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Presenting the (economic) value of patents nominated for the European Inventor Award 2012

Inventor file Josef Bille

1. The invention

1.1 Historic account

Laser surgery (LASIK) of the human eye or devices (intraocular lenses, contact lenses or spectacles) that help improve human vision have benefited greatly by the introduction of the wavefront technology. Wavefront technology is a measurement technology which uses so-called aberrometers to scan the human eye in a very detailed manner for small errors (so-called higher order aberrations). By having a very detailed image of these errors, it is possible to devise much more precise surgery procedures (wavefront-guided LASIK) or to produce tailor-made lenses. Prof. Bille from Heidelberg, Germany, first developed the wave front technology for ophthalmic application on the living eye. This ground-breaking invention and its continuous improvement by Prof. Bille was fundamental for a paradigm change which has been taking place in eye care for some time.

Prof. Bille started working in the field of the invention as early as 1966, when he wrote his master´s thesis ('Diplomarbeit') on short pulse lasers. In 1970, Prof. Bille obtained his PhD from the University of Karlsruhe, and in 1973 his habilitation.

Prof. Bille recounts:

> *"At that time, lasers were something fundamentally new. When I wrote my master´s thesis, the laser had been only around for some six years. Already after my PhD I was thinking about possible areas of application, and application in medicine was one option. But back then the field was not yet ready, and I wasn´t able to get into the field. Nobody was interested."*

After his habilitation, Prof. Bille worked in the chemical industry for around five years. During this time, his work focussed on process automation and adaptive control. The experience proved to be very helpful later on also for eyecare surgery/applications:

> *"Doing laser-based adaptive control was a true novelty. In the defence sector, they used adaptive control and process automation to improve the quality of surveillance, but there were no lasers involved. Another area of application was in astronomy to improve the picture quality of images taken by telescopes."* (Prof. Bille)

In 1978, when he returned to the university sector and became professor at the University of Heidelberg at the Institute of Applied Physics, Prof. Bille used his knowledge of laser-based adaptive control systems, which also included software expertise for image processing, to build short pulse lasers for eye care application. The original idea for a wavefront system for ophthalmic application, i.e. for the measurement of errors in the human eye, came from retinal imaging. The device he built, termed retina tomograph, was presented in 1982 at the annual ARVO (Association for Research of Vision and Ophthalmology) meeting in the U.S. While there was some interest, the technology was seen more as a curiosity, because of the rather crude technology. The lasers needed were so complicated that application in a practitioner´s office was deemed highly unlikely. Nonetheless, together with the German firm Zeiss, the principle of the technology was patented, and in 1986 the respective patent was granted by the U.S. patent office.

Throughout the 1980s, Prof. Bille continued to work on improving applicability of the imaging and measurement system. Slowly, the different pieces of the wavefront technology came together. In 1984, Prof. Bille co-founded the firm 'Heidelberg Instruments' in Germany, which implemented some of the technologies developed so far in the form of prototypes. The firm, being established *"…as a group of several start-up companies focusing on areas of ophthalmoscopy, surface physics, laser* *scanning, confocal microscopy and image processing"*, is now *„...a world leader in design, development and manufacturing of advanced laser based maskless lithography systems for production of photomask, as well as laser direct imaging."* [1]

The development of the wavefront technology obtained a boost after the introduction of the LASIK (laser-assisted in situ keratomileusis) surgical procedure in 1989. The LASIK technology uses a so-called excimer laser operating in the ultraviolet. This type of laser has relatively high energy and is particularly suited for correcting low order aberrations such as myopia, hyperopia and astigmatism. Finer type errors in the human eye (higher order aberrations) can only be tackled if a) these high order aberrations can be measured and b) if there are surgical devices (e.g., lasers) able to work at the needed precision level and performance characteristics.

