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The Origins of the Artificial Cornea: Pellier de Quengsy and His Contribution to the Modern Concept of Keratoprosthesis

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Summary

There has been little recognition of the French ophthalmologist Guillaume Pellier de Quengsy's contribution to the problem of artificial cornea (keratoprosthesis). This fact that he was the first to propose such a device was seldom acknowledged, and usually as a secondary reference. Based on the examination of original texts (1789), this study demonstrates that Pellier not only proposed an essentially correct keratoprosthesis, but also suggested a porous prosthetic skirt, a revolutionary concept which is currently fundamental to artificial cornea research.

Introduction

Opacification of the cornea, due to disease or trauma, is a major cause of blindness in the world population. Transplantation of human donor corneal grafts (i.e., penetrating keratoplasty) has become the main rehabilitation procedure, and its rate of success is generally acceptable in patients not affected by extensive chemical burns, by certain pre-existing conditions and pathologies, or by recurrent graft rejections. In those affected, the likelihood of a successful outcome following penetrating keratoplasty is greatly reduced. Furthermore, there is a high incidence of corneal blindness in economically underdeveloped countries, where the availability of donor corneal tissue is very limited and likely to remain so, as the eye banks generally do not exist and medical infrastructure is often inadequate. An alternative to

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penetrating keratoplasty is prosthokeratoplasty, a procedure in which a damaged cornea is replaced by an artificial cornea, known also as a keratoprosthesis. This allows the problems of graft rejection and donor tissue shortage to be sidestepped, but introduces new problems and challenges of its own.

The idea of an artificial cornea is an old one, and the history of its development over the last two centuries is spiced with peculiarities. Even today, there is still no artificial cornea with proven long-term efficacy and low complication rate. However, research continues, unfortunately limited to a few centres only. Strangely, the identity of the ophthalmologist who originated the idea of an artificial cornea was seldom acknowledged in the literature until the latter half of our century. His name was Guillaume Pellier de Quengsy and he lived in France between 1751(?) and 1835. Also overlooked was the fact that this man, so long ago, suggested a porous structure for the skirt of his artificial cornea. Only now is this idea being put into practice: the relatively few current promising candidates for a functional artificial cornea are based on the concept of a porous skirt. In this paper, we examine the first description of a potential artificial cornea and the revolutionary suggestion of a porous prosthetic skirt. The evidence demonstrates that Pellier de Quengsy is to be regarded as the true originator of both ideas.

Guillaume Pellier de Quengsy and His Main Opus

Guillaume Pellier de Quengsy, Jr. (1751(?)–1835) was a French ophthalmologist, and obviously a distinguished one as Hirschberg reserves for him two full sections in his monumental *Geschichte der Augenheilkunde*[1]. Pellier's father was both a physician and a surgeon, and his brother was an ophthalmologist who moved to the United Kingdom where he eventually became a citizen of Aberdeen. It appears that Pellier was a very dedicated ophthalmologist who practiced his profession in many parts of France. In 1776, he settled in Montpellier where he was to remain until his death. Pellier was primarily an outstanding cataract surgeon. He also treated a large variety of eye diseases and became a prolific author. In 1789, he published the first volume of *Précis ou Cours d'opérations sur la chirurgie des yeux, puisé dans le sein de la pratique, et enrichi de Figures en Taille-douce, qui représentent les*

1 Hirschberg, J.: *The history of ophthalmology,* vol. 3: *The renaissance of ophthalmology in the eighteenth century (part one),* trans. Blodi, F. C./Bonn, J. P., Wayenborgh Verlag, 1984, pp. 327–338.

Instruments qui leur sont propres, avec des Observations de pratique très-intéresantes, a title which can be safely translated as "Abstract or course of the surgery of the eyes, drawn from the depth of practice, and enriched with copper engravings, which illustrate the proper instruments, with most interesting observations from the practice". According to Hirschberg[2], the first volume of 437 pages was followed in 1790 by a second volume of 404 pages. Hirschberg regarded Pellier's course as "the first monograph on eye operations in the world literature"[3]. He also believed that this work was appreciated too little and too late[4].

Pellier's Concept of an Artificial Cornea

For the first time in the recorded ophthalmological literature, the idea of an artificial cornea was promoted by Pellier in the *Troisième démonstration, Article premier* of the first volume of his book[5].

