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Emergent innovation systems and the delivery of clinical services: The case of intra-ocular lenses

J.S. Metcalfe, Andrew James, Andrea Mina *

CRIC, ESRC Centre for Research on Innovation and Competition, University of Manchester, Oxford Road, Manchester M13 9PL, UK

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Abstract

This paper is an exploration of the dynamics of technical change in medicine. We argue that innovation in medicine is a process that is distributed across time, space and epistemic and institutional domains; that it entails the entrepreneurial effort of creative individuals as well as the emergence of correlated understanding among heterogeneous agents whose rules of interaction are contingently instituted in socio-economic systems along unfolding scientific and technological trajectories. We illustrate our arguments through an in-depth analysis of a major ophthalmologic innovation – the intra-ocular lens – that has literally transformed the treatment of cataract in the developed world and has the potential to do so in many developing countries. We investigate the advancement of clinical knowledge about the disease, the development of effective technological capabilities and the co-evolution of the supply capacity and demand of a micro-innovation system emerged along a specific sequence of interrelated problems, and associated solutions, which engaged scientists, technicians, practitioners, regulators and patients alike over a period of around three decades.

Keywords: Innovation systems; Distributed processes; Post-innovation improvements; Medical knowledge; Technological trajectories

1. Introduction

In this paper we trace the development of a radical innovation in the field of ophthalmology, the intra-ocular lens, an innovation that has already transformed the treatment of cataract in the developed world and has the potential to do so in many developing countries (Apple et al., 2000).[1] The cost of this form of visual impairment is immense in terms of loss of human functioning and well-being and in terms of

* Corresponding author. Tel.: +44 161 275 7371.
E-mail address: stan.metcalfe@man.ac.uk (A. Mina).

[1] In 1998, for example, an estimated 4.7 million intra-ocular lenses were implanted worldwide (Hamilton, 2000). Worldwide, it is estimated that some 25 million people are blind while over 110 million suffer from visual impairment due to the presence of cataract.

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lost output in economies, many of which are seriously underdeveloped.[2] The purpose of the paper is to recount the development of the intra-ocular lens not only in its own terms but rather as a peg on which to hang a number of central issues in our understanding of the central role that innovation and the accumulation of new knowledge play in modern capitalism.

We begin by emphasising the fundamental importance of personal and private knowledge existing as electrochemical patterns in individual minds and publicly represented and communicated as information which may or may not be appropriated by enforcement of property rights. What makes possible the coordinated action on which society and economy depend – we argue – is the spread of correlated knowledge between the relevant groups of individuals, that is to say, the emergence of understanding in common so that instructions and questions elicit common answers and common practices in the contexts where activities depends on social interaction (Metcalfe, 2002). The development of the intra-ocular lens is precisely a case of the growth of correlated knowledge in which the original idea and innovation have been diffused worldwide. Because this is a socio-economic problem, it reflects the organisational and instituted contexts in which knowledge grows, in laboratory and clinic, and in the wider society in which the application of knowledge meets a medical need. The several environments and rules of the game in which clinicians developed lenses and operating procedures have influenced greatly the rise to maturity of the overall technology, and we explore these influences in terms of the development of the invention and innovation systems for this procedure. Parallel to and inseparable from the growth of knowledge is the growth of a supply capacity to deliver a new medical service and this dimension connects, inevitably, to the growth of the market and the extension of the division of medical labour. Commercial investments in a new technology are only sustainable if the market supports the necessary returns, and so the development of demand and the role of regulation in instituting demand play an important part in the story.

Yet, as with all radical innovations, the full impact of the intra-ocular lens only follows from the development and the adoption of long sequences of innovations in materials, techniques, equipment and drugs. This sequence is generated within the context of an innovation diffusion process whereby diffusion induces further innovation to define an emergent trajectory of learning and discovery. This process lasted over 40 years from the first implant to the establishment of a standardised procedure on a large scale throughout the advanced nations. Why this was so reflects the nature of the problem sequence and the organisational, institutional and cultural context in which each solution opened up unintended consequences, and thus new problems toward the solution of which creative effort was allocated. Moreover, the context in which problems were identified was inseparable from the extension of clinical practice. Like all medical innovations, application to the human body is a matter of engineering not of science; as with all engineering innovations, feedback from practical application is of the essence of the development of reliable knowledge (Vincenti, 1991). Such knowledge grows in experimental and autocatalytic fashion, as one problem leads to another in the minds of the different individuals who compose the invention and innovation system. In the process, multiple competing solutions are generated and are selected vicariously or by practical trial and error processes.[3] Thus, we employ a frame of reference in which the growth of knowledge is an evolutionary adaptive process, constrained and encouraged by instituted relationships that co-evolve with the growth of knowledge and its application.

It is also central to our argument that invention and innovation systems are not to be presumed, their emergent properties have to be explained. The organisations and individuals from which systems are constituted and the way in which these ‘components’ are interconnected, that is to say instituted, have to be explained with a purpose in mind. In many cases, connection

[2] In terms made familiar by Amartya Sen, the activity of the restoration of sight brings the promise for great improvements in human capabilities, improvements not captured accurately by conventional measures of economic output (Sen, 1999).

[3] It is fundamental to keep awareness that not all the methods have proved to be successful, and, in many cases, lenses have had to be removed or, in extreme cases, eyesight has been lost. As with many medical procedures, the experimental costs are necessarily born by the patients. As a consequence, the risks of any procedure raise questions about the efficacy of regulatory procedures whether by the community of practitioners or by the State.

arises through the self-organisation of knowledge generating processes among like-minded practitioners. In other cases, it arises through the leadership of firms, and in others through the role of government. What we find in the intra-ocular case is that the modes of organisation of the invention and innovation system evolved over time and that the principle cause of the reorganisation was the change in the nature of the innovation problem sequence.[4]

An emphasis on the distributed nature of invention and innovation processes has already had an impact on the study of medical innovation. Blume (1992) and Gelijns and Rosenberg (1995) have characterised the innovation process in medical devices in terms of the interaction between multiple disciplines and multiple agencies with close relations emerging between firms, clinicians and academic scientists. Similarly, Blume's study (1995) of the cochlear implant is concerned with the development of institutional structures to evaluate the feasibility of new devices when their efficacy is strongly contested. The subsequent work of Gelijns and Rosenberg (1999) on CRT scanners, magnetic resonance imaging and endoscopy, makes a clear distinction between the conditions of invention and the conditions that influence the translation of devices into a commercially viable industry. In their account, the strength of local science activity, intellectual property regimes and the characteristics of health care systems play the key explanatory roles.[5]

One rather systematic aspect of medical innovation is the pervasive role of science–industry interfaces. This is in its own rights an increasingly central theme in the innovation literature and although it is not the purpose of this paper to provide an extensive account of such a wealth of contributions, it may nonetheless be useful to recall a few points of relevance to this work as raised in recent studies. In his review of the literature, Carayol (2003) appreciates and explores the great variety of modes of science–industry collaborations. So does Murray (2002), who discusses the co-evolutionary nature of scientific and technological developments in tissue-engineering research. She finds that formal and informal interactions between universities and firms are very intense and contribute to the formation of relatively durable cross-community networks. This is consistent with Meyer-Krahmer and Schmoch's (1998) results on the role of informal and bi-directional knowledge exchanges between universities and industries. Etzkowitz (1998) explores the shifting attitudes of public science employees towards collaboration with industry and refers to the ongoing process of mutual adaptation linked to the emergence of entrepreneurial universities. The tacit, reciprocal, and vastly unrecorded component of science–industry interaction is stressed again by Meyer (2000) while McMillan et al. (2000), confirming the validity of previous studies (see for example Narin et al., 1997), provide quantitative citation-based evidence of an increasing reliance of technological developments on public science.

The case of intra-ocular lenses (hereafter IOL) points to the complexity of these interactions and their shifting nature along emerging, hence non-deterministic, trajectories of innovation (Dosi, 1982). In this case, however, while the changing private vs. public nature of the institutions involved in the innovation process reflects a fundamental aspect of science–industry collaborations mentioned above, institutions involved in the delivery of health services also appear to be fundamental components of the innovation system. We will therefore emphasise the role of clinical practice, which mainly resides in hospitals and heavily relies on direct experience, trial-and-error learning and personal knowledge, over abstract scientific knowledge. As a consequence, instead of focusing on university–firm interactions, and the relation between scientific and technological knowledge, we will stress the co-evolution of clinical knowledge and the technological capabilities, coupled with the supply capacity, of the medical innovation system.