The steps towards a more precise measurement/scanning technology were tedious, and Prof. Bille´s role in the development and uptake of the wavefront technology was fundamental:

- One year before LASIK was introduced, in 1988, Prof. Bille and one if his PhD students, Andreas Dreher, were able to demonstrate that adaptive optics (a special type of which is wavefront technology) could be performed to a living eye with an improved version of the retina tomograph. However, Dreher and Bille were only able to account for astigmatism, because the apparatus then did not use actual wavefront refraction.
- In 1991, Bille and another PhD student, Junzhong Liang, demonstrated for the first time actual wavefront refraction with a so-called Shack-Hartmann aberrometer.
- A further improvement came in the form of patent EP 1059061, which was filed by Prof. Bille and again one of his PhD students, Frieder Lösel under the start-up firm '20/10 Perfect Vision' in 1999. This patent describes an enhanced technology to create topographical maps of the anterior surface of the human eye, which can also measure higher order aberrations in the human eye such as coma or spherical aberration with a cost-effective and easy-to operate apparatus. The patent was eventually sold to the U.S. firm VISX, the market leader for excimer lasers. The patent allowed the two technologies – excimer lasers and wavefront technology – to mate in so called wavefront-guided LASIK. The higher precision of wavefront-guided LASIK can lead to people seeing twice as good as normal human vision under normal light conditions, and up to five times improvements in low light conditions.
- Further refinements have led to the concept and introduction of *all-laser* LASIK, which was pioneered by the firm Intralase. Every LASIK operation takes three steps: creating a flap of corneal tissue, remodelling the cornea underneath the flap with the laser and, finally repositioning the flap. A metal knife traditionally performed the first step of creating a flap, which, according to Prof. Bille, had potential issues in terms of smoothness or overall safety. In all-laser LASIK, a femtosecond laser – an advancement of the picosecond short pulse laser Prof. Bille was working with in the 1980s for his aberrometers - replaces the knife. The all-laser LASIK procedure can be performed again with wavefront-guided measurements.
- Back to the diagnostics area, Prof. Bille further adapted wavefront technology to be used in optical coherence tomography (OCT).[2] Wavefront-guided OCT systems

[1] http://www.himt.de/en/home/

[2] "Optical coherence tomography (OCT) is an optical signal acquisition and processing method. It captures micrometer-resolution, three-dimensional images from within optical scattering media (e.g., biological tissue). Optical coherence tomography is an interferometric technique, typically employing near-infrared light. The use of relatively long wavelength light allows it to penetrate into the scattering medium.

can increase the resolution and accuracy of the three dimensional images obtained along the x and y-axis. Prof. Bille´s invention has been taken up by the firm Heidelberg Engineering (another spin-off of one of his PhD students) – who are now world leader in this technology – and Zeiss.

A novel type of application for the wavefront technology is for intraocular lenses (IOLs) used in cataract[3] procedures (so called wavefront-adapted IOLs): *"Historically, wavefront analysis has been implemented in corneal refractive procedures. Expansion of this technology may soon allow surgeons to choose the most optically appropriate intraocular lens for a patient's individualized wavefront pattern, thus allowing for a 'custom-fitted' intraocular lens."*[4] Such lenses have been already introduced into the market.[5] Furthermore, femtosecond lasers are starting to be used more commonly in cataract surgery. Taken together, the combination of short pulse (femtosecond) lasers and wave-guided IOLs opens a huge market. In fact, Prof. Bille estimates that the cataract femtosecond laser surgery market - addressing primarily the elderly people while classic eye laser surgery typically treats younger patients – may become as much as four times larger than the current excimer-dominated eye laser surgery market.