In the introduction to the *Démonstration*[6], Pellier classifies the corneal diseases into opacification, pustules, blisters, abscess, ulcers, tissue outgrowth, staphyloma "and others". After outlining the topics to be discussed, he deals with the corneal opacification ("fogging") in the first chapter. Pellier considers three species of corneal opacification, i.e., *leucoma albugo* (or "white stain"), *leucoma cicatrix* (or "stain caused by a scar"), and *leucoma nephelium* (or "cloud", "shade"). After presenting his views on the causes of each species, Pellier concentrates on the treatment of the first two conditions. Although he enthusiastically recommends the use of an alcoholic tincture of stag antlers (apparently his discovery), Pellier admits that his treatment fails when the stains are very thick or caused by a scar, a circumstance that makes him propose an artificial replacement for the opaque cornea[7]:

2 Ibid., p. 328. Even before Hirschberg's time, this book was considered rare. A few copies are still in existence in France, the Netherlands, Germany and probably elsewhere. We were fortunate enough to obtain a photocopy of a section of "Troisième démonstration" from the first volume of Pellier's book, which made possible the writing of the present contribution.

3 Ibid., p. 331.

4 Ibid., p. 332.

5 Pellier de Quengsy, Jr., G.: *Précis ou Cours d'opérations sur la chirurgie des yeux, puisé dans le sein de la pratique, et enrichi de Figures en Taille-douce, qui représentent les Instruments qui leur sont propres, avec des Observations de pratique très-intéresantes,* Paris, Didot, 1789, vol. 1, pp. 91–109. The illustrations are explained on pp. 134–135.

6 Ibid., pp. 91–92.

7 Ibid., p. 94.

"When they [the stains] are of this nature, would it not be possible to provide an artificial cornea to replace the natural one, especially when it is sure that the loss of sight comes only from the opacity of this tunic? The case is easy to check. Here [is] the operation that could be attempted without fear, and which should take the form of the artificial cornea that I propose."

After describing the surgical procedure for removing an opacified cornea, Pellier continues[8]:

"Once the cornea was extracted, the surgeon will substitute it with an artificial cornea that should be made up prior to the operation according to the following procedure, and should have all dimensions necessary for the natural one. A piece of very clear glass, thin and smooth, slightly concave inside and convex outside, the diameter being as large as of the removed cornea, is to be placed (see Plate IV, Fig. 2) in a small ring of silver, very thin and well polished, in the same manner in which a spectacle lens is placed into its frame. Around the outer rim of the ring, a groove should be made proportional to the thickness of the natural cornea, so that the sclera, in providing new fluids, could be exactly implanted, and in order to avoid the falling of the [artificial] cornea into the interior of the eye, the external plate of the ring should be made a little larger than the other, such it would lean against the edge of the sclera."

A better description is given in the caption to "Fig. 3, Plate IV"[9].

"The Figure 3 presents a small silver ring, very thin, with two grooves; one is inside the ring; (it has to hold the glass, Fig. 2), the other is outside; it is larger, and has to contain the edges of the [host] opaque cornea. It should be noted that the anterior surface of the ring is a little larger than the posterior one, so that the artificial cornea when inserted could lean against the edges of the sclera, which [the artificial cornea], without this precaution, could fall into the interior of the eye."

Clearly, this was intended as an artificial device to be inserted as a full-thickness corneal replacement, able (in principle) to function as a substitute for the natural cornea.

Pellier also describes in detail a procedure for the surgical implantation of such a device, suggesting and drawing the appropriate instrumentation, and recommends cotton thread for the sutures[10]. However, there is no documentation available to suggest or prove that the author himself ever performed this operation.

In the second half of the *Article premier*, Pellier considers solutions to potential problems with his artificial cornea. He has a key idea when discussing two possible postoperative complications. Pellier believes that abnormal accumulation of aqueous humour may occur due to the failure of the "excreting pores" in the operated cornea (the "second" problem in his exposition), in which case he suggests[11]:

8 Ibid., pp. 95–96.
9 Ibid., p. 134.
10 Ibid., pp. 97–100.
11 Ibid., p. 101.

"This second objection will be completely demolished if we consider that there is always enough interval between the grooves of the silver ring and the body which it contacts, in order to allow the excess of aqueous humour to escape, and [as] we might suspect that they [the grooves] can be blocked by some debris or deposits that this fluid carries, why could not we, in manufacturing the artificial cornea, place several small holes to form pores around the silver ring, which shall serve as natural [pores] !"

