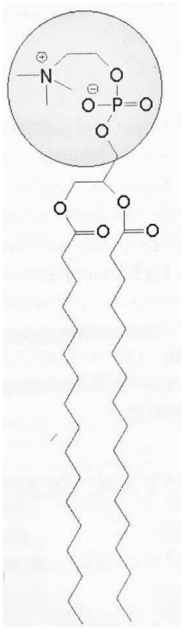


Image 9: Phosphorylcholine molecule. Gheller, 1993

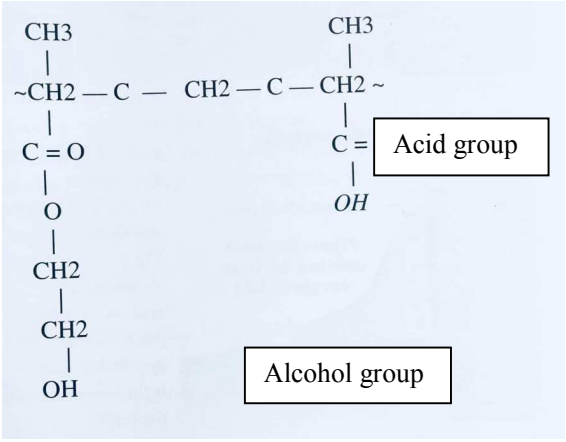


Image 10: example of III group; Gheller,1993.

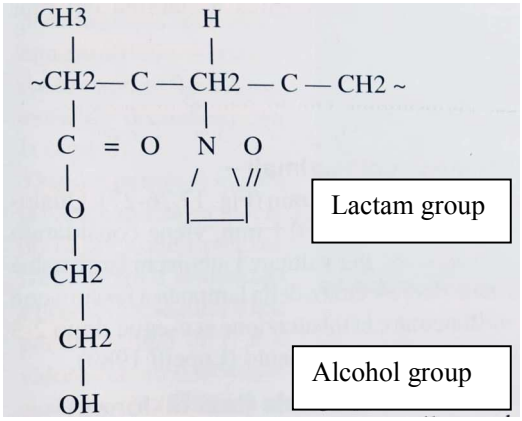


Image 11: example of II group. Gheller,1993

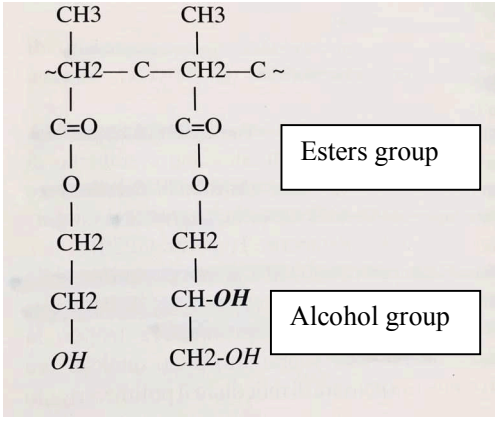


Image 12: example of I group. Gheller, 1993

3.2 RGP contact lenses

There are many reasons why people choose RGP contact lenses, between them we find:

- Visual quality for high astigmatism, Keratoconus and irregular corneas given by the solid refractive surfaces (Formenti, 2018).

- Improved healthcare thanks to the higher oxygen transmissibility that keeps oedema lower than 4%, and to the lower risk to develop corneal staining or keratitis (Formenti, 2018).

Whether we have seen the bright sides of RGP contact lenses, there is one condition that is mandatory when the optometrist decides to introduce RGP in his/her tasks: to know contact lenses' geometry, which means notions on eccentricity, base curve, peripheral curves and other parameters. To achieve knowledge of these data some tools are required: Topographer, biomicroscope and slit-lamp, radius-gauge, sodium fluorescein and cobalt blue filter or UV-lamp are just some of them (Formenti,2018).

Regarding eccentricity, it is good to consider both flat and steep corneal meridians, so it will be possible to select the best contact lens' design (Formenti, 2018).

There are two main designs for RGP contact lenses:

1. Symmetrical design: also called spherical design, it is used if there is not much difference between the two main meridians or when the steeper meridian is less than half of the flatter.
2. Asymmetrical design: when the eccentricity is high between the two main meridians. If the difference is consistent there could be used toric RGP.

The RGP contact lens lands on the cornea between the end of the optic zone (OZ) and the first peripheral curve, creating a thin space filled with tear film which is called "apical clearance" (Formenti, 2018). The depth of this space is measured with Tear Layer Thickness (TLT), observable with sodium fluorescein, a vital dye with very low toxicity if used in low amounts; fluorescein turns from orange to fluorescent yellow if enlightened with cobalt blue light. TLT is important for the prevention against epithelial wounds while maintaining the physiological integrity of the cornea, but it is also essential to rebalance push/pull forces (Formenti, 2018). The optimal range for TLT is between 15 and 20 μm while at the end of the OZ the thickness shall be almost void (Formenti, 2018). There are four main forces acting in RGP contact lenses application, these are explained in Tab. IV.

Tab IV: acting forces when RGP are put in place. Formenti, 2018

Force	**Features**
Eyelid tension	Has balance effects: if the eyelid is higher than the limbus there will be minimum effect, on contrary if the eyelid covers the cornea there will be interactions with RGP contact lenses, those interactions will be less relevant if the eyelid tone is weak.
Tear film compression force	Directly proportionate to TLT value, it has a role in terms of movement. In fact, as TLT gets higher the movement reduces, while if we lower the clearance the mobility will increase.
Edge force	This force acts on the edges uncovered by the eyelid and it is influenced by the lacrimal prism present at the edge of the lens. Although it has a role on the centred location, it is considered a secondary force.
Gravity	Very important when RGP are applied, it depends on the weight of the lens and its diameter.

The ideal movements of the RGP with the balance point located on the corneal pole are regular, with 1,5 mm of width and a speed between .5 and 1 seconds (Formenti, 2018). The fluorescein pattern is smooth under the optic zone, while at its end it is possible to observe apparent touch and proceeding towards the peripheral zone it should be found a green ring with at least 80 microns of depth (TLT) (Formenti, 2018).

Regarding the materials for RGP contact lenses we find:

- PMMA (Poly-methyl-methacrylate): PMMA was invented in 1937 and have been used for rigid contact lenses since 1947. It is not gas permeable and comes from methacrylic acid's esterification with methyl alcohol: its main features are stiffness and hardness combined with optical qualities (Gheller, 1993). PMMA does not react with enzymes nor with tear film products, furthermore it is not able to hold water, so it needs to be hydrated (Gheller,1993).

- CAB (derivatives of cellulose): the first RGP material used in 1968, characterized by flexibility and resistance in collecting bioproducts (Gheller,1993). CAB is cellulose, acetic acid and butyric acid matched together: butyric acid improves flexibility decreasing dimensional stability, which is normalized by adding thickness (Gheller,1993). The hydroxyl groups within cellulose improves wettability: in fact, CAB RGP contact lenses can be hydrated by almost 2% (Gheller, 1993).