Eventually, also application areas such as wavefront-optimised contact lenses and lenses for spectacles are to be noted. There is common consensus that the wavefront technology has had considerable impact in the eye care market, as Dr. Mac Rae, an author of a book on the use of wavefront technology states:

> "*The field has changed so dramatically it has been difficult to keep up…with the wavefront IOLs, wavefront contact lenses and other devices coming down the road… without question, wavefront is the biggest revolution in ophthalmic optics in the last 200 years.*"[6]

1.2 Technological features and major benefits

The human eye works like a camera that uses several lenses to focus rays of light onto the retina, which then initiates a series of chemical and electrical events that trigger nerve impulses. These impulses are carried along the optic nerve to the brain´s visual centres, where they are processed into what we perceive as images. The sharpness of these images can be detrimentally affected by irregularities within the lens or other components of the eye, which cause the light rays to deviate from their desired path.

Detecting which light rays are going astray, and in what direction, is the key function of Prof Bille's device. To do so, a beam of light is focused into the eye to a point on the retina. It is then reflected back out of the eye as a wavefront - passing through the eye´s lens, pupil, anterior chamber, and cornea - before ultimately landing on a sensor located behind hundreds of tiny lenses. Light passing through the lenses´ apertures is concentrated to focal spots on the sensor. If any light is concentrated where it does not belong, the displacement occurs because an aberration within the eye reflected the light improperly. Noting this displacement, a computer is then able to create an accurate, three-dimensional map of the eye´s visual system, irregularities included.

Confocal microscopy, another similar technique, typically penetrates less deeply into the sample.", cited from Wikipedia (http://en.wikipedia.org/wiki/Optical_coherence_tomography)

[3] "A cataract is a clouding that develops in the crystalline lens of the eye or in its envelope (lens capsule), varying in degree from slight to complete opacity and obstructing the passage of light. Early in the development of age-related cataract, the power of the lens may be increased, causing near-sightedness (myopia), and the gradual yellowing and opacification of the lens may reduce the perception of blue colours. Cataracts typically progress slowly to cause vision loss, and are potentially blinding if untreated. The condition usually affects both eyes, but almost always one eye is affected earlier than the other." (taken from Wikipedia)

[4] http://www.ncbi.nlm.nih.gov/pubmed/18545013

[5] http://www.aao.org/publications/eyenet/200501/feature.cfm

[6] http://www.aao.org/publications/eyenet/200501/feature.cfm

2. The market

2.1 General market considerations

The prime invention of Prof Bille of an aberrometer enjoys a high level of success and widespread usage for refractive surgery:[7]

> *"Eye care has known a number of major technological innovations in recent years. Aberrometers have made it possible for the first time to measure higher order aberrations in the clinic. This breakthrough has been a runaway success with refractive surgeons from the outset, and now there is a growing realisation in the market that the type of precision and detail offered by aberrometers is increasingly needed in the general practice as well. There is a growing number of new correcting elements based on information coming from aberrometry. Best known are Lasik and IOLs; aberrometers can help making a sharper prescription. Contact and spectacle lens manufacturers are under tremendous pressure to offer custom correction solutions. Aberrometers have been the key enablers for this trend. It is clear that aberrometers are an essential part of the forward-looking ophthalmic practice."*

Market researchers assess the size of the European market for diagnostic and interventional ophthalmic devices – of which aberrometers are part of – to be worth some € 650 million in 2010.[8] Leading firms in the market for ophthalmic devices are Alcon, Bausch & Lomb, Carl Zeiss, Haag-Streit, Medtec and Oculus. The corresponding report for the U.S. addresses also contact lenses and gauges the market to be worth some US$ 5 billion by 2017.[9]

The market itself is driven primarily by demographic trends – which make the market correlate with the e.g. prevalence of myopia – and by general economic development/business cycle development.[10]

Laser surgery, the prime field of application of aberrometry, represents a high-cost, discretionary purchase. A number of papers have linked respective volume of surgical procedures to consumer confidence or to stock prices. On the supply side, the market is considered very competitive:[11] *"Leaders in the market strive to meet the demands of the industry and continue to invest 7% to 15% of total sales into research and development efforts...long-term success is gained by focusing on improving technology and by enhancing productivity, patient outcomes, and reducing health costs to both patients and providers."*

In terms of diagnostic use alone, Prof. Bille estimates that there are around 5,000 to 7,000 OCT devices sold each year. He notes that there is a clear tendency to replace the old-fashioned slit lamps in practitioner offices by OCT devices, even if they cost much more (around € 100,000 vs. € 3,000 for a slit-lamp), because the advantages clearly outweigh the costs.