Pellier then contemplates the possible loss of transparency in the prosthetic glass core, following implantation (the "fourth" problem in his exposition). He refutes this possibility on the basis that the glass surface will be permanently lubricated and maintained moist by the "various humours, and particularly by the aqueous which regenerates by natural laws"[12], a process that supposedly will maintain its transparency. However, as a preventive measure, he again recommends the fabrication in the prosthetic silver ring of "small holes more or less close to each other to serve as natural pores"[13] in order to maintain the circulation of lubricating humours.

Thus, albeit for the wrong reasons, Pellier came up with a concept which is central to modern keratoprosthesis research: porosity of the prosthetic periphery. Aqueous humour is continuously produced by the ciliary body epithelium through a complex active transport process. Pellier was mistaken in two respects, namely when suggesting that the outflow pathway for the aqueous humour is through the cornea, and also when assuming – as a consequence – that the aqueous humour is a wetting as well as a lubricating agent for the external surface of the cornea. Although the aqueous humour does leak through the corneal endothelium to reach stroma and supply nutrients, it is pumped back into the anterior chamber by the endothelial metabolic pump, with the result that normal stroma is maintained relatively dehydrated. (Without this mechanism, the corneal stroma swells and looses its transparency.) The diffusion of a small amount of aqueous into the cornea cannot be considered a major pathway for the drainage of this fluid. The majority of aqueous (70–90%) leaves the anterior chamber through the trabecular meshwork into Schlemm's canal, and then through the collector channels into the episcleral veins, while the rest exits through the uveoscleral pathway, i.e., the posterior coats of the eye. It is also now well established that the corneal epithelium is maintained wet and lubricated by the precorneal tear film which comprises an aqueous layer sandwiched between much thinner mucoid (deep) and lipid (superficial) layers. The contribution to the precorneal film of the aqueous humour that diffuses into the cornea is negligible, if any at all.

12 Ibid., p. 102.
13 Ibid., p. 103.

In Pellier's day, the physiology of the cornea was unknown, leading to his erroneous arguments in favour of peripheral porosity and his desire to promote aqueous leakage. Modern ophthalmologists would regard the leakage of aqueous humour as incompatible with successful prosthokeratoplasty, as it indicates poor healing, epithelial downgrowth, infection, and usually precedes the rejection of a keratoprosthesis. Although a porous skirt as such is a revolutionary idea, Pellier failed to recognise its real purpose and significance. The holes that he suggested to be drilled through the silver holding ring would allow the aqueous humour egress but would not promote the biointegration of the prosthesis. Recent research emphasizes the need for an interconnecting network of channels in the material used for the skirt of keratoprostheses. This contiguous porous structure allows the incorporation of the prosthetic material into the host biological substrate through cellular invasion and growth across the interface between material and tissue.

Subsequent refinements, however, do not rob Pellier of his right to be credited with the first conception of an artificial cornea, with the design of a transparent optic core of natural dimensions, and with the suggestion that the core could be surrounded by a porous skirt. But, over 150 years after his death, Pellier's hint that his idea would be "easy to check" and that surgery "could be attempted without fear" perhaps deserves a wry smile.

Recognition of Pellier's Proposal in the Nineteenth and Twentieth Centuries

It seems that the attempts in the nineteenth century to use a glass artificial cornea were not prompted by Pellier's ideas, which were either unknown to, or ignored by, his European colleagues. Nussbaum, who was the first to report the insertion of glass keratoprostheses in animal and human corneas[14], did not mention Pellier, nor did the few surgeons who subsequently attempted prosthokeratoplasty using quartz devices (Heusser[15], von Hippel[16], Salzer[17]). In the United States, Baker reported[18] the maintenance of a glass

14 Nussbaum, J. N.: «Die Cornea artificialis als Substitut für die Transplantatio corneae empfohlen», *Zeitschr. Wiss. Zool.* 5, 1854, 179–187.

15 Heusser, T.: «Ein Fall von Cornea arteficialis», *Denkschr. Med.-Chir. Ges. Kant. Zürich,* 1860, 127–129.

16 von Hippel, A.: «Über die operative Behandlung totaler stationärer Hornhaut-Trübungen», *Graefe's Arch. Ophthalmol.* 23, 1877, 79–160.