We attempt to do so in the following way. The innovation problem sequence of the IOL serves as our probe, which we use to interrogate the technical literature, and guide the interview process with firms, clinicians, surgeons and hospital managers. The method is comparative and historical and combines qualitative and quantitative data extracted from a variety of primary and secondary sources. Beside the relevant medical literature and the interview materials,

[4] Innovation problem sequences are reflected, in good part, in the birth, growth, stabilisation and decline of the innovation systems organised around them; again, this is in part a question of evolutionary adaptability (Coombs et al., 2003; Tether and Metcalfe, 2003).

[5] That innovation processes are distributed is common to all of these accounts; that distributedness is a problem in epistemological, organisational, institutional and cultural dynamics is less well understood, and forms one focal point for this paper.

national surveys on technology diffusion have been consulted for the US and UK. Furthermore, two datasets, one of papers and one of patents, have been constructed by key-word searches and used to complement the analysis of the epistemic evolution of the problem sequence as profiled in appreciative accounts. The paper dataset includes papers on intra ocular lenses and procedures extracted from the Institute of scientific Information (ISI) covering the period 1965–1999. The patent datasets contains 707 documents of patents granted over the period 1976–2002 extracted from the US Patent Office. Finally, institutional sources (OECD, FDA and NHS documents[6]) have been used to investigate the regulation of ophthalmologic practice, the creation of demand and the nature and constraints of adoption decision.

Before embarking on the detailed account of the invention, innovation and diffusion of the intra-ocular lens, it may help to summarise the main points. The innovation of the IOL has radically transformed the conception, design and delivery of a major medical service, the removal of cataracts combined with their replacement by a functioning lens. This has brought great benefit to countless patients and has greatly increased the efficiency and effectiveness with which the clinical procedure is carried out.[7] It has been achieved by the creativity of individual clinician inventors combined with the development of a transnational medical–industrial complex that has changed radically the innovation system in this field of ophthalmic medicine. A procedure originally based around pioneering 'hero-surgeons' deploying 'craft technique', has evolved into a 'routine, quasi factory' procedure capable of being effected in a local medical centre by clinician nursing staff, whose education and training have correspondingly changed.[8] This is indeed a fundamental transformation of a service activity and its skill base. How this happened is the major concern of this paper.

The rest of the paper is arranged as follows. In part 1, we briefly outline the cataract condition, the 'problem sequence' that the IOL 'solves' and the innovative vision of the pioneer of the procedure, Harold Ridley. In part 2, we trace the evolution of the problem sequence from the work of Ridley's followers to the revolution of foldable lenses. In part 3, we highlight how the emergence of correlated understanding shapes the dynamics of the micro innovation system. In part 4, we explore the relevance of demand and regulation in the development of IOL. Part 5 reflects upon some of the wider implications for the study of sector specific innovation systems.

2. Part 1: innovation and the problem sequence

2.1. The problem of cataract and Harold Ridley's solution

Cataracts, the clouding of the eye's crystalline lens are the most frequent cause of defective vision in later life. Ultimately resulting in blindness, cataracts are severely disabling for otherwise active people and, between the ages of 52 and 64 there is a 50% chance of their occurrence while by the age of 75 some 70% of the population have cataracts. With an ageing population in the world, the significance of an effective cure is not easily overestimated.[9] Although surgical treatment of cataracts dates back to the Middle Ages, and possibly to Egyptian times, until the 1940s the state of the art was so poor that only the effectively blind could benefit from the available procedures, which entailed great risks of infection and collateral operative damage.

At the time of his invention, Ridley was the senior eye surgeon at Moorfields Hospital in London, the then leading eye hospital in the UK. Ridley's contribution entailed the creation of a new surgical technique, the design of a new implant, and the use of new materials.[10] In the first half of the 20th century the dominant operative method followed by cataract surgeons was the

[6] Detailed references are to be found in Section 4.

[7] For the patient, an operation that imposed months of incapacity is now recovered from in a matter of hours. For health services, there has been an enormous increase in capital and labour productivity associated with the increased patient throughput and the ambulatory nature of the modern procedures.

[8] In effect, IOL implants have evolved into a commodity provided in a mass market, albeit a highly regulated one, that mixes public and private provision in different proportions according to country.

[9] Although ageing is the major factor in cataract formation (senile cataracts), it is evident that their incidence is also influenced by lifestyle factors (smoking and alcohol consumption), the use of particular drugs (steroids), diabetes and exposure to UV radiation (West and Valmadrel, 1995). Some cataracts in young people have genetic causes and occasionally the eye's lens has to be removed for other reasons as with traumatic injuries.

[10] We might say, following Usher (1929), that he followed a process of cumulative synthesis to realise his invention.

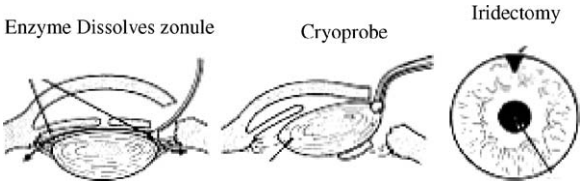

Fig. 1. Intracapsular cataract surgery.

intra-capsular cataract extraction (ICCE) procedure in which the entire lens is removed within its capsular bag (see Fig. 1). Ridley had formed the view that ICCE was a technique inferior to the alternative of extra capsular cataract extraction (ECCE), in which the lens capsule is left in situ, and his key insight involved inserting the plastic lens into the capsular bag. Crucially, he believed that the prevailing lens extraction procedure was 'but halfway to a cure which is complete only when the lost portion is replaced' (Ridley, 1951, p. 617).[11]

The choice of PMMA (acrylic) as the lens material is an instructive example of the role of the unexpected in the innovation process. Wartime injuries to pilots had indicated that perspex 'shrapnel' would lie 'inert' in the eye, producing minimal pathological or chemical reaction.[12] Here there was an ideal material, inert, and light (almost the same specific density as eye fluid). Yet, industrial perspex clearly would not do as it contained too many impurities, so, lacking the requisite chemical knowledge, Ridley joined forces with John Pike of Rayner and John Holt of ICI to develop 'Perspex CQ' (Clinical Quality) a suitably purified form of PMMA. Ridley, Pike and Holt, collaborated on the use of ECCE technique, the design of the rigid lens, its manufacture from PMMA (Perspex), and the insertion of the lens in the posterior chamber of the eye. The three worked together in secret and on a non-commercial basis (for fear of the wrath of fellow clinicians) and Rayner agreed to manufacture the lens and supply them on a cost only basis.[13] Ridley implanted the first IOL in a 45-year-old woman on 29 November 1949 and within the following 17 months treated another eight cases with the ECCE technique. When he announced his results to the British Ophthalmic Community Conference in Oxford in 1951, not unexpectedly, the response from leading eye surgeons was almost uniformly hostile.

2.2. Technical hurdles and opposition

The nature of the professional hostility to this innovation is an intriguing aspect of the story and it is not entirely irrational. Ridley's IOL was a double innovation in terms of conception and surgical procedure, it was a radical alternative to established practise and it challenged an established viewpoint that cataract extraction using ICCE was the best that could be achieved. As a new technique, it placed great demands on the skill of the surgeon and created major risks during and after the operation. Furthermore, in the early years the first lenses were too thick and heavy.[14] Furthermore, they were turned by hand and, consequently, varied from copy to copy. No method existed for sterilising the lens, thus post-operative inflammation posed severe limitations to the success of the new surgical practice.[15] Dislocation (the slippage of the implant out of the line of sight), primarily due to damage to the posterior capsule or zonule during surgery, constituted another major problem that was not solved satisfactorily for many years.

Cataract surgery is not a theoretically grounded science, theory does not predict how an individual patient will respond to any method, so it is not entirely unreasonable that experience should dominate the worldview of its practitioners or that professional reaction is conservative.[16] Furthermore, the question arises of

[11] There was a general presumption among the ophthalmic community of the time against inserting foreign bodies in the eye. However, there was at the time a partial exception to this rule, the plastic contact lens, invented in the 1930s, a device that is placed on the eye and is removable at will. Ridley's lens was also of plastic, though it was placed in the eye and was permanent. It is clear that Ridley was well aware of the design and use of plastic contact lenses and he was known to be turning them on a lathe in 1946 as an alternative to a moulding process (Ridley, 1946). No doubt, his general inventive awareness provided him with important complementary knowledge.

[12] Apparently, Ridley was mistaken in this conclusion in that most aircraft canopies were made of glass, which is equally inert. However, the general conclusion turned out to be correct.

[13] Here we find the first tentative shaping of a local distributed innovation process, bringing together the complementary capabilities of the clinician, the technician and the industrial chemist.

[14] A Ridley lens was 2.4 mm thick, and weighed 108 mg, compared to the latest generation of lenses, at the time of writing, that are 1 mm thick and weigh 15 mg (Patel et al., 1999).

[15] This problem was not solved until 1957 when Ridley introduced caustic soda as the medium for sterilisation.