- Siloxane co-polymers: created to satisfy the demand of better oxygen permeability, during the Seventies appears the first combination of PMMA and silicon. Siloxane can be matched with CAB, HEMA, VP to bond with more oxygen, though loosing hydrophilicity, which is the weakest point of these materials (Gheller, 1993).

- Fluoride-acrylates and fluoride-silicon-acrylates: among these materials fluoride switches with hydrogen and bonds with carbons, this changing makes the polymer much harder and improves interactions between eyelids and contact lenses, meaning more comfort and less adhesion of debris while achieving the possibility to reduce contact lenses' thickness (Gheller,1993). Within the merits of these polymers we find the great oxygen permeability that makes them worthy to be used in exchange with silicon (Gheller,1993). The weak points of fluoride-acrylates are the fragility while polishing the lenses plus the sensibility to high temperatures which ruins their wettability (Gheller,1993).

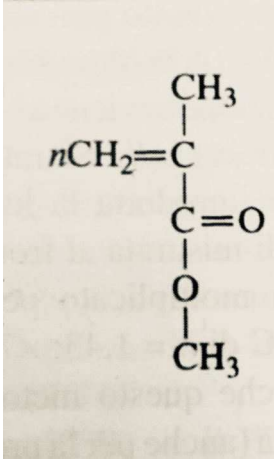


Image 13: PMMA. Gheller, 1993

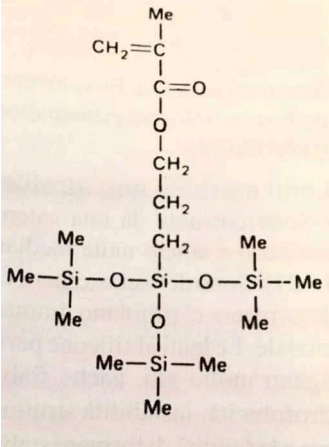


Image 14: PMMA + Silicone. Gheller,1993

3.3 Findings in SCL wear among Diabetic subjects

One feature extensively assessed for what concerns diabetic corneas is the slow recovery from endothelial oedema: by using soft hydrophilic contact lenses with low Dk, it has been possible to find data about corneal oedema in diabetic subjects: as the tissue was stressed with these SCL, diabetic corneas did not react as healthy corneas did (Saini et al., 1996). Hypoxia signs like endothelial folds and striae are not always due to contact lens induced oedema, in fact they have been observed even among those who did not wear contact lenses (Efron et al., 2001). Among the corneal complications due to soft contact lenses use between diabetics, we find endothelial issues: chronic endothelial oedema might occur, causing storage of lactate and high levels of CO_2: the main consequence to this condition is the reduction of pH (Hyun Sung Leem et al., 2011). The area CV of the polygonal cells appears to be higher among diabetic SCL users than in diabetic subjects who were not wearing them, while the cellular density seems lower; furthermore, the central corneal thickness does not show many differences between diabetic SCL users and diabetic without SCL (Hyun Sung Leem et al., 2011).

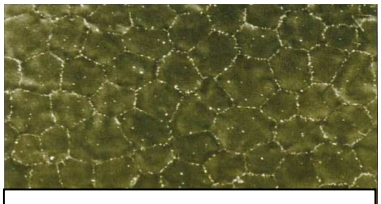


Image 15: healthy endothelium. Al-kott, 2013

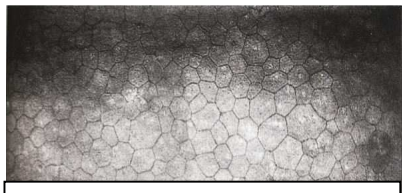


Image 16: Poleomorphism and polymegathism. Al-kott, 2013

It could then be said that morphological changings in endothelial cells are caused by soft contact lenses use, while central thickness and endothelial cells density depends only on Diabetes Mellitus (Hyun Sung Leem et al., 2011).

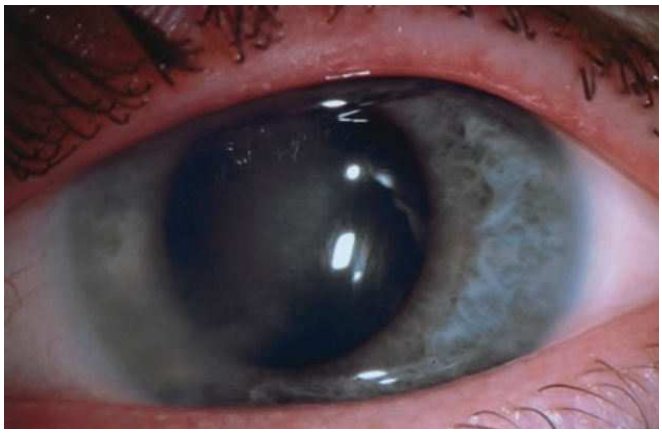


Image 17: contact lenses induced oedema. Al-Abbadi, 2017

Regarding low corneal sensitivity among diabetics, it must be said that this condition gives higher risks of corneal ulcers or abrasions and it slows corneal wound healing as a secondary effect (Efron et al., 2012). The damage in terms of sensitivity becomes greater if coinciding with severe neuropathy, this means that good hyperglycaemia control and absence of neuropathy should let diabetic corneas without appreciable signs of sensitivity's decline (Efron et al., 2012). The rate of discomfort seems to be higher between those who are both diabetics and users of contact lenses. This finding represents a strange data because the diabetic cornea's sensitivity should be lower than the healthy one. This misunderstanding might come from errors regarding the aesthesiometer sensibility, but another reason to this mistake could be the lens interacting with the eyelids rather than the cornea: diabetic eyelids, indeed, are often prone to blepharitis and other infections (Efron et al., 2001).

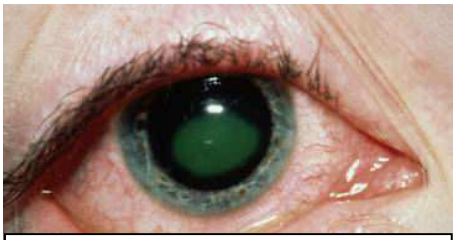


Image 18: Corneal abrasion. McQueen, 2010

One study tested SCL use between diabetics, Hydrogel SCL have indeed been worn by both diabetics and non-diabetics for one year: diabetics showed less corneal transparency, blurred vision and less comfort than healthy subjects (Efron et al., 2001). Whether diabetic subjects were more sensitive to SCL wear than non-diabetics, it has not been found a significant feedback regarding Contact Lenses Acute Red Eye (CLARE), hyperaemia, staining or eyelids alterations (Efron et al., 2001).