17 Salzer, F.: «Über den weiteren Verlauf des in meiner Arbeit über den künstlichen Hornhaut-Ersatz mitgeteilten Falles von Cornea arteficialis, sowie des von Schröder'schen Falles», *Zeitschr. Augenheilk.* 3, 1900, 504–509.

18 Baker, A. R.: "Some remarks on transplantation of the cornea and allied subjects", *Am. J. Ophthalmol.* [Ser. 2] 6, 1889, 1–10.

keratoprosthesis for two years in a human patient; he was aware of Nussbaum's and Heusser's experiments, but did not make any mention of Pellier's proposal.

We were almost ready to conclude that probably none of the nineteenth century ophthalmologists knew about Pellier's suggestion, when we came across a report in the extracts from the 1856 records of the Boston Society for Medical Improvement. This communication[19], which was prepared by Dr Burnett and read to the Society by Dr Bethune, describes in detail Nussbaum's experiments with glass keratoprostheses. Importantly, the participants' discussions following this presentation are quite relevant to our subject. Thus, Dr Williams remarks[20] that the editor of a French medical periodical (*Union Médicale,* Paris) strongly criticized Nussbaum's experiments qualifying them as "worthy of a German brain". (A century later, this statement will make Robert Day to blame posthumously the editor for "conveniently forgetting, such is national pride, that a Frenchman had originally proposed" an artificial cornea[21]). Williams also mentions[22] a letter published in the same periodical by Deval (an ophthalmologist of authority in Paris, see Hirschberg[23]) who claims that Nussbaum's experiments have nothing of novelty, as similar glass devices were implanted previously in animals. It is not specified, however, by whom, and when, these trials were done. The records of the Boston gathering end with a note[24] from the meeting's Secretary, which is equally important for our discussion. The brief comment reveals that Pellier's proposal was actually known to the great French surgeon Malgaigne who mentioned it in the 1843 edition of his *Médecine opératoire* and also provided the information that this idea had not been applied to animals or human patients. Based on these observations, we assume that in the decade between Malgaigne's note and Deval's letter some experiments must have been performed in France to insert glass keratoprostheses in animal corneas. However, at this stage, we know neither by whom these experiments were done, nor whether they were inspired by Pellier's suggestion.

At the beginning of our century, it was Hirschberg who, as a result of his own search, re-discovered and briefly described Pellier's proposed artificial

19 Burnett, W. J.: "Recommendation of an artificial cornea as a substitute for the transplantation of the cornea", *Extr. Rec. Boston Soc. Med. Improvement* 2, 1856, 69–74.
20 Ibid., p. 73.
21 Day, R.: "Artificial corneal implants", *Trans. Am. Ophthalmol. Soc.* 55, 1957, 455–475.
22 Burnett (n. 20).
23 Hirschberg, J.: *The history of ophthalmology,* vol. 7: *The first half of the nineteenth century (part three),* trans. Blodi, F. C./Bonn, J. P., Wayenborgh Verlag, 1986, pp. 213–217.
24 Burnett (n. 19).

cornea[25]. About the same time, Magitot, in the introduction to one of his early major papers[26], after asserting that previous graft transplantation experiments proved the tolerance of corneal tissue to foreign matter, continues[27]:

> "Resuming an idea that seems to belong to the French oculist Pellier de Quengsy (1789) and which was never put in practice, various authors proposed and attempted in the last half of the nineteenth century the placement in the leucomatous cornea of genuine small prosthetic devices."

Although not referenced, which suggests that Magitot never saw the original text, this statement will contribute essentially to the recognition in the modern times of Pellier's contribution.

Due to the low rate of success of glass or quartz keratoprostheses and following the first successful human penetrating keratoplasty performed in 1905 by Zirm[28], the attention of ophthalmologists was diverted from artificial implants to donor corneal transplants; work on artificial cornea almost ceased during the first half of the twentieth century. The only notable review[29] of this period, covering both penetrating keratoplasty and prosthokeratoplasty, clearly indicates this situation; it also fails to mention Pellier's proposal.