[16] On the conservatism of craft technologies see Martin (2000). As with many medical procedures it is a matter of engineering in a heterogeneous environment.

the intergenerational distribution of risks and benefits associated with a new procedure whereby the risks born by patients in early experiments is more than compensated in the long run by the increasing aggregate benefit of future patients. Value judgments may differ widely. This is precisely the dilemma that the rules and norms of the profession are meant to deal with and these rules, as accumulated social capital sunk in the profession, will constrain and channel the acceptance of new methods to make life difficult for innovators. In the case of Ridley, opposition was so strong that by the late 1950s he was close to abandoning the implantation of IOLs.[17]

Yet, Ridley's innovation did ultimately sweep the world and he was awarded one of the last English Knighthoods of the Second Millennium for 'pioneering services to cataract surgery'.[18] By the end of the 20th century the IOL had become the standard complement to cataract surgery which itself had become one of the most frequently performed outpatient operations in the advanced industrial world (Linebarger et al., 1999). A major survey of the histopathology of IOLs opines that, 'lens implantation is among the safest major procedures in modern surgery' (Apple et al., 1984). How and why did this transformation take place? Part of the answer is provided by the emergence of a community of IOL practitioners. With a little support from the industry, usually in terms of the limited manufacture of their idiosyncratic lens designs, this group of enthusiast 'hero-surgeons' formed the basis of a series of highly localised micro-innovation systems introducing new variants on a trial and error basis and communicating the outcomes in the professional literature, at conferences and in personal visits to their respective medical centres.

2.3. The eye as a 'design space' and the emergence of a practitioner community

IOLs are not unique in the fact that Ridley's radical invention and innovation has spawned a sequence of incremental innovations and the development of a range of complementary technologies. IOLs are a textbook case of the latent potential implicit in a radical innovation, the identification of a design space that could be explored by other innovators. Indeed, it is only in the light of this subsequent process of exploration that the radical nature of the innovation became manifest. One of the key factors in lens' design is its intended location in the eye and different surgeons were in effect contesting the ideal design location. Fig. 2 illustrates the main options, which are three in number: anterior chamber lenses; posterior chamber lenses located in the capsular bag; iris-supported lenses fixed in front of or behind the pupil.

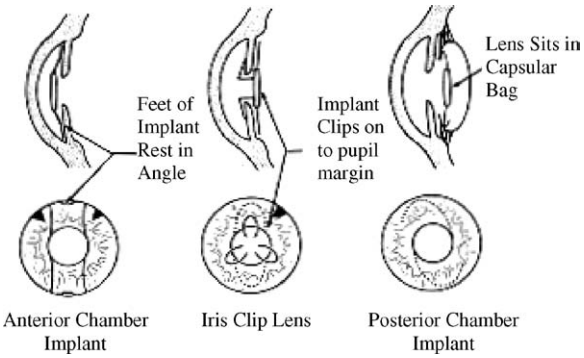

Fig. 2. The eye as a design space: lens implant configurations.

The original Ridley lens was located in the capsular bag within the posterior chamber of the eye and relied on the ECCE operative technique. This was a risky procedure that led to a number of complications, including displacement of the lens, post-operative opacification of the posterior capsule and iris atrophy from contact with the optic. These complications, together with the demanding nature of the technique, encouraged surgeons to experiment with lenses placed in the anterior chamber, the first of which was implanted in 1952 by Baron, and was followed by many other designs.[19] The most significant development here was the placement of the lens in the anterior eye chamber, a different portion of the design space. Strampelli, working in Rome, implanted the first widely accepted anterior chamber lens in 1953. Other clinicians followed his lead, including the eminent Barcelona based surgeon, Barraquer, although by the time he presented his results at the Oxford Conferences of 1956 and 1959, it was

[17] See Duke-Elder (1959) on the scope of professional hostility and Ridley (1964) for evidence of his perception of the opposition encountered and self-evaluation of the results obtained.

[18] Times of London for the 31 December 1999.

[19] Different lens designs were compatible with less demanding surgical techniques, and we find one leading surgeon suggesting that, by comparison, implantation in the anterior chamber 'was child's play compared to Ridley's technique' (Binkhorst, 1959, p. 570).

clear that the anterior chamber lens was creating new design problems. The size and curvature of the lens was crucial to its success although no accurate method existed for measuring the magnitude of the anterior chamber. Consequently, problems arose from the rigid lens touching and irritating the inner surface of the cornea, the endothelium. The resulting corneal dystrophic effect was to undermine the case for anterior chamber lenses but, for a while, they were the ascendant design (Barraquer, 1956, 1959).[20]

The other major development in design was the introduction of iris-supported lenses; the first, in 1953, Epstein's 'collar-stud' lens, followed by Binkhorst's 'iris-clip' lens in 1958.[21] The logic behind the iris clip design was the desire to avoid a major complication of posterior chamber lenses, their propensity for dislocation, and of anterior chamber lenses, the damage they inflicted on the cornea. As Binkhorst expressed the point, 'Therefore I designed an implant which, in a harmless way, is entirely supported by the iris diaphragm and does not touch the angle at all, nor other related structures' (Binkhorst, 1959, pp. 573–574).[22] Between June 1956 and the Oxford presentation of 1959 he had carried out 19 implants and he clearly considered that his design was a major advance on the then prevailing alternatives. However, despite the initial promise and success of this design, long-term, multiple complications in relation to the stability of the lens and iris reaction have lead to their eventual abandonment.[23]

It is clear that in the years immediately following the announcement of Ridley's invention and innovation there occurred a great deal of creative, experimental endeavour. The ferment of inventive activities that was emerging around lens insertion techniques in the early 1960s led to the foundation of the International Intra-Ocular Club.[24] Meeting first in London in 1966, it formed the basis for the identity of the early community and subsequently became the European Society of Cataract and Refractive Surgeons, which now contains over 2500 members in 100 countries and publishes its eponymous journal. Within this community, many other 'hero-surgeons' emerged as inventors cum innovators seeking to improve on Ridley's design. The role of formal and informal interactions taking place within the framework of this community scarcely needs be emphasised. As is rather systematically the case for practice-based disciplines, such as surgery, communication of tacit knowledge via personal connection and direct interaction is pivotal for medical progress to occur. Ophthalmology is no exception. It is largely by personal, tacit and often unrecorded co-operation that individual knowledge comes to be more highly correlated and is built into a body of shared understanding. Shared understanding contributes to the formation of standards and influences the institutional framework in which trial and error experimentation is translated into accepted norms of practice. However, to take this innovation from within its hero surgeon community required much more than the activities of a professional society: it required further distributed innovation of technique, innovation that created a step change in the

[20] Numerous developments occurred to find a solution to this problem including lenses with more flexible haptics, and lenses with open or closed nylon loops to lessen the irritation to the angle of the chamber (Dannheim and Barraquer designs). Choyce made important innovations in his search to improve the Strampelli lens, settling on a design with a rigid lens and flexible loops, and he worked closely with Rayner Ltd. to develop the technology. In 1960, he reported that the improvements in the success of the IOL procedure were due to standardised machine made lenses, better sterilisation methods, more experience in the design of the lens to fit the eye and in the choice of patient (Choyce, 1960). Interestingly, two of his lens designs (the M8 and M9) were the first IOLs to gain approval from the FDA in the early 1970s.

[21] Binkhorst visited Ridley to understand the new methods, implanted copies of his lenses and then, dissatisfied with the size and weight of the early Ridley lens, he began a search for improvements.

[22] The acrylic lens only 0.6 mm thick was placed in front of the pupil and held in place on the iris by wire loops. Also important as a designer of iris clip lenses was the Russian ophthalmologist Fyodorov, the pioneer of radial keratotomy. After correspondence with Epstein he also developed his own design of lens, the so-called 'Sputnik' lens.

[23] In this regard, sketching the stream of successful ideas, artefacts and procedures is as important as recalling attempts that did not succeed because failure is an integral part of evolutionary processes of creative destruction (Metcalfe, 1998).

[24] Interestingly, the competition between cataract surgeons over the best design and location of an IOL did not exhaust the logical possibilities for the treatment of aphakia following cataract surgery. The major competing alternative, the contact lens has already been alluded too above. During the 1950s and 1960s the use of and knowledge about the properties of PMMA contact lenses grew apace. Duke–Elder's text refers to their use, post cataract surgery, as easy and safe. Yet this apparently promising solution failed. Contact lenses are an interesting part of the IOL story for it is clear that without the common notion of a plastic lens the Ridley invention could not have occurred.

possibilities of application. It is to the sequence of innovations complementary to Ridley's that we now turn.