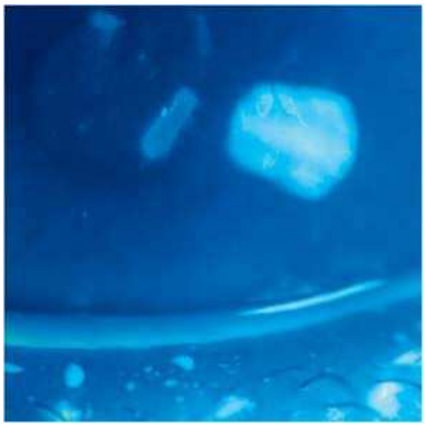


Image 19: Corneal erosion in a soft lens wearer with tear deficiency, diminished corneal reflex from drying.
https://entokey.com/primary-fitting-and-wearing-problems/

Among the damages induced by Diabetes Mellitus we find epithelial fragility, which leads to easier wounds on the anterior surface, especially when contact lenses are in place: this condition creates debates on whether apply contact lenses or not (Efron et al., 2001). Furthermore, it is an evidence that diabetic tear film is rich in polysaccharides, which means more adherence of cellular debris to the lenses (Efron et al., 2001). Another struggle for diabetic corneas is the small production of tear film, which translates into higher rates of contact lenses' dehydration: losing hydration for the contact lens means keeping liquids from the cornea (which is yet poor in tear film), this situation brings lots of troubles to the corneal tissue, especially at the level of epithelium (e.g. Staining). (Gheller, 1993)

3.4 RGP contact lenses wear among diabetic subjects

There are opposite opinions on whether RGP contact lenses are better than SCLs for people affected by Diabetes Mellitus. At first, RGP were not recommended because of their low O_2 content, this was in order to protect endothelium against the damages that could have occurred because of its fragility; today we might say that both CLs types have pros and cons. For some aspects, RGPCLs represent the best-fit lenses: they hardly split, provide better tear film turnover beneath their posterior surface and attract very low quantities of bioproducts, toxins and pathogens rather than SCLs (Efron et al., 2012).

While using soft hydrogel contact lenses for extended periods, 100 aphakic subjects were observed to determine the odds rate in contracting ulcers caused by infections; four people contracted ulcers and three of them were diabetics (Eichenbaum et al., 1982). This leads to think that diabetic subjects are more prone to develop infections while using contact lenses, especially if applied for extended periods. Diabetes indeed has been indicated as a risk factor in developing contact lens induced microbial keratitis, which is one of the worst contact lenses complications, typically caused by *Pseudomonas Aeruginosa* and *Staphylococcus Aureus*. At this point, it would be appropriate to keep in mind that RGP contact lenses partially eliminate risks related to infections thanks to their tight texture and polymers (Efron et al., 2012).

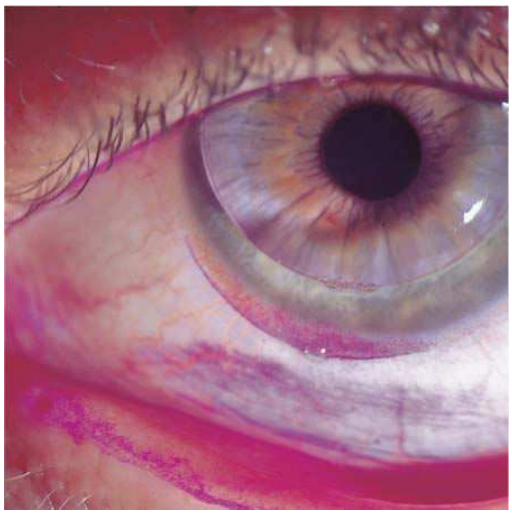
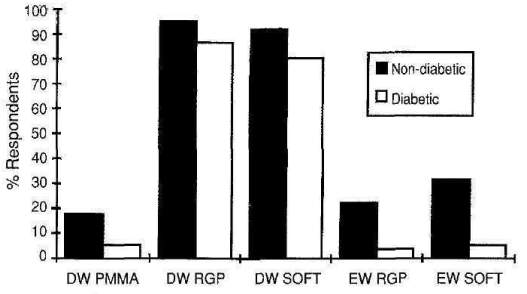


Image 20: Tear deficiency, hard contact lens, rose bengal staining, abrasion below the limbus caused by the lens because of tear deficiency.
https://entokey.com/primary-fitting-and-wearing-problems/

While the lower rate of infections is a great feature of RGP contact lenses, their rigidity and hardness can be considered a weak point when we speak in terms of Diabetes Mellitus. The reason why RGP can be stated as unsafe is the possibility to inflict injuries by scratching the edges against epithelium if they are not smooth enough, causing corneal erosions (Efron et al., 2012). Another struggle determined by rigidity and edges of RGPCLs is the discomfort caused when superior eyelids touch the lens while blinking: once again the design of RGP contact lenses can cause irritation and discomfort to the person diagnosed with D.M. as we know that diabetics have sensitive eyelids and high rates of eyelids' infections (Efron et al., 2012). Although SCLs seem the best choice in terms of comfort, there is a study made among UK practitioners which shows us their preference for RGPCLs, due to their lower infection rate: the 62% of the interviewed would apply RGPCLs, while the 38% would choose SCL (Efron et al., 1997).



Contact lens types (and modalities of wear) respondents would consider fitting to patients. DW = daily wear; EW = extended wear; PMMA = polymethyl methacrylate; RGP = rigid gas permeable; SOFT = soft lens.

Image 21: Efron et al., 1997

One particular design for RGP contact lenses is orthokeratological RGP with reverse geometry: these lenses are used for myopia control or cosmetic compensation of refractive errors, mostly myopia and hyperopia, by flattening and steepening corneal cells in order to add or subtract corneal thickness (Formenti, 2018). This procedure is dangerous for healthy people and even more unsafe for diabetics (Formenti, 2018): the practitioner should consider what have been said before about diabetic corneas and their predisposition to injuries before deciding to apply such lenses. Among the

contraindications to RGP and orthokeratological contact lenses' use we find low corneal sensitivity which is a feature of diabetic corneas; if the loss is severe these contact lenses should then be avoided (Efron et al., 2012).

3.5 Glucose sensing contact lenses

A conspicuous number of researches were made over the past 30 years to project contact lenses with the specific ability to read and monitor the amount of glucose within ocular tear film, but nowadays none of them have been commercialized yet; all the literature available concerns experimental studies as there are some limits for which better solutions are required. The last great example of contact lenses as glycaemia recording tool is promoted by Google ft. Novartis with its licence for the development of "Glucose sensing contact lenses". Although the project is ground-breaking, researchers are far away from finding the light: struggles have been found in biocompatibility, circuit's reception of the signal and sensor's readings of glucose. (Ascaso et al., 2016)