There were three factors which eventually, by the fifth decade of this century, triggered the resumption of development work on an artificial cornea, on a background of post-war increase in disease, dietary deficiency and industrial accidents. Firstly, the limitations of penetrating keratoplasty became more fully appreciated. Secondly, the problems associated with eye banks were recognized. Finally, the introduction of synthetic polymers as keratoprosthetic materials offered new and improved avenues for design and manufacture, and virtually marked the beginning of the modern period in the history of artificial cornea development[30]. The first polymer to be used in

25 Hirschberg (n. 4).

26 Magitot, A.: "Recherches expérimentales sur la survie possible de la cornée conservée en dehors de l'organisme et sur la kératoplastie différée", *Ann. Ocul.* 146, 1911, 1–34.

27 Ibid., p.1.

28 Zirm, E.: «Eine erfolgreiche totale Keratoplastik», *Graefe's Arch. Ophthalmol.* 64, 1906, 580–593.

29 Forster, A. E.: "A review of keratoplastic surgery and some experiments in keratoplasty", *Am. J. Ophthalmol.* 6, 1923, 366–375.

30 Strictly speaking, it was Dimmer who used for the first time, at the end of the last century, a polymer as a keratoprosthetic material (see Dimmer, F.: «Zur operativen Behandlung totaler Hornhautnarben mit vorderer Synechie», *Ber. Versamml. Ophthalmol. Ges. Heidelberg* 20, 1889, 148–163; Dimmer, F.: «Notiz über Cornea arteficialis», *Klin. Monatsbl. Augenheilk.* 29, 1891, 104–105). He made a keratoprosthesis in the shape of a hat from a thin sheet of celluloid, and implanted it into the corneas of four human patients. Celluloid, the first plastic developed commercially in the world, is a blend of nitrocellulose (a modified natural polymer), camphor and stabilising agents, actually not a fully synthetic polymer. It was, unfortunately, not a good choice as a biocompatible material: within four months, Dimmer's devices were extruded from the host corneas. However, this is probably the first attempt ever to use a man-made polymeric material in a biofunctional (i.e., not cosmetic) prosthetic device.

keratoprostheses was poly(methyl methacrylate), better known as Perspex or Plexiglas, an event which was not exempted from historical controversy[31]. The enthusiastic revival of interest in keratoprosthesis research was followed by a significant increase in the number of topical publications; eventually, this brought about the recognition of Pellier's original ideas. In his opening lecture[32] at the 69th Congress of the Ophthalmological Society of the United Kingdom and affiliated societies (1949), the great Swiss ophthalmologist Franceschetti acknowledged Pellier as the first who "had the idea of putting a transparent material in an opaque cornea", indicating Magitot's above mentioned paper as a bibliographic source[33]. Inexplicably, Franceschetti gave 1771 as the year of Pellier's proposal.

As in a chain reaction, all subsequent major reviews on artificial cornea acknowledged Pellier. Most of them employed secondary bibliographic sources, mainly Franceschetti's paper (such as Cardona[34] and Hruby[35]), some perpetuating the incorrect date (1771 instead of 1789). Other authors cited Cardona's paper[36] as a secondary source (Barber[37], Barron[38], Donn and Cotliar[39]). Pellier's proposal was also mentioned in other reviews[40], without any supporting references. Finally, some authors (Day[41], Henderson and Giles[42], Mannis and Krachmer[43]) indicated Pellier's book as a primary bibliographic source, to which they apparently had access. Retrospectively, we can say that Pellier's inspirational idea has eventually received its long overdue recognition.

