M. Soledad Cortina
Jose de la Cruz
Editors

Keratoprostheses and Artificial Corneas

Fundamentals and Surgical Applications

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Foreword

Why do we need an artificial cornea – a keratoprosthesis – when standard corneal transplantation (PK) is so easy to perform surgically and is so time-tested and well established? After all we have learned over a century how to prevent infections, suppress postoperative inflammation, and now effectively replace diseased corneas layer by layer.

Is that not enough? No – and the reason is related to the exaggerated notion we often have of the long-term outcome for PK, worldwide. In the affluent developed world, PKs are largely performed for endothelial dysfunction in eyes with little inflammation, and here the 5-year outcome with clear grafts seems to be in the range of 60–90 %, depending on where performed. In developing countries, where 90 % of the corneal blind live, corneal damage tends on the average to be much more severe and the eyes more inflamed. There, outcomes after PK (when resources allow) are poorly documented but tend to be dismal long-term. Also, worldwide, severe chemical burns and autoimmune diseases are rarely helped by corneal allograft.

Thus, for a large portion of the world's cornea blind, probably at least 100,000 new cases per year, a PK cannot restore vision even if repeated, and we clearly need a simple and inexpensive back-up "rescue" procedure of some kind. Here a keratoprosthesis should have a prominent place, but other alternatives are also being pursued such as stem cell transplants or buccal mucosa, followed by keratoplasty, or tissue constructs, scleral contact lenses, etc.

The concept of a keratoprosthesis as a definitive sight-restoring solution for a severely opaque cornea is quite obvious, but throughout history it has been very difficult to implement safely. Infection, tissue melt, glaucoma, retinal detachment, and even total loss of eye have been frequent. Not until the last two decades has it become justified to implement keratoprosthesis surgery on a routine basis in PK failures. Still, credit should go to many past surgeons with bright minds who have patiently added building stones toward what we have now.

Thus, keratoprosthesis implantation has now been developed into an at least moderately safe procedure for the long-term, except in autoimmune diseases and other heavily inflammatory situations. It has become included in recent ophthalmic textbooks, but it has not previously been the subject of a single monograph. This void has now been filled by this elegant treatise, ably edited by Drs. Cortina and de la Cruz, in which basic surgical and

epidemiological aspects are covered in depth by experts. The participants should be congratulated for producing a detailed surgical guide as well as what should be a profound basis for the next generation's developmental work in this rapidly expanding field. We have to realize that we have so far reached only a few steps in this very promising area. We should encourage coming generations of clinician-scientists to translate our present insights into applying KPros on a massive sight-saving scale – especially in the developing world. This monograph will serve as a great inspiration!

Claes Dohlman
Harvard Medical School
Boston, MA, USA

Preface

Visual rehabilitation is a major challenge in those patients whose damaged or diseased cornea is not amenable to penetrating keratoplasty. For over two centuries, those engaged in the field of artificial cornea have tried to address these important challenges. In recent years, we have seen a tremendous step forward that makes us believe we finally have options to offer patients suffering from corneal blindness.

The history of keratoprosthesis spans from the initial work of French ophthalmologist Guillaume Pellier de Quengsy (1751–1835), who first described the concept of an artificial cornea in 1789, to modern advances in integrated and nonintegrated keratoprostheses from such luminaries as José Ignacio Barraquer Moner, Hernando Cardona, Benedetto Strampelli, Giancarlo Falcinelli, and Claes Dohlman. Throughout this time, different keratoprostheses have seen their fair share of successes and failures. In the last three decades, advances in corneal transplantation techniques, instrumentation, identifying risk factors, and modifications in current keratoprosthetic devices have helped improve the long-term outcomes for patients who would otherwise have little to no options of visual rehabilitation.

As improvements in keratoprosthesis surgery have occurred, a unified source of knowledge has become necessary to assist future keratoprosthesis surgeons. Additionally, keratoprosthesis surgery is becoming a standard procedure in most academic institutions. This book is the first comprehensive textbook dedicated solely to keratoprosthesis surgery. It offers an in-depth review of all keratoprostheses in use today. Special attention is given to the Boston Keratoprosthesis (KPro), which has become the most commonly used artificial cornea in the United States and worldwide under the stewardship of Claes Dohlman, MD, PhD.