3. Part 2: the evolution of the problem sequence

3.1. The next steps

No innovation takes place or diffuses in isolation and the determinants of success for new medical procedures often reside in the development of complementary techniques, drugs and devices. This is certainly the case for the IOL. Of all the developments that have transformed Ridley's innovation and operative method into a mass procedure, by far the most important has been the adoption of phakoemulsification techniques for cataract extraction, which in turn triggered the development of new kinds of lenses. This radical and complementary process innovation has enabled a step change in the treatment of cataract, effectively removing the bottleneck presented by craft operative procedures.

3.2. The trigger invention: phakoemulsification

The originator of this technology was Charles Kelman, a Professor of Clinical Ophthalmology in the USA (New York). Kelman had established his credentials as an inventor in the 1960s, with the development of a sophisticated cryoprobe for the removal of cataracts. In 1963, he turned his attention to the question of the benefit to patients of a procedure that would reduce the size of the incision in the eye. His attempts to develop rotating mechanical cutting devices bore no fruit until by chance he realised upon a possible solution in an ultrasound device.[25] He experimented for many years with the idea of using ultrasound, that is to say the high frequency energy of a vibrating needle to fragment a cataract, which would then be sucked clear of the eye through a much smaller incision (2–3 mm) than that traditionally associated with the ECCE technique (10–11 mm).[26] Improvements followed quickly and the first crude machines were made available commercially in 1970, signalling the shift in the locus of leading edge of commercial cataract innovation to the USA.[27] The device was patented in collaboration with an engineer, Anton Banko, and consisted of the ultrasound needle, a supply of irrigating fluid, a pump to evacuate the debris from the liquefied cataract, and a control mechanism for the surgeon (Kelman, 1973, 1991).[28]

In presenting his method to the British Ophthalmological Society in 1970, Kelman (1970) claimed that its main benefit was the dramatic reduction in time lost by the patient. Even with the best ECCE techniques of the day, 4–8 days would be spent in hospital with a 6-month recuperation period at home, while, with 'phako', the patient left hospital the day after surgery and could be fully active immediately. The professional literature soon carried papers by other surgeons who reported outcomes similar to those achieved with the ECCE technique (Hiles and Hurite, 1973). Thus, was born the technique that transformed cataract surgery. We have seen, in fact, how Ridley's intention of replacing the ICCE technique with the ECCE alternative had failed, and that his preferred method of locating the IOL in the posterior chamber soon fell into disfavour. Yet by the end of the twentieth century, ICCE is defunct in the advanced countries (although not in the developing world) and the posterior lens is the standard fitting. Furthermore, cataract extraction is a standardise procedures performed by trained nursing staff on an ambulatory basis. Much of the explanation for this change is

[25] Again, we find many competing routes to the solution of this problem. Well after Kelman succeeded with his method, others continued to search for a mechanical solution. In the 1970s, for example, surgeons at Moorfields reported on the use of a technique called lensectomy, in which the lens is cut mechanically and then aspirated. It was claimed to be cheaper than the phako technique and required less skill to perform although it could not be used with hard cataracts (Kanski and Crick, 1977). It failed to catch on.

[26] It is worth noting that the use of aspiration to remove cataracts long predated its application by Kelman but it was then restricted to the removal of soft cataracts, those typically experienced in patients under thirty. Certainly, aspiration was well understood in the 1930s and Schere (1960), in a paper, explained the use of a hollow needle and a hand syringe to remove a cataract while only creating a small incision. This method was widely used in the USA in the 1960s and its less invasive nature allowed rapid healing and the fitting of contact lenses to the younger patients (Rice, 1967). The significance of the Kelman innovation is that it tackled the problem of hard cataracts, and thereby opened up a very large market for treatment.

[27] They were manufactured by a company called Cavitron Surgical Systems, long since disappeared from the record.

[28] The apparatus was soon improved by the incorporation of piezoelectric technology and ways of controlling the rate at which material is aspirated from the eye without causing major fluctuations in pressure.

found in the growth of knowledge about phakoemulsification and the matching pattern of its diffusion.

Tracing the spread of phakoemulsification is not easy, records are sparse and the fact that many procedures were and are carried out in private clinics makes it difficult to paint an overall picture. However, on the bases of surveys and secondary data on clinical procedures, sufficient fragments can be assembled to give a broad assessment that suggests that the method took off on the way to becoming the dominant operative technique in the US around 1983. In the US as late as 1969 the predominant method of cataract extraction was the ICCE procedure, which usually required a 2–4 day stay in hospital. By 1984, the picture had changed considerably because a national survey (Dowling and Bahr, 1985) reported that 64% of surgeons used the ECCE method and that 75% inserted IOLs in more than half their patients, while 66% of surgeons inserted IOLs in 90% or more of their patients. Moreover, 30% of the reporting surgeons performed ambulatory surgery, that is to say, the patients were day patients, and we can infer that many, if not all, of these cases involved the use of phako methods. Norregard's et al. (1998) more limited survey figures suggest that by 1991 the proportion of operations using phako in the USA had risen to 66%. Similarly, Jaffe et al. (1997) report that phako was used in over 85% of operations by 1994. More recent figures from the American Society of Cataract and Refractive Surgeons suggest that, in 2000, phako was the procedure of choice for 97% of surgeons (Leaming, 1998). The upshot is that, in the USA today, cataract surgery is the most frequently performed surgical operation for individuals over 65, with some 0.5 million procedures taking place in 1984 and 1.3 million procedures in 1996 (Apple and Sims, 1996).

These charges in operative technique from the early 1980s onwards are also reflected in the shifting balance between preferred lens designs. The return of the posterior chamber lens and the simultaneous decline of iris-clip lens, however, began well before the phako method became established.[29] The following Table 1 shows the rapidly changing proportions in which the different lens designs were used in the USA between 1978 and 1984 (Stark et al., 1984).

Table 1
Use of competing lens designs USA (%)

Lens type	1978	1984
Anterior chamber	25	30
Posterior chamber	4	69
Iris fixation	52	<1
Iridocapsular	19	<1

Source: Stark et al. (1984).

The phako method also spread quickly to the UK but only after a lag of some ten years. By the early 1970s, Arnott reports that an estimated 7000 phako operations had taken place worldwide and that he had carried out 40 in the UK (Arnott, 1973). He later reported on the growth in the use of the technique at Charing Cross hospital in London. Of some 113 operations in 1973, only 21 used phako, while, by 1976, this method accounted for 118 out of 138 operations (Arnott, 1977). However, it seems that the practice did not spread beyond the few pioneers. Apparently, the method of resource allocation in the UK health care system constrained the rate of adoption because of a fear among managers that the potential demand could not be met. Beginning around 1990 adoption did take off and rapidly. A national survey in 1997, covering operations on ca. 18,500 patients, found that 77% of operations in 100 UK hospitals used phako but with considerable variation in usage between hospitals, covering the range from 10% to 99%.[30]

No doubt part of the explanation for the slow initial diffusion of phako lies in the need to acquire expensive suites of equipment combined with the need to acquire the necessary skills.[31] Nevertheless, there is more to the argument than the slow adjustment of the forces of potential supply to latent demand. Again, as with all radical innovations, the acceptance of this innovation depended on a sequence of post-innovation improvements to the technology. Space constraints do not allow us to delve into a detailed analysis of these complementary innovations, but among the various

[29] The return of the posterior lens, located 'where nature intended', was in part also a consequence of improved lens design to which lighter materials and better methods of fixation were crucial. Shearing's J-loop lens, with a flexible haptic introduced in 1977, turned out to be the emergent dominant design and remains so to this day, although there have been a continuous stream of improvements in the materials and shape of the haptic element to better locate the lens.

[30] The survey also found that 70% were surgical day cases (Desai et al., 1999).

[31] This, in spite of Kelman's effort to provide short courses to aspiring surgeons and independently of any conservatism of the ophthalmic profession.

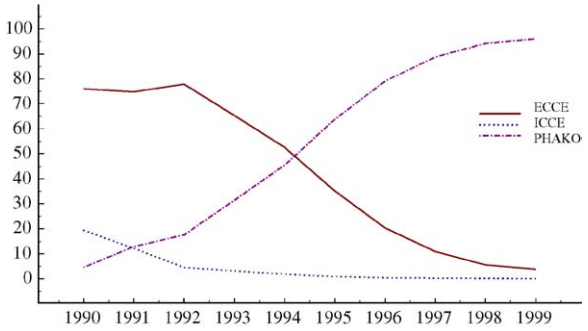

Fig. 3. Diffusion of cataract extraction techniques in the UK.

post-innovation improvements it may worth mentioning at least engineering development in the supply of phako equipment; the introduction in the early 1980s of viscoelastics[32] to reduce post-operative complications and the development in the late 1980s of a new surgical technique (known as continuous-tear anterior capsulotomy[33]) which dramatically improved the safety and success rate of the procedure. While the latter was the result of the imagination of creative surgeons, the former stemmed from the applied research of specialised suppliers with competences in the area of physics, engineering and material sciences. This is not the knowledge base of the typical clinician so the locus of invention and innovation necessarily moved to the firms competing in the market for these machines.