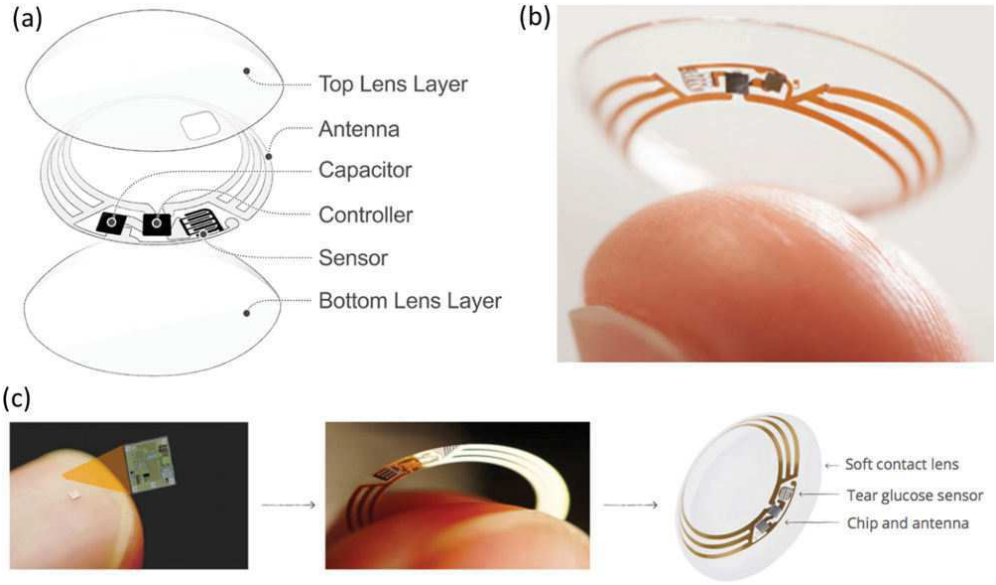


Image 22:The contact lens sensor under co-development by Google and Novartis. It measures glucose concentration in tears using a miniaturized electrochemical Image 7: example of Silicone-hydrogel. Back et al., 2011 sensor embedded into a hydrogel matrix. a) A schematic of the contact lens sensor, showing the electrical circuitry of the sensing system. b) The contact lens sensor prototype. c) The wireless chip, which is mounted, with the sensor, onto an electronic ring, and then embedded into the contact lens. Google X, 2014.

There are many benefits in promoting the development of such devices, the first above all is that using a contact lens to monitor glycaemia is painless if compared with skin's pierces made with standard glucose monitoring devices, for which blood is needed. Whereas blood is the first source of data, glucose could be found even within tears, urine, sweat and saliva. Regarding urine and saliva, glucose is difficult to measure because of too much water content within these fluids. On the opposite, sweat and tears are present only in small quantities along the body, which means a difficult collection of glucose through the day (Efron et al., 2012). Another struggle for glucose sensing contact lenses is the sensibility of glucose reading's sensors: the percentage of glucose found in tears is 10% of blood glucose, which means the device shall be ten times more sensitive than blood glucose monitoring devices. It must be added to this evidence another problem to glucose sensing contact lenses: changings in tear film's percentage of glucose occurs about 10 to 30 minutes after blood glucose changings, which means less specific data and management of acute glycemia, especially in presence of hypoglycaemia (Efron et al., 2012).

Chapter IV

A Survey on contact lens wear among diabetics

After some researches on literature about Diabetes Mellitus and contact lens wear, it has been decided to carry out a small survey on contact lenses' use between both healthy and diabetic people: the aim was to point out eventual differences and see if diabetics used RGPCLs more than healthy people, according to other studies. 39 anonymous questionnaires were proposed, of which 20 were given to healthy people who wore contact lenses and 19 to diabetics: only 9 diabetics out of 19 wore contact lenses or had worn them but then quitted. The questionnaires were personally proposed to healthy people during an internship in Noventa Padovana (PD), which took place in Ottica Mario, while questionnaires among diabetics were left to the staff of Borsatti Pharmacy near Pordenone (PN). It took from April to July 2018 to collect these data, the main problem was found in obtaining a minimum number of diabetic contact lenses users to compare with those unaffected by Diabetes Mellitus. It must be said that this study does not provide any objective data on the ocular condition of both healthy and diabetics, as no clinical instruments were used to asses results; although the lack of objective measures, parts of Efron's grading scales were used in questionnaires to get more relevant subjective data.

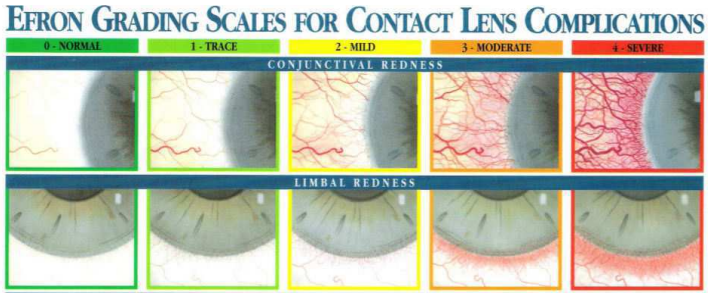
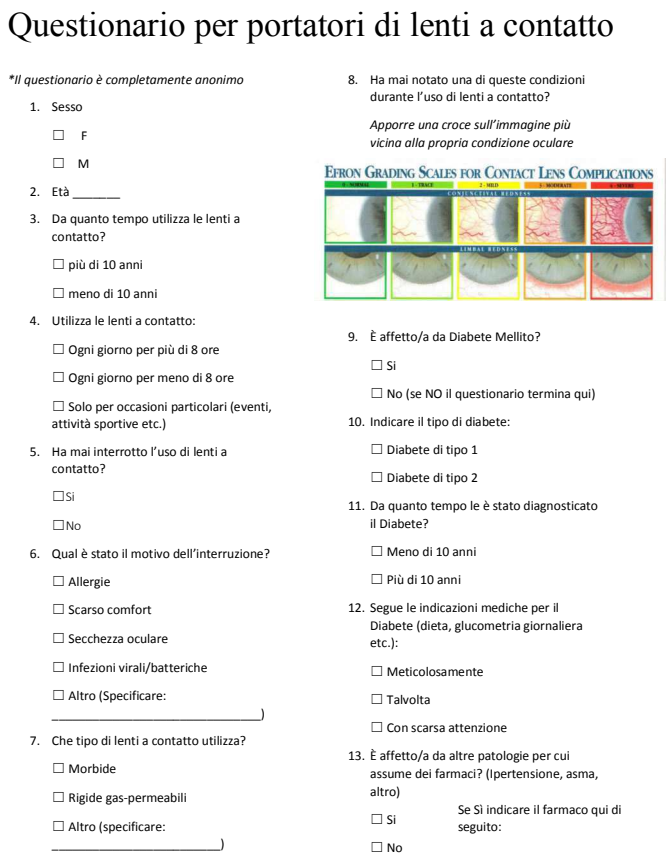


Image 23: Part of the Efron's grading scale used to find out if both healthy and diabetic subjects ever experienced one of these clinical pictures while using contact lenses. The answer consisted in marking the most similar picture.

This survey was not representative of the Italian condition as all the information were collected between Veneto and Friuli Venezia Giulia, so it is not possible to extend these results to the entire Italian population.

At the end of the survey and its analysis, it has been found that diabetics more likely used RGPCLs rather than SCLs when compared with healthy subjects who wore contact lenses (p value <0,05). Furthermore, it has been pointed out how diabetics answered they stopped using contact lenses at least one time mostly because of dry eye symptoms (11% of the sample) and discomfort (11% of the sample), while healthy subjects mainly marked allergies (5% of the sample), discomfort (10% of the sample) and viral/bacterial infections (10% of the sample).