31 Chirila, T. V./Crawford, G. J.: "A controversial episode in the history of artificial cornea: the first use of poly(methyl methacrylate)", *Gesnerus* 53, 1996, 236–242.
32 Franceschetti, A.: "Corneal grafting", *Trans. Ophthalmol. Soc. U.K.* 69, 1949, 17–35.
33 Ibid, p. 29.
34 Cardona, H.: "Keratoprosthesis. Acrylic optical cylinder with supporting intralamellar plate", *Am. J. Ophthalmol.* 54, 1962, 284–294.
35 Hruby, K.: «Künstliche Hornhautimplantate (Keratoprothetik)», *Wiener Klin. Wochenschr.* 92, 1980, 227–233.
36 Cardona (n. 34).
37 Barber, J. C.: "Keratoprostheses: past and present", *Int. Ophthalmol. Clin.* 28, 1988, 103–109.
38 Barron, B. A.: "Prosthokeratoplasty", in: Kaufman, H. E./Barron, B. A./McDonald, M. B./ Waltman, S. R. (eds): *The cornea,* New York, Churchill Livingstone, 1988, pp. 787–803.
39 Donn, A./Cotliar, A. M.: "Cardona keratoprosthesis", in: Hornblass, A./Hanig, C. J. (eds): *Oculoplastic, orbital, and reconstructive surgery,* Baltimore, Williams & Wilkins, vol. 2, pp. 1271–1286.
40 See Tudor Thomas, J. W.: "Considerations affecting technique and results in keratoplasty", *Trans. Ophthalmol. Soc. U.K.* 75, 1955, 473–513; Leibowitz, H. M./Trinkaus-Randall V./ Tsuk, A. G./Franzblau, C.: "Progress in the development of a synthetic cornea", *Prog. Retin. Eye Res.* 13, 1994, 605–621.
41 Day (n. 21).
42 Henderson, J. W./Giles, C. L.: "Keratoprosthesis: current status", *Am. J. Med. Sci.* 253, 1967, 239–242.
43 Mannis, M. J./Krachmer, J. H.: "Keratoplasty: a historical perspective", *Surv. Ophthalmol.* 25, 1981, 333–338.

The Concept of a Porous Prosthetic Skirt

In spite of the extensive, albeit delayed, recognition of Pellier as the first ophthalmologist ever to propose an artificial cornea, none of the authors mentioned his additional suggestion concerning a porous prosthetic rim, likely because of the unavailability of the original text. The very few who apparently had access to Pellier's text either did not expand their reading too far, or, probably, did not find the idea interesting.

Ever since the revival of keratoprosthesis research in the fifth decade of this century, some devices were developed having supporting plates (or flanges) around the transparent optical cylinder, which were perforated or fenestrated, or made of meshworks. It was hoped that the voids provided will facilitate the growth and integration of the host tissue into the peripheral zone of keratoprosthesis. Generally, these core-and-skirt devices did not improve significantly the clinical outcome of prosthokeratoplasty, as the large holes in the plates did not encourage the tissue proliferation much better than a non-perforated plate. Perhaps, if they had been aware of Pellier's suggestion of pores, these workers would have obtained different results, although we do not know what size Pellier envisaged for the pores. It seems that simple perforations in the prosthetic skirt are not sufficient for improving the maintenance of an artificial cornea. The host tissue should blend with, or integrate into, the prosthetic skirt in order to induce a tight interpenetration between them. This idea was expressed for the first time by Salzer[44], in describing what we call now biointegration:

> "Finally, the question arises whether it would not be better to use in the manufacture of the [prosthetic] frame a material which is not completely insoluble, but one which is able, to a certain degree, to promote scar formation. For, the single reason presently recognized as causing, in principle, the impossibility to carry out artificial corneal replacements is not the proliferation of tissue around the frame, but its disappearance."

Although closer to our time of rapid exchange of scientific information, Salzer, who talked about biointegration but not about peripheral pores, was ignored by his colleagues, as was Pellier much earlier, who advocated the pores but was not able to deal with the concept of biointegration. Metaphorically, their ideas came together at the end of the 1980s, when some research groups developed and experimented core-and-skirt keratoprostheses with porous polymeric skirts[45]. There is no proof, however, that this modern concept was inspired by Pellier's or Salzer's ideas.

44 Salzer, F.: «Beiträge zur Keratoplastik V. Zur Biologie der Hornhautverpflanzung», *Arch. Augenheilk.* 101, 1937, 450–481.

45 See Chirila, T. V.: "Modern artificial corneas: the use of porous polymers", *Trends Polym. Sci.*, 2, 1994, 296–300; Chirila, T. V.: "Artificial cornea with a porous polymeric skirt", *Trends Polym. Sci.*, 5, 1997, 346–348.

Conclusion

The material presented in this paper should help us to achieve a better understanding of Pellier's place in the history of artificial cornea. Although his work did not inspire directly the subsequent research, this study leaves one in no doubt that Pellier de Quengsy was the first to envision the possibility of replacing an opaque cornea, and to propose an essentially correct design for an artificial cornea. This study also demonstrates, for the first time, that Pellier suggested a porous periphery in an artificial cornea, an idea which is the foundation of contemporary keratoprosthesis research.

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