Fig. 3 shows the diffusion curve of phako-based extraction procedures in the UK in the 1990s. Here we see the decline of ICCE to negligible proportions by the early 1990s when ECCE 'ruled the roost'. Initially, the new method displaced ICCE procedures but from 1992 onwards, the substitution is against the handicraft ECCE method.[34] By 1999, phako has risen to dominance in the UK health system. Data for Manchester Eye Hospital, a large teaching hospital, cast interesting local light on the national picture. In 1991, four phako procedures took place out of a total of 3246 cataract operations. By 1996, the phako proportion had risen to 52% and to 90% by 1999 out of a total of 4102 operations. Over the entire period since 1991 virtually all those cataract operations were followed by the insertion of an IOL.

3.3. Foldable lenses: a revolution complete

It is pointless to make a small incision with the phako technique in order to remove the cataract, if one has to make subsequently a larger incision to insert a conventional, rigid or semi-rigid PMMA lens. The development of the modern lens well illustrates the point that the solution of one problem often opens up a design space for new problems, so knowledge builds on knowledge in an autocatalytic fashion but, crucially in this case, the new knowledge lay beyond the ken of clinicians. The dominant solution in these problem sequences has seen the latest stage in IOL development, the innovation and adoption of foldable lenses that are 'injected' into the eye and unfold within the capsular bag. This innovation can be said to complete the revolution in cataract surgery begun by Ridley in 1949.

As with Ridley's lenses, the first generation of foldable IOLs were poorly manufactured and suffered many decentrations after insertion. Subsequent generations are thinner, have better haptics to stabilise the optic in the eye and have greater biocompatibility, as a result of greater understanding of the interaction between the new materials, acrylic and silicone, and the biochemistry of the eye. That firms are now the dominant players in the innovation system in this field is nowhere more apparent than in the design of the modern lens and the choice of material from which it is manufactured.[35] Much learning has occurred in the

[32] The absorptive properties of viscoelastic materials help prevent damage to the corneal endothelium and to the posterior capsule during the emission of ultrasounds in the course of a phako procedure.

[33] Two clinicians, Gimbel and Neuhann, introduced it independently in the late 1980s, and it has since become the standard method for opening up the anterior portion of the lens capsule.

[34] The classic sigmoid curve reflects the logistic law that necessarily applies to all diffusion processes within populations of competing technologies, although the logistic law does not imply that each technology diffuses along a logistic curve. For references and further discussion of an extensive literature see Geroski (2000) and Metcalfe (2004).

[35] Furthermore, in line with what Gelijns and Rosenberg (1999) have observed in relation to the medical device industry more generally, a noticeable geographic shift has taken place also in the domain of IOL-related devices. While the first two decades of the innovation are essentially a European story the next three decades are told primarily in the United States with the involvement of major ophthalmic multinationals rising to dominate the industry. All of these

industry, and by the mid-1980s, Allergan, for example, introduced its three piece silicone lenses with UV filters incorporated in the material to prevent opalescence of the lens in situ. The second generation of silicone IOLs has further enhanced biocompatibility and they are thinner still. Side by side with the development of the new materials has been the development of new instruments, for example, to inject the foldable lens into the capsular bag.[36] Silicone is not the only new material made available, Alcon (a subsidiary of Nestle) markets acrylic foldable lenses (Acrysof). These lenses unfold more slowly within the eye, can be produced with a thinner optic and have many of the desirable attributes of PMMA. Yet further innovations are to be expected in materials and lens design in the future but here our account must stop, for the Ridley inspired revolution is virtually complete, at least in the high-income countries. What have we learned about the medical invention and innovation process?

The development and diffusion of the IOL is a powerful example of the interplay between innovation and an emergent division of labour in this medical area. As Young (1928) insisted, the division of labour requires a systemic response that goes beyond adjustment within particular activities to include the changing and emergent relationships between a number of complementary activities. This emergent division of labour is reflected in the growth of knowledge, the changing organisation of practice, the growth of demand, and, for our purposes most importantly of all, the creation of a micro innovation system that emerged around the IOL guided by the relevant problem sequence.

4. Part 3: aspects of the growth and transformation of medical knowledge in the IOL micro-innovation system

4.1. Composition, substitution and complementarities

While there is no obvious way to infer the development of knowledge in the minds of individuals, we can follow systematically the growing body of codified representations of personal knowledge placed in the public domain. This information, in the form of papers, patents, device evaluations and professional demonstrations of method, can provide invaluable insights on the development of correlated understanding within the community of practitioners and the supplying firms. It must be remembered, however, that placing information in the public domain is not placing knowledge in that domain, however tempting it may be to draw that equivalence. This is especially clear when knowledge, such as clinical/surgical knowledge, heavily depends on practice. This is in part the reason why we have so far emphasised practical co-operation, personal connections, and informal exchanges. These appear to be especially important in phases of early development of micro-innovation systems where knowledge is unstable and standards contested. At the same time, it cannot be denied that as the system grows, the representation, communication and protection of private knowledge through publishing and patenting become essential factors in shaping the nature of further knowledge as well as the scope for its future applications.

In the following section of the work, we integrate the evidence gathered in our interviews and in the relevant medical literature by examining how the growth and transformation of clinical and technological knowledge for the treatment of cataract is reflected in the codified traces of research activities contained in medical papers and patent documents.[37] We examined scientific papers listed by ISI between 1965 and 1999, and 707 patents granted by the US Patent Office between 1976 and 2002. By means of simple statistics, we profile the main trends and explore the nature and change of composition, substitution and complementarity effects among the creative efforts of medical scholars and inventors. The main goal of this exercise is to provide evidence of the complex epistemic nature of the prob-

firms have a major presence marketing and distributive presence in Europe but the preponderance of their innovation activity remains in the North American system.

[36] Interestingly, these developments are based in materials science and the biotechnology of the eye not upon engineering knowledge.

[37] Patent analysis is an especially well-established technique for the study of science and technology and a wealth of contributions discuss their uses and limitations. Time constraints and the limited methodological ambition of this paper do not allow us an in-depth discussion of the vast body of literature on the topics. Pavitt (1985), Griliches (1990) and Jaffe and Trajtenberg (2002) are the authoritative and well-known reviews to which we refer the reader.

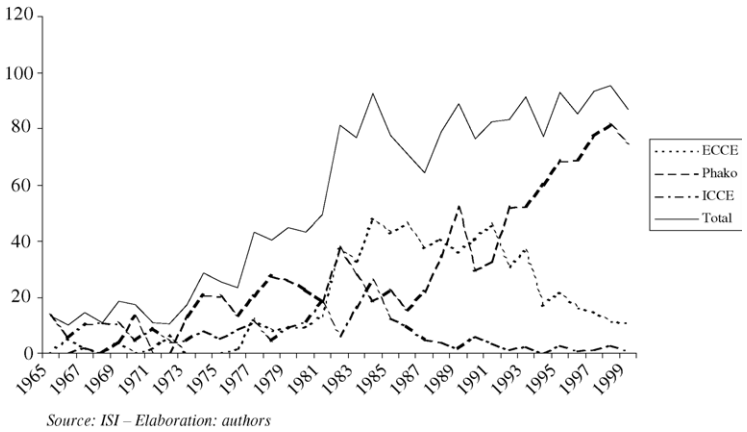

Fig. 4. Distribution of IOL research publications 1965–1999.

lem sequence.[38] The following results corroborate the qualitative findings insofar presented.

Fig. 4 shows the proportions of all papers in the field of IOLs and cataract surgery that refer to at least one of the three main surgical methods that can deployed for cataract extraction procedures: ICCE, ECCE, and phako. Note that the trends broadly reflect actual practice in hospitals and clinics as reported in Fig. 3. This is not insignificant because it constitutes clear evidence of the interdependency and co-evolution of medical research and clinical trial-and-error practice. The steady rise of papers referring to phako methods from the early 1970s is immediately apparent, as is the relative unimportance of references to ICCE, which was the well-established and thus uncontroversial practice of the profession. References to ECCE, Ridley's preferred method, begin to increase in the late 1970s, peak around the late 1980s and then decay away as phako continues its rise in importance. The joint growth of ECCE and phako related papers reflect the shift to placing the lens in the posterior chamber, 'where nature intended'.