Paragraph one will discuss the methods and analysis used for the collected data, while paragraph two and three will both summarize the results found for heathy and diabetics, followed by a discussion and conclusions drawn by this survey.



Questionario per portatori di lenti a contatto

**Il questionario è completamente anonimo*

1. Sesso
   - ☐ F
   - ☐ M
2. Età _____
3. Da quanto tempo utilizza le lenti a contatto?
   - ☐ più di 10 anni
   - ☐ meno di 10 anni
4. Utilizza le lenti a contatto:
   - ☐ Ogni giorno per più di 8 ore
   - ☐ Ogni giorno per meno di 8 ore
   - ☐ Solo per occasioni particolari (eventi, attività sportive etc.)
5. Ha mai interrotto l'uso di lenti a contatto?
   - ☐Si
   - ☐No
6. Qual è stato il motivo dell'interruzione?
   - ☐ Allergie
   - ☐ Scarso comfort
   - ☐ Secchezza oculare
   - ☐ Infezioni virali/batteriche
   - ☐ Altro (Specificare: _____)
7. Che tipo di lenti a contatto utilizza?
   - ☐ Morbide
   - ☐ Rigide gas-permeabili
   - ☐ Altro (specificare: _____)
8. Ha mai notato una di queste condizioni durante l'uso di lenti a contatto?

   Apporre una croce sull'immagine più vicina alla propria condizione oculare

9. È affetto/a da Diabete Mellito?
   - ☐ Si
   - ☐ No (se NO il questionario termina qui)
10. Indicare il tipo di diabete:
    - ☐ Diabete di tipo 1
    - ☐ Diabete di tipo 2
11. Da quanto tempo le è stato diagnosticato il Diabete?
    - ☐ Meno di 10 anni
    - ☐ Più di 10 anni
12. Segue le indicazioni mediche per il Diabete (dieta, glucometria giornaliera etc.):
    - ☐ Meticolosamente
    - ☐ Talvolta
    - ☐ Con scarsa attenzione
13. È affetto/a da altre patologie per cui assume dei farmaci? (Ipertensione, asma, altro)
    - ☐ Si — Se Sì indicare il farmaco qui di seguito:
    - ☐ No

Image 24: Example of the anonymous questionnaire used to collect data.

4.1 Methods and analysis

The model used to analyse data obtained by the survey was a linear regression model, the independent variable was the group of subjects (Diabetics, coded as 1 and healthy subjects coded as 0). In addition to this variable, other features of the group were used to track a profile of the samples: sex, age, interruption of CLs, EGSCLS, type of CLs.

The first model concerned the duration of contact lenses' use (for how long the interviewed was using CLs): regarding this model the only relevant parameter was the Group. The group presented a negative result and a "p" value of 0,0476, implying that diabetics were using contacts for less time if compared with healthy subjects.

Tab V: statistical analysis

Dependent Variable: **Tempo**

Parameter Estimates

Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > |t|
Intercept	Intercept	1	11.60046	6.07968	1.91	0.0695
Group	**Group**	**1**	**-12.35881**	**5.89123**	**-2.10**	**0.0476**
Sex		1	3.28175	4.92339	0.67	0.5120
Eta	Eta	1	0.21586	0.15745	1.37	0.1842
Interruzione	Interruzione	1	6.42921	6.39718	1.01	0.3258
TipoLAC		1	11.49266	7.13996	1.61	0.1217
Efron	Efron	1	-3.72517	3.37956	-1.10	0.2823

The second model concerned the daily use of CLs: in this analysis Time was also used as an independent variable. Within this reading of the data the Group-parameter had no significance, meaning there was no difference between the samples in terms of daily CLs use. Surprisingly, it has been found a correlation with the Time-parameter ($p < 0.05$): those who were using contact lenses for more years also used them for 8 or plus hours per day.

Tab VI: statistical analysis

Dependent Variable: **Utilizzo**

Parameter Estimates

Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > |t|	
Intercept	Intercept	1	1.81180	0.46622	3.89	0.0009	
Group	Group	1	0.39513	0.45842	0.86	0.3985	
Tempo	Tempo	1	0.03079	0.01514	2.03	0.0549	**B**
Sex		1	0.32361	0.35323	0.92	0.3700	
Eta	Eta	1	-0.01202	0.01165	-1.03	0.3138	
Interruzione	Interruzione	1	-0.16828	0.46472	-0.36	0.7209	
TipoLAC		1	0.51928	0.53620	0.97	0.3438	
Efron	Efron	1	-0.15895	0.24660	-0.64	0.5262	

4.2 Results for healthy subjects

7 males and 13 females answered the questionnaire avoiding parts reserved to diabetic subjects, the mean age of this healthy sample was 34,5 years (SD +/- 11,35 yr.) with the younger being 18 and the older 52.

Questions were made about:

- the amount of time spent wearing contact lenses during the day;
- what kind of contact lenses they used between RGP and SCL;
- if they have never stopped to use contact lenses and why;
- if they have never recognized one or more of the Efron's grading scale's pictures while wearing contact lenses

The subjects were asked for how long they had worn contact lenses: only 4 out of 20 answered to have worn them for less than ten years, which means most of the group consisted in long-standing contact lenses' users.

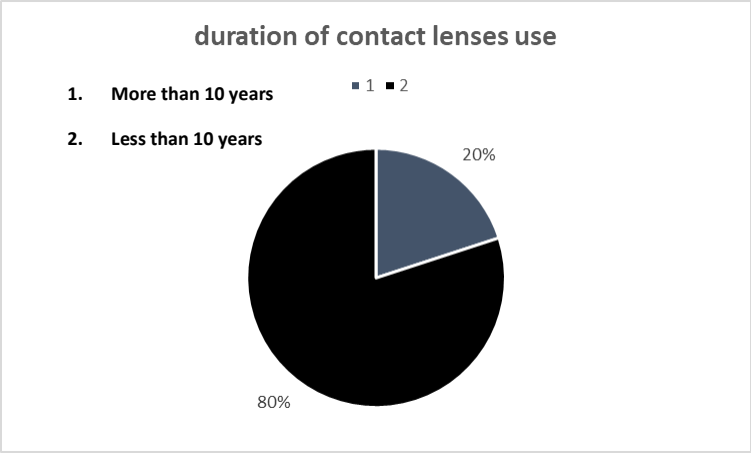


Image 25: This pie chart shows how many healthy subjects used cl for more than 10 years compared to those who wore them less than 10 years.

55% of the interviewed claimed to wear contact lenses for more than 8 hours every day, while the 40% was wearing them occasionally (e.g. Sports, ceremonies); only one person answered to wear CL daily but for less than 8 hours.