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[7] Imagine Eyes.com (2011): Frequently asked questions (FAQ) about wavefront aberrometry, http://www.imagine-eyes.com/content/view/29/56/

[8] http://www.businesswire.com/news/home/20111118005577/en/Research-Markets-European-Markets-Ophthalmic-Devices-2011

[9] http://www.businesswire.com/news/home/20110411006543/en/Research-Markets-U.S.-Market-Diagnostic-Ophthalmic-Devices

[10] http://www.medicaldevicestoday.com/2009/02/difficult-days-for-laser-vision-correction-market-and-amo.html

[11] http://www.mddionline.com/ophthalmic-market-rise

Concerning the cataract market, the number of cataract surgeries worldwide in 2007 is estimated at 14 million.[12] This surgery represents over 70% of eye surgeries. According to Prof. Bille, premium lenses (the market segment addressed by wave-guided IOLs) already account for 70% of the lenses sold in the U.S.; in Germany the share amounts to 10%. Eventually, Prof. Bille sees market penetration of premium lenses globally at 50% on average.

2.2 Direct economic impact

A measure of the direct economic impact of Prof Bille´s invention is the number of start-ups Prof. Bille has co-founded, mostly with some of his former PhD students. There were five such start-ups formed. Three firms are now larger companies with around 250 employees each and a yearly turnover of € 100 million. Taken together, Prof. Bille´s inventions have helped create around 1,000 jobs in these firms and have led to yearly combined turnover of € 300 million.

3. The role of patents and Intellectual Property Rights (IPR)

3.1 Motives and benefits of patenting and employed IPR strategy

For Prof. Bille, patents have been essential for the development and uptake of the inventions:

> *"Patents are important for a variety of reasons, but two stand out: First, to set up a start-up firm there is the need for venture capital. But it would not be possible to obtain such capital if we had no patents. In fact one could say that writing a business plans equates to writing patents. Secondly, without patents, large competitors would quickly absorb the technology and we would not have had a chance to enter the market."*

Enforcement of patent rights can be an issue in this industry. According to Prof. Bille, a patent litigation would be an economically feasible option only if the firm has a yearly turnover in the order of US$ 100 million, in order to sustain the litigation process. This means that especially for small firms patent litigation and enforcement is an issue. However, without the patents it would be not possible to actually enter the market at all. There is a time window of around 2 to 3 years at the beginning, where the patent actually protects the invention and where there is hesitation on the side of competitors to infringe the patent (there is, of course, also the power of the involved venture capital firms behind the start-up to be considered). And one natural option is then also the sale of the patent (or the firm whose business is based on the patent) to a competitor who is in a better position to enforce the patent rights.

One can conclude, therefore, that the patents in this field are most valuable for the inventor in the beginning of the commercialisation process and their value, on average, tends to decrease with time. *"As the technology is a puzzle of many different parts which get patented over time, it could very well happen that a particular patent is so far ahead of the time of application, that by the time you get to actual commercialisation, patent life has expired,"* explains Prof. Bille, *"you need to be able to cope with that. Other patents in the portfolio will have to compensate for that."*

Prof. Bille reckons that patents are also important because purely scientific publications would not push the technology forward. Many technological aspects that need to be tackled in the transition from the (basic) research phase to application in a practitioner´s office would most likely not even be accepted for publication in journals.