We are deeply grateful to all the contributors, who have so generously shared their experiences and insight in this book, which we hope will help other cornea surgeons in their journey through the field of the artificial cornea. Our goal was to make this book a standard reference that provides the technical expertise acquired by years of experience, and we are very proud to have contributions by such a distinguished group of authors.

We would like to thank Springer for its support of this edition in what we hope will be the main reference source of keratoprosthesis surgery.

In closing, we would like to thank our spouses, Agustin and Sylvia, for their continuous love and support throughout the many long hours of work, which has allowed us to dedicate the time needed to accomplish this project, and to our children Benjamin, Nicolas, Tobias and Francisco, and Javier and Gabriella, to whom we dedicate this book.

Chicago, IL, USA
April 2014

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Part I

Introduction and History of PKP and KPRO

The History of Keratoplasty: A Brief Overview

1

Mark J. Mannis

Contents

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The histories of keratoprosthesis and corneal allograft (penetrating keratoplasty) are complex and intimately intertwined. Of the two procedures, keratoprosthesis predates penetrating keratoplasty by almost a century and, as such, plays an important role in the development of corneal transplantation. For the contemporary corneal surgeon interested in keratoprosthesis surgery, understanding the historical landmarks of both keratoplasty and prosthokeratoplasty is important to the recognition of the obstacles we face to finding a successful artificial cornea.

1.1 Keratoprosthesis and Keratoplasty

The history of keratoprosthesis will be covered in detail in a subsequent chapter. However, the story of corneal transplantation begins with the notion of an artificial replacement for the opaque cornea. As such, any history of penetrating keratoplasty must open with a description of the earliest concepts for replacement of the opaque cornea, using a corneal prosthesis.

While the notion of restoring clarity to an opaque cornea appears as early as 200 AD in the writings of Galen, the first mention of trephination of the cornea to create an opening and the placement of a clear prosthesis emanated almost simultaneously in the late eighteenth century from England

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Fig. 1.1 Erasmus Darwin (1731–1802) (Image courtesy of Mannis and Mannis [1])

and France. In 1795, Erasmus Darwin (Fig. 1.1) theorized that a central corneal opacity could be removed with a quill serving as a trephine and that a bit of glass shaped like shirtsleeve stud could be placed into the hole made by the quill, serving as a clear window [2]. There is, of course, no evidence that Darwin ever attempted this procedure. Across the English Channel in Montpellier, France, Guillaume Pellier de Quengsy, a surgeon renowned for his cataract surgery, published a monograph on ophthalmic surgery in which he described in great detail a glass corneal prosthesis along with an array of surgical instruments used in its implementation [3] (Fig. 1.2). There is very scant evidence to suggest that this was actually performed.

There are several books and papers that provide detailed reviews of the history of penetrating keratoplasty. In this brief chapter, we can only touch on some of the highlights, but the reader is encouraged to explore other sources for more detailed information [1, 4–13].