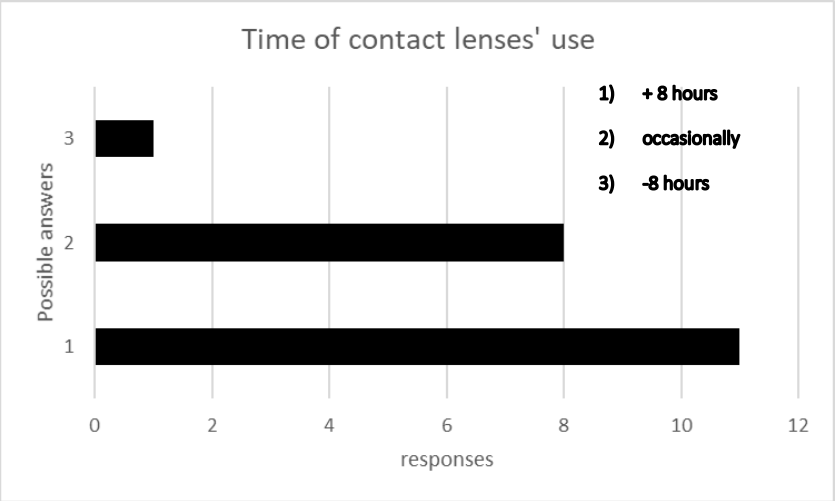


Image 26: The histogram represents CL's time of use per day among healthy subjects.

Everyone who answered the questionnaire was wearing SCL, except two people that used RGP contact lenses instead. It was then possible to assess that this sample preferred soft contact lenses, even though explanations for this choice were not asked.

Within the analysis, it has been found that 35% of the interviewed interrupted CL use at least one time. Below are reported the reasons of these interruptions:

Tab. VII: reasons why 7 people stopped using CL. * The percentage refers to a total of 20 subjects

Interruption of contact lenses use because of:				
Allergies	**Dry eye**	**Discomfort**	**Viral/bacterial infections**	**Other reasons**
5%*	0	10%*	10%*	10%*

Zero per cent of the people stopped using contact lenses because of dry eye, while only one person interrupted due to allergies; 2 people dropped because of discomfort and the same thing went for viral or bacterial infections and other unspecified reasons. 35% is a high percentage of people dropping contact lenses use, but it might be due to the little number of people recruited for this study, which could have enhanced the amount of bias while redacting, answering and analysing questionnaires.

The latest data collected were about having seen at least one time, while using contact lenses, one or more conditions present in Efron's grading scales (EGSCLC) about conjunctival and limbal hyperaemia. These were subjective responses as none of the subjects reported optometric diagnosis to validate their assessments.

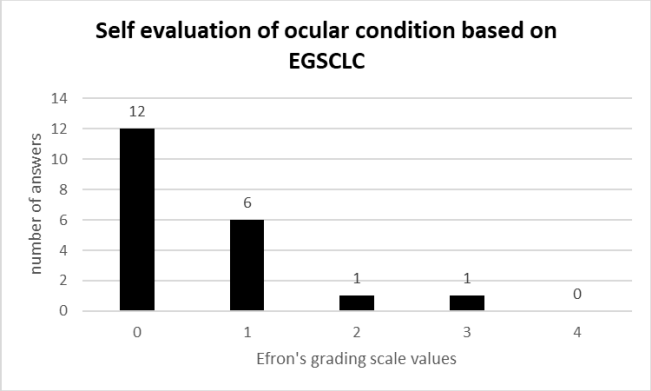


Image 27: Graphical representation of self-measured eye condition.

By looking at this graphic we can see how most of healthy subjects answered grade 0, which means they had never seen traces of hyperaemia while using contact lenses. Surprisingly, 30% of the samples marked grade 1, declaring to have seen traces of hyperaemia, while no one pointed out grade 4 (severe) and only two people marked respectively grade 2 and 3 (mild and moderate hyperaemia).

From this first analysis it has been possible to say that healthy subjects wore mostly SCLs, every day for more than 8 hours per day, moreover they have never seen excessive redness around limbus or conjunctiva except for 2 people. To conclude, 35% of the interviewed stopped using CL mostly because of discomfort and infections. The next step in this study will be to analyse data collected among those affected by Diabetes Mellitus, as it will be seen in the following paragraph.

4.3 Results for diabetic subjects

Nineteen questionnaires were proposed to diabetic subjects in order to collect data about contact lenses' use, unfortunately only 9 out of 19 was wearing them or had worn them before. If we consider that 5.3% of Italian population is affected by Diabetes Mellitus (Istat,2017), it becomes easy to understand how little the percentage of diabetics who

wear contact lenses can be, this has been pointed out as the main struggle in finding diabetic people using contact lenses. To analyse data concerning this sample, diabetic subjects were divided in two sub-groups: CLs' users and non-CLs' users:

The mean age of non-CLs' users (5 females and 5 males) was 50,4 years with a standard deviation of +/- 27,7 years, the younger was 12 and the older 90; the mean age of diabetics with contact lenses (4 females and 5 males) was instead 51,7 years (SD +/- 29,3 years) with the younger being 21 and the older 90.

It is known that almost 90% of those affected by D.M. have Type 2 Diabetes, while the other 10% have Type 1 Diabetes: the percentage of T1 and T2 D.M. was measured within the sample, but it was found that 52,7% of the interviewed had T1D.M. while 47,3% was affected by T2D.M.: these data led to say that the diabetic sample collected during this small survey was not representative of the population. Between the CLs' users 55% had T1D.M., again the percentage was too high if compared with population's data.

To the entire diabetic sample questions were made about:

1) Duration of Diabetes Mellitus: It has been asked if D.M. was diagnosed less or more than the previous ten years, this question was proposed to see if there were differences among CLs' users with Diabetes for more than 10 years and those with the smaller duration. The 40% of non-CLs' users had diabetes for more than 10 years, while among CLs' users the percentage was 66.7%.

2) Insulin intake: One of the questions was about exogenous insulin intake; this was a "yes or no" question to track a profile of the sample: 60% of non-CLs' users was taking insulin and the 55.5% of CLs' users was taking it too.

3) Diabetes' control: During the questionnaire diabetic subjects were asked to rate their ability to follow the prescriptions, with three possible answers. The aim of this question was to check literature: with poor diabetes' control, there might be higher rate of discomfort and even drop out. Diabetic subjects, indeed, are more prone to discomfort and injuries while using contact lenses, this fragility aggravates when there is poor Diabetes' control. From this perspective, data about diabetic CLs' users will be discussed in the next pages to see if they are

consistent with literature faced in chapter three. The following graphics represent what has been answered both between CLs' and non-CLs' users:

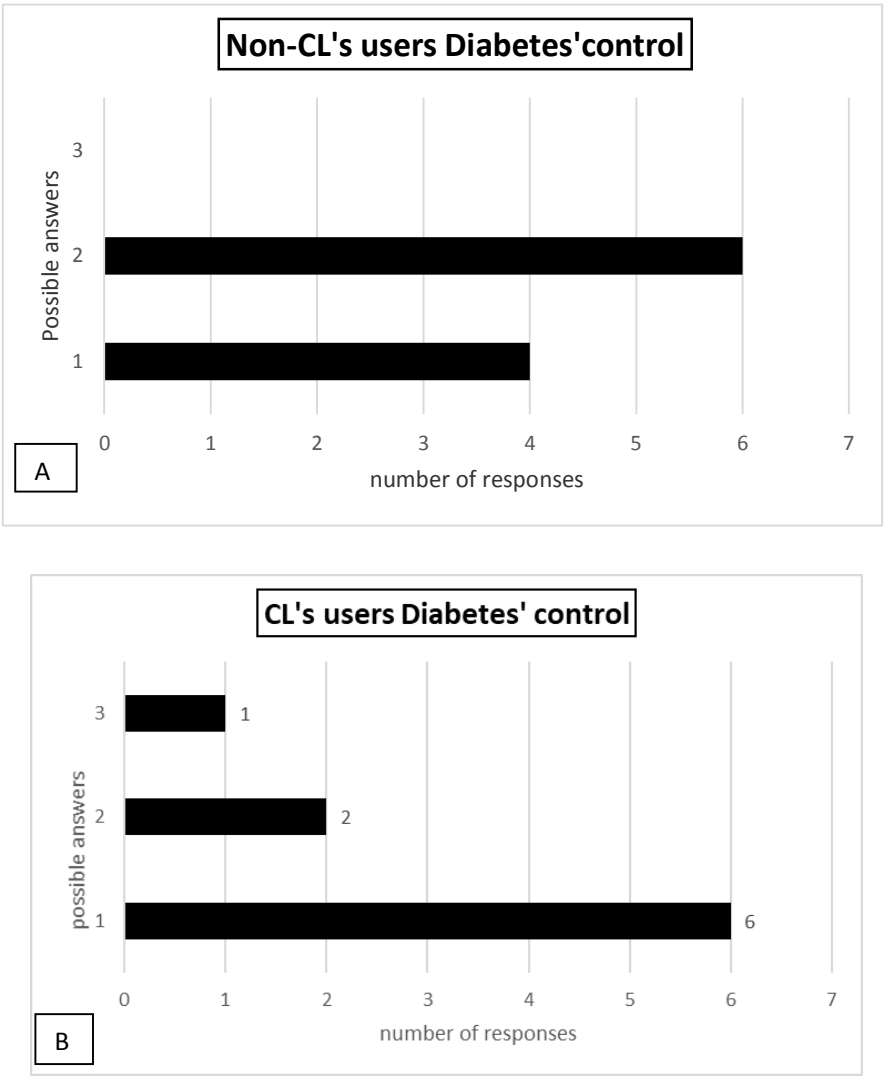


Image 28: Answers collected between non-CL's (A) and CL's (B) diabetic samples. The y-axis represents three possible answers to the question "How do you monitor your Diabetes in agreement with your prescription?" Number 1 matches "Carefully" while number 2 is for "Sometimes I do not follow the prescription" and number 3 "I don't care" .

4) Other pathologies with pharmaceutical therapies: The last question on Diabetes Mellitus concerned the presence of pathologies in addition to Diabetes, for which different therapies were followed by the subjects, it was also asked to write which kind of medication they were assuming. It is known that some

medications can cause diminished production of tear film, with consequently dry eye diseases. Between these prescriptions we find anti-hypertensive medications, antihistamine, birth-control drugs and others (Gheller, 1993). Between both the non-CL's diabetic and CL's diabetic samples 3 people for each group were following other therapies, all of them were suffering from hypertension, for which beta blockers were required.

Regarding contact lenses' use among diabetics, the same questionnaire as healthy subjects was proposed for a further comparison between healthy and diabetic CL's users. The 55% of the sample had worn contact lenses for more than 10 years; when it was asked about the daily time of use 55% again answered more than 8 hours per day, while the 22,5% for less than 8 hours per day and the last 22,5% had worn them occasionally.

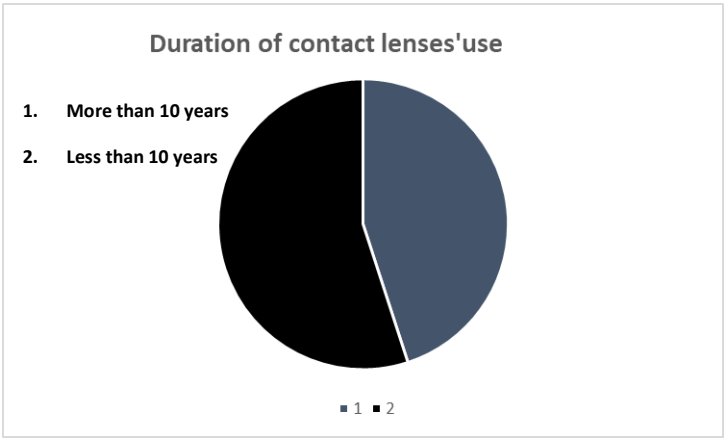


Image 29: This pie chart shows how many diabetic subjects were using CL's for more than 10 years compared to those who wore them less than 10 years.

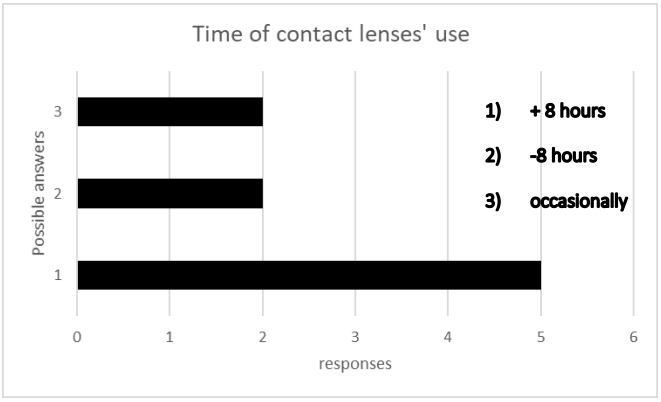


Image 30: histogram about daily contact lenses wear among diabetic subjects

The 45% of diabetic CL's users answered to wear RGP contact lenses when it was asked what kind of contact lenses they wore, while 55% answered to wear soft contact lenses. It was interesting to find out that 55% of the group interrupted using contact lenses at least one time, the tab showed below represents what has been answered.

Tab.VIII: reasons why 5 people out of 9 stopped to wear contact lenses. * the percentage refers to a total of 9 contact lenses users

Interruption of contact lenses use because of:				
Allergies	**Dry eye**	**Discomfort**	**Viral/ bacterial infections**	**Others**
0	11%*	11%*	0	33,3%*

The last question was the self-evaluation of the ocular condition based on EGSCLC: it was asked whether these subjects had ever seen one of the conditions pictured in Efron's scales, exactly as it was for the healthy sample.