The growth of understanding clearly accelerated in the late 1970s exactly in phase with the beginnings of rapid diffusion of the IOL into clinical practice. If we add together the three categories of papers charted in Fig. 4, we have the proportion of the total of IOL and cataract surgery papers that refers to operative technique. In the late 1960s this total was less than 20% of all papers, the inference being that most papers were then concerned with matters such as lens design or reports of complications once lenses have been fitted. The interest in matters of technique then rises almost year on year and accounts for 90% of published papers by 1999. To put this information in perspective we have calculated the total number of papers in cataract surgery over the period since 1947. At that date they run at an annual rate of ca. 150 papers per annum, rise to a peak of 350 in 1960 and settle down to a more or less constant rate of 250 papers in the early 1980s.[39]

Patents offer a second window on the development of understanding with the added dimension that they reflect the growth of ideas with potential commercial value. Many of the pioneering IOL surgeons, as we have already suggested, patented their lens designs and operating instruments but, over time, there have been significant changes in the role of the surgeon inventors; as the community of practitioners has grown, a sub-division of specialised IOL surgeons has emerged and an increasing proportion of firms account for the majority of the patents granted. Fig. 5 shows the trend in US patents for IOLs from 1976, following the date

[38] Given the exploratory nature of this exercise, we deploy very simple techniques for the analysis of paper and patent and emphasise the epistemic side of the innovation processes to the detriment of the institutional and geographical dimensions of the micro-innovation system. However, in a separate paper some of the authors use newly developed bibliometric methods for the analysis of large citation networks and investigate the economic, institutional and geographical distributedness of medical innovation systems (Mina et al., 2004).

[39] The shift from 'product' to 'process' is entirely in line with product cycle models of the innovation process, see for example, Utterback (1994).

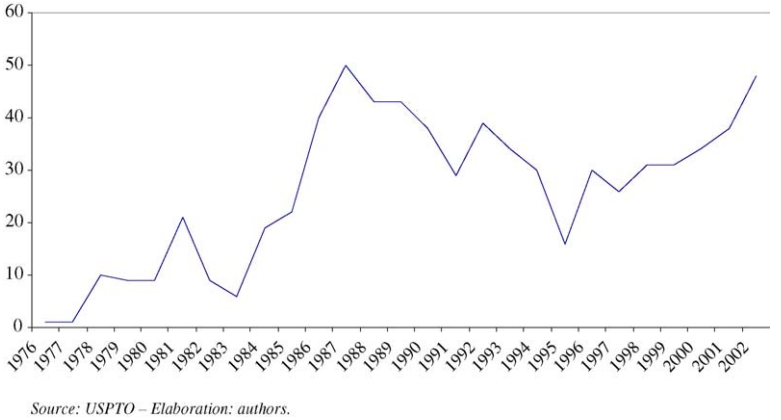

Fig. 5. IOL patents 1976–2002.

Table 2
Distribution of patents across categories 1976–2002

	N				%			
	Design	Materials	Tools	Methods	Design	Materials	Tools	Methods
1976–1983	41	5	12	8	62	8	18	12
1984–1995	223	53	68	59	55	13	17	15
1996–2002	67	24	86	61	28	10	36	26

of invention of Kelman's invention, to 2001. We can see the considerable acceleration that took place after 1983, roughly corresponding to the emergence of commercial innovation systems.[40]

The patent record also allows an assessment of the shifting balance of inventive effort as a further check on the evolving problem sequence. Beside its aggregate growth, we have identified the composition of patenting activity in the field of IOLs. Table 2 shows the distribution of patents across four categories, lens design, materials used in the making of lenses, methods of performing cataract surgery and tools, primarily for inserting foldable lenses into the eye. The proportionate growth in patents on methods and tools reflects the trigger effect of phako, and the decline in the relative importance of lens design patents suggests that this dimension of the problem sequence is relatively settled.

Figs. 6 and 7 show the extent of substitution effects in the composition of lens characteristics.

They illustrate respectively the rising relative importance of patents in relation to posterior chamber lenses, confirming the switch to the 'Ridley model', and the proportionate increase in patents concerned with deformable lenses.[41] It may be interesting to notice that while the problem of lens location seems settled in 1995–1997, it in facts re-emerges from 1998 (although the number of location-related patents decreases in absolute terms). Examination of the patents granted after 1998 reveals that research on alternative locations was triggered by the need to accommodate the impossibility of placing lenses in the preferred location of posterior chambers because of local tissue damages.

In Table 3 we see the significant correlations between these three groups of patents published over the period 1981–2001, while in Fig. 8 we show the corresponding linear regression surface. In spite of its elementary nature, this exercise clearly signals the presence of connected and co-evolving aspects of the

[40] The relevant patents have been retrieved by the US Patent Office between May and December 2002 via targeted thematic searches. The patents have been fully inspected and reclassified by functions and by characteristics.

[41] In the case of deformable lenses, the takeoff in activity is dated ca. 1984. Between 1981 and 2002 a (cumulative) total of 74.8% of the IOL patents are based on the use of deformable material.

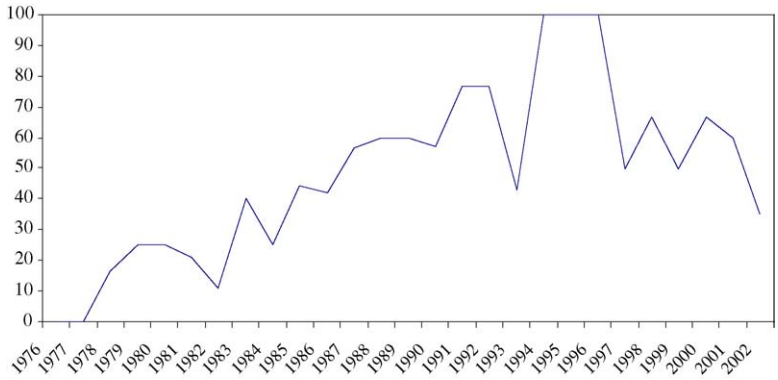

Fig. 6. Proportion of posterior chamber lens 1976–2002.

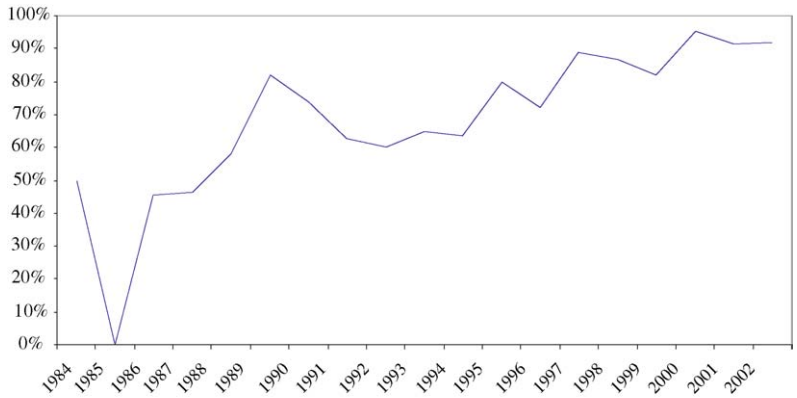

Fig. 7. Proportion of patents classed as deformable 1984–2002.

Table 3
Correlation between different groups of lens patents 1981–2001

		Tool	Phaco	DEF
Tool	Pearson correlation	1	0.746**	0.752**
	Significant (two-tailed)		0.000	0.000
	N	20	20	20
Phaco	Pearson correlation	0.746**	1	0.668**
	Significant (two-tailed)	0.000	0.000	0.001
	N	20	20	20
DEF	Pearson correlation	0.752	0.668**	1
	Significant (two-tailed)	0.000	0.001	
	N	20	20	20

** Correlation is significant at the 0.01 level (two-tailed).

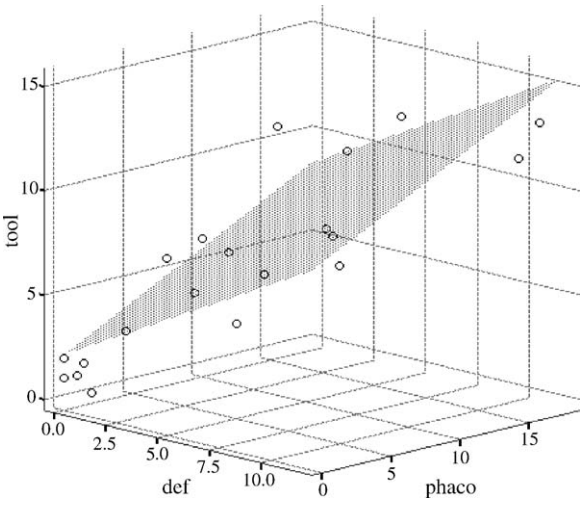

Fig. 8. Regression surface for complementary groups of patents 1981–2001.

problem sequence where advances in one component are strongly associated with advances in the others. Inspection of the patent documents allows confirmation that the correlation is of causal nature, as made explicit in the 'Description' sections of the documents.