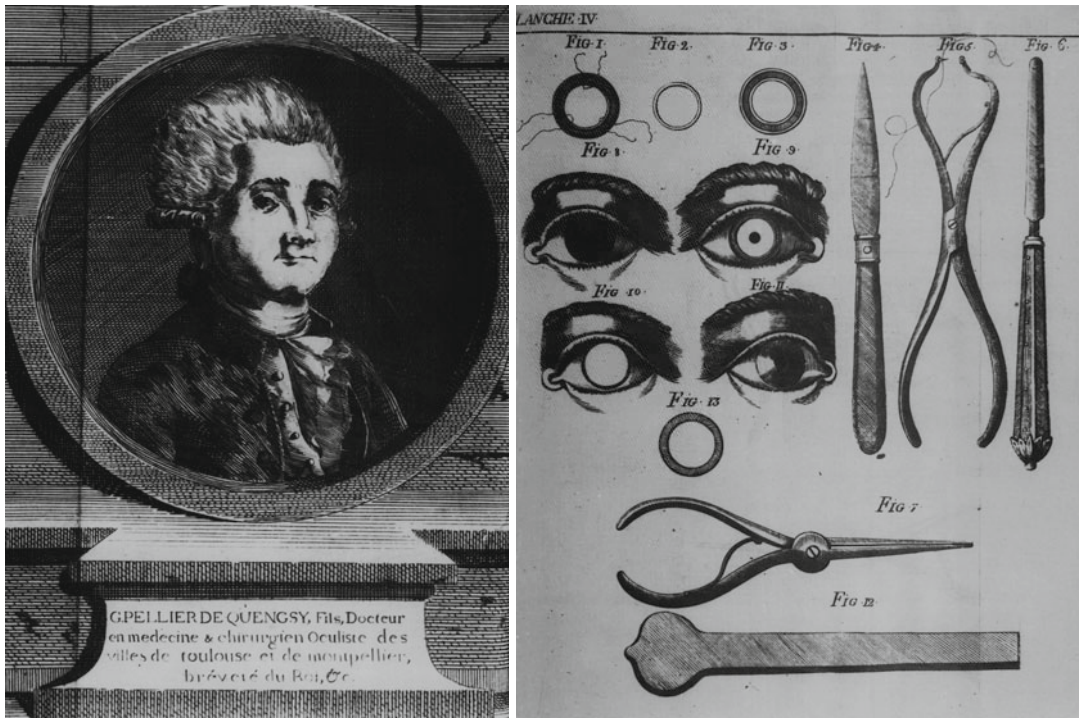

Fig. 1.2 Guillaume Pellier de Quengsy (*left*) (1751–1835) and his instrumentation (*right*) for prosthokeratoplasty (Image courtesy of Mannis and Mannis [1])

1.2 Keratoplasty: Experimentation in the Nineteenth Century

If the end of the eighteenth century witnessed the vision of prosthokeratoplasty, the first half of the nineteenth century was a time of intense experimentation. There is considerable controversy over who first replaced the opaque cornea with living donor tissue. In 1813, Karl Himly (1772–1837) first suggested replacement of the opaque human corneas with clear animal corneas. However, Franz Reisinger (1768–1755) is generally given credit for the first graft, and he coined the term "keratoplasty," a term he used to describe the replacement of the cornea with animal tissue (1824) [14].

Johann Dieffenbach (1792–1847), also recognized as the father of strabismus surgery, documented extensive animal experimentation with keratoplasty in chickens, rabbits, and doves, but concluded that corneal transplantation was in the realm of fantasy [15]. Optimistic reports by Thome stimulated the Irish ophthalmologist Samuel L.L. Bigger to travel to Germany to learn the techniques firsthand. His capture by Sahara Bedouins in 1837 led to a series of experiments during his captivity in which he used the direct suturing of homografts in gazelles [16]. The grafts were relatively successful, but Bigger did not appreciate the significance of the use of homograft material or the value of direct appositional suturing.

After the first three decades of experimentation in the nineteenth century, interest in the feasibility of keratoplasty declined, largely due to discouraging results. There was a concomitant resurgence of interest in the keratoprosthesis with the discouraging results of keratoplasty, and in the 1850s and 1860s, Nussbaum, Heusser, and von Hippel, among others, devised and employed glass keratoprostheses which they implanted in patients with varying degrees of temporary success [17].

However, it was the work of Arthur von Hippel, a strong advocate of lamellar keratoplasty, who profoundly altered the keratoplasty procedure (Fig. 1.3). Unfortunately, von Hippel was an advocate of heteroplasty, and his work