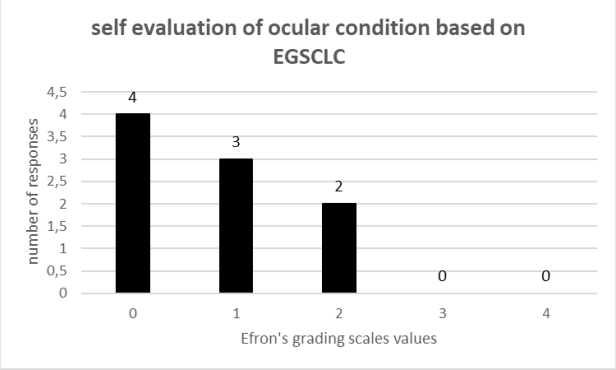


Image 31: Graphical representation of self-measured eye condition.

4.4 Discussion and conclusions

The aim of this small survey was to find any eventual difference between healthy and diabetic contact lenses' users and to see if the diabetic sample agreed with literature for what concerns the higher number of RGP used among diabetics. In 1997, a study on Diabetes Mellitus and contact lenses was published ("A survey on contact lens wear among diabetic patients in the United Kingdom"). Within this latest survey was assessed that practitioners preferred to apply RGP contact lenses rather than SCL on

diabetic corneas; these considerations were made possible by proposing questionnaires between both diabetics and practitioners in UK (Efron et al., 1997). Although in our analysis practitioners were not involved, it has been compared the number of RGP prescribed among healthy and diabetic samples.

To see more clearly all the results obtained by this analysis a summary tab will be reported in the next page and further assessments will follow.

Tab.IX: comparison between the answers given by both healthy and diabetic CL's users.

	Healthy sample	**Diabetic sample**	**"P" Value**
Mean age	34.5 SD +/- 11.35	51.7 SD +/- 29.3	P = 0,5120
Duration of CL's use	• 80% more than 10 years • 20% less than 10 years	• 55% more than ten years • 45% less than ten years	
Daily use of CL's	• 55% + 8 hours per day • 5% - 8 hours per day • 40% occasionally	• 55% + 8 hours per day • 22.5% - 8 hours per day • 22.5% occasionally	
RGP vs. SCL use	• 90% SCLs • 10% RGP	• 55% SCLs • 45% RGP	P= 0,0559
Interruption of contact lenses	• 35% yes • 65% no	• 55% yes • 45% no	P= 0,4223
Reasons for CL's interruption	• 5% Allergies • 0 Dry eye • 10% discomfort • 10% Viral/bacterial infections • 10% other reasons	• 0 Allergies • 11% dry eye • 11% discomfort • 0 Viral/bacterial infections • 33 % Other reasons	
EGSCLC self-	• 60% grade 0	• 44.5% grade 0	P=0.6858

evaluation	• 30% grade 1 • 5% grade 2 • 5% grade 3 • 0 grade 4	• 33.3% grade 1 • 22.2% grade 2 • 0 grade 3 • 0 grade 4	

The mean age of the two groups was different: between diabetics, indeed, the older person who has been interviewed was 90, while among the healthy subjects the older was 52. It is known that T2 Diabetes Mellitus afflicts mostly older people, in this analysis the percentage of T2 diabetics was 45%, this could explain why the mean age of diabetic subjects differs from that collected among healthy contact lenses' users.

It is clear now that we cannot say these samples are age-related, furthermore the Standard Deviation is higher within the diabetic sample because of the smaller range of subjects recruited for this analysis.

The time spent wearing contact lenses was over 10 years for the 80% of our healthy sample, this implied a strong propension to long-standing contact lenses' use: for diabetics the propension was not that strong as only the 55% of them was wearing CL for more than 10 years. The exact same percentage (55%) of both diabetic and healthy subjects was wearing contact lenses for more than 8 hours per day, but we found a big difference between the two samples: only the 20% of healthy CL's users was wearing RGP CL, against the 45% of diabetics. Using Fisher's exact test, it has been found a correlation between these data on Soft and RGP contact lenses, as the "p" value was lower than 0,05.

Although there are no objective data supporting this analysis, if we compare the responses of our samples with Efron's study "A survey of contact lens wear among diabetic patients in the United Kingdom" made in 1997, it seems that still today RGP contact lenses are preferred for the best-fit on diabetic corneas.

In chapter three it has been explained that diabetic people who wear contact lenses might have higher rates of CL's drop out: this might be due to discomfort caused by interactions between eyelid and contact lens or dry eye symptoms, which occur as the

production of liquids decreases, probably because of a lacrimal gland's neuropathy (Kyung-Chul Yoon et. al., 2004). Within this survey, we found that 55% of diabetic subjects stopped using contact lenses at least one time mostly as a consequence of discomfort (11%), dry eye (11%) and other reasons which were indicated by all the subjects as "old age" (33%). These latest data were different from those collected among healthy subjects: indeed, 35% of them also stopped wearing CL's at least one time, but the 5% did it because of allergies, while the 10% because of discomfort; the same 10% was found also for viral or bacterial infections and other unspecified reasons. These data, collected by proposing a subjective questionnaire, had no statistical relevance as the "p" value was found higher than 0,05. Regarding the self-evaluation of the ocular condition while using contact lenses it has been found that 60% of the healthy sample marked grade zero, while 30% marked grade 1 and 5% marked grade two as well as grade three. The condition among diabetic CL's users was similar: 44.5% marked grade 0, 33.3% marked grade1 and 22.2% marked grade 2, none of the subjects took in consideration grade 3 and 4. As we compared these percentages, no relevant differences were found except the fact that none among diabetics marked grade 3. The statistical analysis pointed out again a "p" value higher than 0,05.

To conclude, this survey showed that diabetics seem to wear RGP more than healthy subjects and that those who was wearing contacts for more years, also used them the more during the day. It must be specified that although these data are in accordance with literature, there are no objective measurements that can be used to validate any of these assessments.

Conclusions

While studying literature in order to achieve knowledge of a broad topic like Contact Lenses and Diabetes Mellitus, it has been highlighted that there are few researches in this field of interest. Even if this might be due to the struggle in finding diabetics who wear contact lenses, it clearly emerges that is of vital importance to improve knowledge on cornea abnormalities caused by the combination of Diabetes Mellitus and contact lenses' use.

Today we still don't know which solutions are better for diabetics who whish to use contact lenses, as there are different data and opinions about this matter and even practitioners are divided in different schools of thought. For example, some practitioners think that soft contact lenses are better regarding comfort and money expense, but others say that RGP contact lenses are the safest in terms of infections and oxygen intake (which, indeed, seems the more reasonable thought).

The aim of this analysis was to review the literature concerning this argument and to see if what said in those researches was in accordance with a small survey made among Italian diabetics. Indeed, it has not been found a single Research pursued in Italy. The evidences which were pointed out in this analysis on Diabetes Mellitus and contact lenses, in accordance with literature, highlighted how diabetics seem to have more fragile corneas and how their rate of discomfort with CL seems to be higher if compared with healthy people.

Although the clinical condition of diabetic corneas is well-known and widely explained in literature, there are still a lot of questions coming to mind if we introduce contact lenses beside the pathology: further analysis and then answers have to come before being certain with giving contact lenses to people affected by Diabetes Mellitus.

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