4.2. Division of knowledge, division of labour and interdependecies

That Ridley's revolution was a revolution within the design space of the eye with multiple strands of invention and innovation required for its realisation is confirmed by this epistemic data. The correlated growth of patents and papers shows the very considerable shifts over time that took place in the body of correlated knowledge across this community. The move to foldable lenses placed in the posterior chamber by means of the phako method is one interrelated aspect of the same revolution in which the solution of one problem opens up new problems that find their solution in the inventive division of labour. This division of labour in the production of private knowledge and public understanding is strongly co-ordinated by the practices that define the field and is paralleled by a second division of labour in the organisation of the delivery of the service.

A procedure that at the beginning of the 1980s required a general anaesthetic and a 5–7 day period of hospitalisation using the ICCE method, could take place with a local anaesthetic and a 1–3 day hospitalisation using Ridley's preferred ECCE method, an improvement of itself. Yet with the adoption of phako, surgery is carried out now by training nursing staff, on a day basis, under local anaesthetic and with a very short recuperation period. As a result, both the number of beds and nurses absorbed by cataract surgery has declined very sharply.[42] The cost savings in terms of capital and labour are clearly considerable. When taken in conjunction with the decline in postoperative complications, following the return of posterior chamber lenses and the improvements in lens quality, the transformation in the service for the patient is precisely immeasurable.

One of the most striking features of this division of labour is the interdependence between the deliverers of health-related services and the manufacturers of lenses and related ophthalmic equipment. It marks the transition from localised invention systems to the innovation system of today, where large firms dominate and channel the innovation process along commercial lines.[43] In the early days it was the 'hero surgeons', Ridley, Kelman, Fyodorov and many others, who drove the field forward with the fundamental changes in perspective embodied in the concept of the IOL. Trial-and-error clinical experimentation and growing clinical experience have been the forces behind both radical developments in IOL technologies as well as incremental developments within established design trajectories; the medical clinic or hospital has been a primary locus for the design of lenses and the accumulation of experience from the earliest days of the industry.

Even with the emergence of the medical–industrial complex, the manufacturers of IOLs and related equipment remained heavily dependent on clinicians as a source of inventions although the balance of advantage was changing. This highlights the fact that – in a professional community where peer opinion is critically

[42] In some UK hospitals the time from admission to leaving the hospital after the operation has been reduced to around 2–3 h. At the Manchester Eye Hospital in 1991, for example, all the patients were inpatients, while by 1999 only 13% fell in that category. In 1980, this same Manchester hospital maintained ca. 175 beds but by the late 1990s, this number had fallen to 26.

[43] This interdependency takes a number of forms: the role of ophthalmic surgeons in the commercial innovation process; the role of ophthalmic surgeons in testing new designs for regulatory purposes; the role of pioneering surgeons in legitimising new designs and practices within the surgical community.

important – the views of leading surgeons can have an important influence on the diffusion of practices and selection of designs. The companies recognise this fact and build it into their innovation strategies. The leading surgeons are courted. They are encouraged by companies to use their products and the views of the leading inventors are taken seriously. Companies sponsor events at the leading ophthalmology conferences and those supplements to the leading journals in which the merits of the various products are debated. Good platform speakers are at a premium, particularly where they are held in high esteem by their peers, and are regarded as influential within the professional community.[44]

What is also worth emphasising is that, even during the period of what we call craft-based innovation, new developments depended upon these mutual interdependencies but on a much smaller scale. Thus, Ridley's pioneering innovation in surgical technique relied on the ability of ICI to develop clinical quality materials and on Rayner's ability to manufacture the lens itself—no trivial task in the late 1940s. The importance of these mutual interdependencies in the innovation process supports the work of scholars such as Lundvall (1988), Constant (1980) and von Hippel (1988), who emphasise the sharing of information within communities of practitioners who 'learn by interacting' in the context of user–producer relationships and in this doing directly shape the competence landscape of the emergent innovation system.

5. Part 4: the market for cataract surgery: demand, need and regulation

To the extent that the IOL is a story of increasing returns in the production and use of knowledge, we would expect that the scale of demand and the way demand is instituted play an important role in the unfolding of technique and practice. In this section, we explore the dynamics of the emerging IOL invention and innovation system and the forces in relation to the demand for IOL implants, the regulation of the practice and the development of commercial interests that shaped the system. This invention and innovation system did not exist naturally, it had to be instituted and the focus for its construction was the emerging problem sequence.

As with any dimension of economic life that is based on a division of labour, the growth in scale and composition of demand is a vital part of the story and the IOL is no exception to this rule. The nature, size and growth of the market are fundamental determinants of the way health care is delivered and of the supporting innovation process. This is equally so in relation to cataract surgery and the implementation of innovations in IOLs. However, the market for treatment has its own peculiarities expressed in the way the participants make decisions and the rules, formal and informal that govern the activities involved. In this case, four factors interact to determine the demand for the IOL procedure. These are the population at risk, the clinical procedures and routines that translate physical need into economic demand, the wider regulatory rules for the procedure and, the instituted norms for allocating health care resources to IOL treatment.

It is clear that the determinants of the pool of need and the rate of surgical removal of cataracts will vary from country to country but that, in all cases, the principal driving factor in adding patients to the pool is the age profile of the population. In the populations of the advanced countries, the incidence of cataract in the overall population lies in the region of 17–18% and the predominant need for treatment is in those over 65 years of age (Desai et al., 1999). That the population of advanced countries is growing older on average is an important factor in shaping the ongoing evolution of demand for cataract surgery. In the OECD region for example, 13.3% of the population in 1999 was over 65, a proportion that stood at 8.9% in 1960. As per capita incomes have increased, along with expectations of an active and long retirement, so has the pressure from patients for this operation to be performed. At the same time the more routine nature of the procedure and the increasing clinical confidence of positive outcomes means that patients in lower age brackets and with less acute conditions are operated upon.

While need is a physiological matter, its translation into demand depends also on the prevailing standard of visual acuity as assessed by professionals, and this in turn is related to their knowledge of and access to available techniques that work. The translation of patient need into demand for cataract surgery and the insertion of an IOL depend crucially on the prevail-

[44] The close connection between academia and large corporations is not without problems. For thorough discussion, see Blumenthal (1994).

ing clinical rules of assessment and these depend on the technologies of treatment open to clinicians. If the threshold of acceptable visual acuity is lowered this will expand, perhaps considerably, the pool of potential patients deemed to benefit from cataract surgery. In Denmark, for example, the number of annual cataract extractions increased by 350% between 1980 and 1991, with a change in the surgical threshold cited as the principle source of this increase (Norregaard et al., 1996). The advances charted above have transformed the need/demand relationship. One need only reflect on the hazards of the early procedures and the limitations of aphakic spectacles to see the point that, prior to the IOL, demand would necessarily be suppressed whatever the scale of need. Thus, one of the unforeseen developments, one that reflects the success of the technology, is the implantation of IOLs in patients who can expect many years of life with the lenses. Increasing life expectancy in the advanced countries means that an implant in a 50 years old may be expected to function for another 20–30 years. Furthermore, intra-ocular lenses are today implanted in patients whose vision has been only marginally affected by cataracts, patients, for example, who are still able to drive a car.

A further factor affecting the growth of the IOL market is the particular ways in which countries fund medical services. In most of the advanced countries medical care is either funded by the state from general taxation supplemented with charges for medical prescriptions, as in the UK, or it is financed by charges on patients that are met from insurance payments, as in the USA. As has long been understood these financial rules break the link between patient benefit and the opportunity cost of treatment and they have become something of a *cause celebre* in health economics (Newhouse, 1992). In state funded systems, this typically leads to rationing of treatment with rationing decisions being in the hands of clinicians and medical system managers. In insurance-based systems, payments are typically set to cover the costs of treatment. In both cases, health professionals determine the relation between need and demand, and this is as true of cataract surgery and the IOL as it is of any other major area of treatment. However, the constraints that they face differ in the two cases. In the UK, health care bureaucracies determined the timing of the expansion in demand, while in the USA it is the insurance companies through their rate setting rules that incentivise physicians to perform particular procedures. In both cases pressure to cut costs has been an important factor in accommodating the growth of demand. As early as October 1984, for example, the Medicare system in the state of Rhode Island was prescribing that all cataract/ IOL surgery should be carried out on an ambulatory basis to qualify for public reimbursement. No doubt, other States followed quickly and encouraged the adoption of phako techniques (Dowling and Bahr, 1985). Similarly, in the UK in 1985, the NHS issued a directive to the effect that 80% of cataract surgery should be performed on a day basis thus encouraging the use of phako methods and the search for the more efficient scheduling of operations.