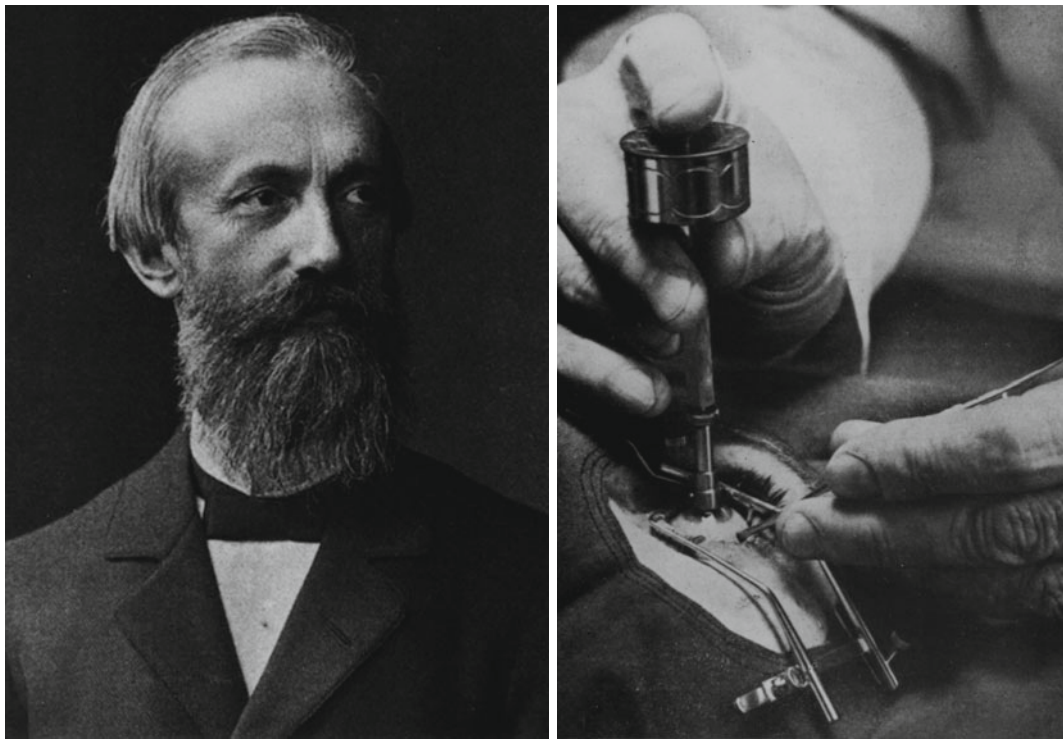

Fig. 1.3 Arthur von Hippel (*left*) (1841–1916) and his mechanized trephine (*right*) (Image courtesy of Mannis and Mannis [1])

bolstered the trend to xenografting. Nonetheless, he made a major contribution to the technique of keratoplasty by inventing a mechanized trephine that greatly improved the procedure from a technical/surgical standpoint [18, 19].

In 1872, Henry Power (1829–1911) reported both xenografting from rabbits to humans and human allografts with some degree of success. His report stimulated renewed interest in tissue transplantation. Ernst Fuchs (1851–1930) reported a series of 30 penetrating grafts with poor results, using both animal and human tissues. Despite the fact that he recognized the superiority of human tissue as graft material, xenografts, with marginal success, continued to dominate the field into the first decade of the twentieth century [20].

What the nineteenth century demonstrated was a storm of creativity in corneal replacement that was limited primarily by a lack of understanding of basic physiology including the role of the corneal endothelium and basic function of the immune system in graft rejection. No doubt, the lack of suitable technology, the von Hippel trephine notwithstanding, also hampered successful keratoplasty. This would begin to change rapidly at the beginning of the twentieth century.

Fig. 1.4 Eduard Konrad Zirm (1863–1944) (Image courtesy of Mannis and Mannis [1])

1.3 The Early Twentieth Century: Successful Penetrating Keratoplasty

The turning point for penetrating keratoplasty came from an unlikely place—a small town in Moravia far from the great centers of European medical science. The now celebrated successful penetrating graft performed by Eduard Konrad Zirm (1877–1944) defined the principles of modern corneal transplantation [21] (Fig. 1.4). Using the cornea from the enucleated eye of an 11-year-old boy, Zirm performed bilateral penetrating grafts in a 45-year-old farm worker who had sustained bilateral alkali burns 16 months earlier. Although this was his only reported case, Zirm defined the basic requirements for successful penetrating keratoplasty including the exclusive use of human donor tissue, strict asepsis, the avoidance of antiseptic agents in contact with the donor cornea, protection of the graft using gauze moistened with physiologic saline, the use of overlay sutures, and the judicious selection of cases. Despite his report, lamellar grafting continued to dominate the field for the next two decades.

The importance of Zirm's case report with his articulation of surgical principles was its influence on the great schools of ophthalmic clinical science including the work of Tudor Thomas in England in the 1920s, Anton Elschnig and colleagues in Prague, and Vladimir Filatov in Odessa [22, 23]. Both Elschnig and Filatov had been advocates of lamellar keratoplasty. However, with the report of Eduard Zirm, they turned to partial penetrating keratoplasty.

It was Elschnig (1863–1939) who reported successful penetrating keratoplasty in 1914 (Fig. 1.5). His series of over 180 transplants reported a 22 % success rate, and he defined many of the principles of pre-, intra-, and

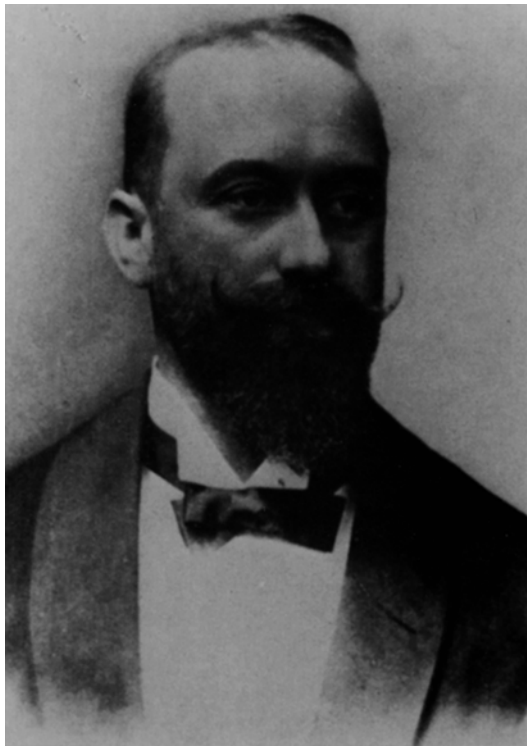

Fig. 1.5 Anton Elschnig (1863–1939) (Image courtesy of Mannis and Mannis [1])

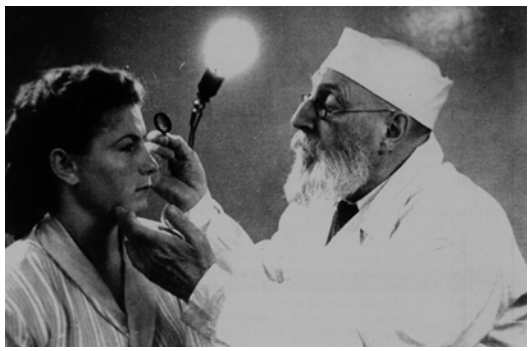

Fig. 1.6 Vladimir Filatov (1875–1956) (Image courtesy of Mannis and Mannis [1])

postoperative management of penetrating grafts [24]. In Odessa, Vladimir Filatov (1875–1956), encouraged by the reports from Elschnig in Prague, studied penetrating keratoplasty systematically (Fig. 1.6). During a career in which he performed over 3,000 corneal transplants, he devised novel instrumentation, advocated direct suturing techniques, first employed cadaver corneas presaging the development of eye banks, and appreciated the importance of the ocular surface by protecting the graft with an egg membrane [25, 26]. The innovations of Elschnig, Filatov, and others in the 1930s and early 1940s began to define the surgical principles that would lead to successful penetrating keratoplasty.

1.4 The Mid-Twentieth Century: Refinement, Standardization, and the Spread of Keratoplasty

While there were many important figures whose names resonate in the history of keratoplasty including Paufique and Charleux (France), Tudor Thomas and Rycroft (UK), Arruga and Barraquer (Spain), Imre (Hungary), Franceschetti (Switzerland), and Vannas (Finland), the focus of keratoplasty moved in large part to the United States.

Ramon Castroviejo (1904–1989), a mercurial Spanish ophthalmologist who moved to the United States in 1929, became a strong vocal advocate of penetrating keratoplasty (Fig. 1.7). A prolific surgeon practicing in New York City, Castroviejo made numerous innovations in surgical instrumentation, which became standard implements in keratoplasty still employed today. The miniaturization of instrumentation anticipated the introduction of the operating microscope, which would only become used two decades later. Castroviejo experimented with different graft shapes and, for many years, employed the signature square graft with considerable success. With complete conversion to direct appositional suturing, the circular graft again became standard in the field [27, 28].