Regulation of the market has been the third important factor extending the market for IOLs. Regulation is part of the instituted framework in which medical innovation takes place and, in the case of IOLs, the development of formal government regulatory frameworks paralleled but lagged behind the emergence of the medical industrial complex and this, in turn, lagged behind the self-regulation imposed by the clinical profession. In this sense the regulatory system, the market and the innovation sequence co-evolved. More forcefully, the development of regulatory institutions was essential to the growth of the market since it provided the assurance of a stable framework within which clinicians, patients, hospitals and suppliers could interact with a more developed sense of trust and correlated understanding. Effective and efficient devices and operative procedures provide benchmarks for quality and performance and facilitate the transfer of the understanding of practice to other surgeons.

These standards do not exist naturally; they are discovered in an extended process of trial and error learning that reflects the engineering like nature of the medical knowledge. Within this process, the creation of a sub-community of practitioners is a crucial step. Thus, Ridley and his fellow pioneers had to create their standards through co-production with the activity, medical outcomes and procedures and new understanding were joint products. As we have seen above they visited each other, they communicated through papers and they attended professional meetings to present and evaluate each other's work; by the early 1960s, the community was sufficiently well identified to set up its own professional associations. As Savage (1994) and Langlois and Savage (2001) have pointed out, pro-

fessional networks are neither firms nor markets they are a distinctive organisational form particularly well suited to the trial and error accumulation of knowledge via practice, and the sharing of information on non-competitive terms. The community becomes as it were the instituted framework for collective learning.

The significance of this process is that concerns amongst the ophthalmology community about the safety and propriety of inserting a foreign body into the eye loomed large from the very beginning of the IOL story. Thus, we have noted that Harold Ridley and his hero surgeon colleagues faced the criticism of Duke Elder and the ophthalmology establishment in the UK, while the professional community – not least in the United States – was to long remain sceptical about the efficacy and ethics of the IOL. Indeed, this professional scepticism, backed-up by considerable clinical evidence of the problems and difficulties associated with the procedure, limited the diffusion of the IOL in the early years and provided the stimuli to improve the innovation. However, it was impossible to confine the norms and process of regulation within the ophthalmic community. Most significant of all was the emergence of a network of consumer activists in the USA, including Ralph Nader, which challenged the very basis of the ophthalmic community, namely its professional autonomy and the principle of self-regulation of practice and patient welfare.

Critics of the IOL procedure argued that IOLs had never been properly tested in animals or clinically investigated under properly controlled clinical trials. The consequence, they claimed, had been serious damage to the eyes of many patients including induced glaucoma, severe corneal disease, inflammation and infection. Trial, not surprisingly given the engineering nature of the medical knowledge, had resulted in error and the issue had become the regulation of practice to produce permissible error bounds. This challenge to professional codes of practice strained relationships within the ophthalmic community in the United States over an already controversial practice.[45] The direct consequence of this deep controversy was the extension of the regulatory powers of the FDA to include IOLs, among other medical devices, in the 1976 Medical Device Amendments. The objective of these 1976 Amendments was to ensure the safety and effectiveness of medical devices by requiring manufacturers to register with the FDA and follow quality control procedures.[46] Paradoxically, it was the extension of the regulatory regime that was to underpin the growing acceptance of the IOL procedure in the medical community and by the medical insurance industry. Regulation no doubt constrained sharp practice but it also helped institute the market by adding an implicit minimum quality mark to the procedures, radically reducing uncertainty among patients, ophthalmic professionals and insurers alike.

This confluence of events, defined by an aging population structure, a radically changed supply capability, and the regulation of practice and devices to make the market, underpinned the rapidly growing scale of practice and so provided the economic incentive for private firms to make large-scale investments in the cluster of techniques around cataract surgery and the insertion of IOLs. As reflected in the patent statistics, these changes came together in the early 1980s in the USA. In the process of making these investments, private firms have transformed a craft-based innovation system into a medical–industrial complex that transcends national borders. The crucial point is that the transformation of the relationship between an abstract concept of need and a concept of effective medical demand depended on the related transformation of a radical innovation into a routine medical procedure. Growth of the market stimulated the search for a new division of labour and this is reflected in the emergence of a modern micro innovation system.

6. Part 5: the wider questions

We find it helpful to conclude with some of the wider questions towards which this study points. Our interest in this case lies in part in it being an important example

[45] An editorial in one ophthalmology journal declared: ‘This has placed ophthalmology in the eye of a surgical storm’. A pioneer of the technique in the US commented: ‘Even the most enthusiastic advocate of this procedure would agree that this has polarized the American ophthalmic community like nothing else in recent memory’ (both quoted in Jaffe, 1999).

[46] In 1978, the US Food and Drug Administration (FDA) initiated the largest clinical study on IOLs ever conducted. This resulted on 11 December 1981, in the Rayner-designed and manufactured Choyce MkVIII and MkIX lenses becoming the first IOLs to be approved by the FDA as safe and effective (Rayner, 1999).

of the interdependence between the service economy and the manufacturing economy. The medical sector is properly regarded as one component of the service economy with primary and secondary care affecting most individuals at some stage in their lives, while innovation in the conception and delivery of new treatments is a central aspect of modern health care systems. However, these innovations are increasingly dependent on the interaction between the clinical delivery of health care services and a manufacturing system that develops and delivers new drugs and new instrumentation and devices to enhance the delivery of clinical services. So close is the degree of supply chain interdependence that the medical service economy and the medical industry economy are effectively one, as the link between cataract surgery and the prophylactic use of IOLs serves to illustrate. Thus, service innovation is premised on complementary innovations in manufacturing, and those manufacturing innovations are shaped by clinical innovations and related co-developments in the delivery of services. It is thus quite unhelpful to think of this economy as constituted by independent service and manufacturing sectors. What we are dealing with are knowledge intensive medical services and the innovation systems that sustain them and transcend traditional sector boundaries.

A second rationale behind this study is that it enables a critical evaluation to be undertaken of the idea of a distributed innovation system and the processes by which it is instituted (Coombs et al., 2003). We have found that the relevant system is constituted at a number of interdependent levels. There is a national level defined by the characteristics of a particular national healthcare system, characteristics that differ significantly across countries. There is a medical sector level which cuts across national boundaries and is integrated by two factors: the operation of trans-national medical device firms; the international community of clinical practitioners. Linking the two levels are the external organisational arrangements of particular firms each with their own networks of suppliers and clinicians competing for business from hospitals and private clinics. Now no innovation system is formed without cost or without purpose. Rather, a division of labour is created and develops over time in order to stimulate the growth and application of knowledge and understanding. It is a distributed process of innovation that is continually evolving and shaping the accumulation of new knowledge and understanding, and much new knowledge accumulates in the context of 'market' processes.[47]

We argue that there are two important, interrelated aspects of the process by which the IOL medical innovation system has emerged and developed. First, the level and attributes of national demand were important to the shaping of this dynamic division of labour. As we have seen, the relation between demand and need is itself dependent on the prevailing clinical technology and health care management practices. It is an instituted relationship shaped by regulation. Secondly, the competitive activities of rival firms are central to the way the innovation system develops. The process of competition is reflected in the attempts of rival firms to build their own 'local' concentrations of innovation resources. That is to say, they develop proprietary micro-innovation systems as part of their strategies to support their ongoing search for competitive advantage.

Two consequences follow. We find competition to create different firm specific systems of innovation, each one drawing its support from wider networks of knowledge generating resources. Thus, competition between rival firms leads to contests for access to knowledge, expertise and skill held at national and sector levels of the ophthalmic medical innovation system. Secondly, to build firm specific innovation systems requires significant investments not only in internal capabilities but also, for example, in the training of clinicians in the use of proprietary equipment and in the provision of clinical facilities. To build these relationships adds to the fixed costs of innovation and to the sources of increasing returns as the market for ophthalmic services expands. Hence, a key element in the development of the current configuration of leading firms is the large scale of the USA market for lens implantation

To conclude, the most important aspect of this case study is the fact that the innovation system has co-evolved with the development of technology and practice around specific problem sequences. The innovation system has been variable in form and geographic focus, variable in terms of the relative importance of surgeons and firms in the innovation process, and variable in relation to the understanding required to 'solve' the inno-

[47] For recent discussion of disaggregated varieties of innovation system see Freeman (2002) and Malerba (2004).

vation problems of the moment. It was exhibited self-organisation and a capacity to for self-transformation. National institutions and organisations have played an important role in the sense of providing knowledge and other inputs into innovative activity and in framing the possibilities for innovation. However, national organisations do not form innovation systems. Innovation systems depend on interaction for a purpose, and the linkages that define the pattern of interaction are constructed and friable. Thus, the development of IOL innovations is best understood in terms of evolving innovation systems focused around a constellation of related problems: the problems of human sight in those of more mature years.

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