Contemporary with Castroviejo and also practicing in New York City, Richard Townley Paton (1901–1984) founded the first eye bank, the Eye-Bank for Sight Restoration [29] (Fig. 1.8). The quiet but deliberate Paton who had trained with Wilmer at Johns Hopkins dedicated much of his professional life to the concept of eye banking, beginning with collecting tissue from executed prisoners to the founding of a public institution, which

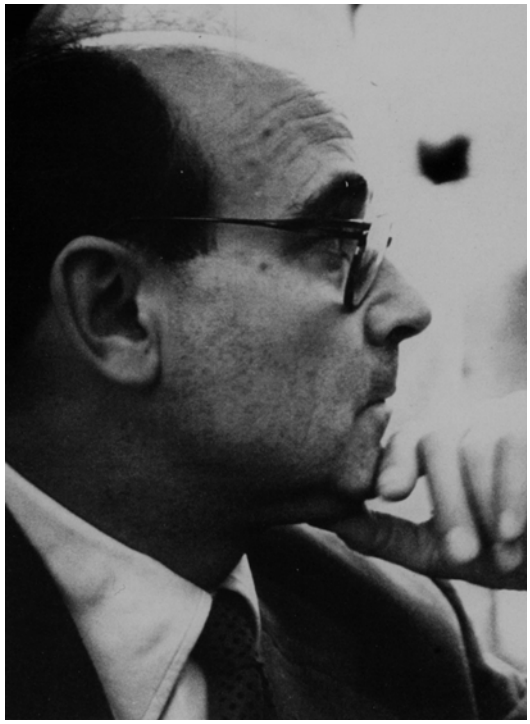

Fig. 1.7 Ramon Castroviejo (1904–1987). (Image courtesy of Mannis and Mannis [1])

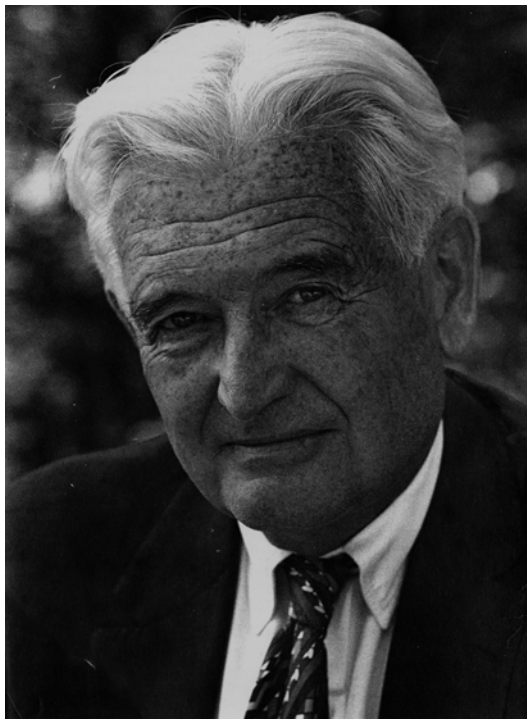

Fig. 1.8 Richard Townley Paton (1901–1984) (Image courtesy of Mannis and Mannis [1])

eventually stimulated the most successful and productive eye banking system in the world. Paton founded the eye bank in a period amidst considerable public criticism and controversy but recognized the importance of a source of reliable, safe, and equitably distributed tissue for transplantation.

1.5 The Second Half of the Twentieth Century: Biological and Technical Refinements

Keratoplasty was met with increasing success over the latter half of the twentieth century. Two important biological insights enabled increasing success. One was a clear appreciation of the function of the corneal endothelium in the maintenance of corneal clarity. The work of David Maurice and others in this realm significantly changed the way in which corneas were handled by surgeons and greatly boosted the success of corneal grafting.

The work of Medawar and colleagues elucidated the basis of immunologically mediated graft rejection, and the "maladie du greffon" (graft sickness) was identified as a phenomenon of immunity. The reports of Edward Maumenee and Ali Khodadoust describing and defining the clinical entity of graft rejection eventually led to the employment of immunosuppressive agents [30]. The use of topical corticosteroids, introduced by Maumenee, revolutionized penetrating keratoplasty.

In the 1960s, Richard Troutman and Dermot Pierse introduced the operating microscope to ophthalmic practice. In combination with the microscope, the further miniaturization of instrumentation and the introduction of monofilament nylon sutures in the 1970s greatly enhanced the technical success of corneal surgery. Other developments in ophthalmic surgery, such as the introduction of viscoelastic agents, further enhanced the efficacy of penetrating keratoplasty by protecting the endothelium during the surgical procedure.

Technical advances were not limited to the pre- and intraoperative phases of keratoplasty. Corneal astigmatism post-keratoplasty was recognized as a major obstacle to functional vision