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12 http://www.moria-surgical.com/MORIA-SURGICAL-CORPORATE-PRESENTATION-CATARACT-MARKET_378.htm

Prof. Bille´s patent strategy is to patent first in the U.S. with priority filings. This is because most venture capital firms are located in the U.S. and, naturally, their interest is to have patent protection in the U.S. Another reason for the focus on the U.S. is that U.S. patent law have broader patentability criteria, which extend also into methods (e.g., new surgical procedures). Eventually, Prof. Bille underlines that, in particular in the past, the time from application to actual grant of the patent was faster in the U.S. Now, with the increasing backlogs at the patent offices, mere patent applications often fulfil the same role as did granted patents in earlier times. Interestingly, Prof. Bille and the associated firms hardly consider China for patenting, *"...as in our optical field there are no Chinese manufacturers to speak of."* (Prof. Bille).

Prof. Bille writes all his patent applications himself also because *"...because it is fun to do so."* He has hardly used external support from the university. In the beginning, there was not even support. *"The situation is now changing, but being professional at the university technology transfer offices - fast, unbureaucratic – is an issue for a lot of universities in Europe and also in the U.S., where the situation is further developed."* (Prof. Bille)

3.2 Patent statistics and patenting trends

Prof. Bille has applied for 74 patents since 1982, all related to the diagnostics and surgery in particular for eyes. The frequency of filing activity is indicative of a continuous R&D and commercialisation process. 28 of the inventions led to filings using the world-PCT route. 49 inventions were applications with the European Patent Office. Of the 49 European patent applications, 14 patents are still in force.

Major markets – as identifiable by the countries in which patent protection was sought – comprise the U.S., Europe (Germany, the UK and France) and Japan. Since around 2005, applications have also been filed in Eastern Asian as well as in Central and South American markets. Prof. Bille has filed his patents together with different firms. There have been as many as 15 firms with whom Prof. Bille has written patent applications; most applications were filed with the firm Technolas Perfect Vision (formerly 20/10 Perfect Vision).

A common measure for patent value is the number of times a patent is cited. The number of times Prof. Bille´s patents are cited – 683 times by other patent applicants – is a clear indication of a high value of these patents.

All patents of Prof. Bille are classified in the IPC technology class A61B-003/103.[13] In this patent class, there have been as many as 1,082 patents filed. While there were 177 patents application submitted in this class in the 1980s, there have been as many as 426 applications since 2000. Particular spikes in patent filing activity can be observed between 1989 and 1991 (on average 55 patent applications per year) and between 2000 and 2003 (on average 58 patent applications per year). Major patent applicants are Canon (166 patent applications), Topcon (Japan) with 166 patent applications and Carl Zeiss with 83 applications. AMO Manufacturing/VISX and Bausch & Lomb – firms with which Prof. Bille collaborated on some of the patents – are ranked fifth and sixth, respectively, on the list of patent applicants in this IPC class.

4. Conclusions

The available evidence suggests a high value of the patented technologies, with clear economic and societal impact, as evidenced by the up-take of the invention in medical

[13] Apparatus for testing the eyes, Objective types, i.e. instruments for examining the eyes independent of the patients perceptions or reactions, for determining refraction, e.g. refractometers, skiascopes

practice or the establishment of firms with a total employee workforce of 1,000 and € 300 million combined annual sales.

Success factors were, according to Prof. Bille:

- Perseverance: *"You need to stay for a long time in a technology field and be prepared to deal also with moments of defeat. You have to have a lot of staying power, and usually there are many tedious steps to be taken."* (Prof. Bille)
- Close interaction between inventors and users: *"There is a necessity to stay in touch with the users, in my case the eye specialists and ophthalmologists. This requires a good knowledge of the market, establishing trust-worthy relationships. This takes time."* (Prof. Bille)
- Unconventional approaches: Being prepared *"…to swim against the tide"* is, according to Prof. Bille, also an important success criterion.
- *Good IP strategy:* For Prof. Bille, patenting was a modular process, and each patent was a small piece of a technological puzzle. From a financial point of view, this process is burdensome and there was clearly the need to be able to cope with this process financially. Venture capitalists' backing is essential in this context.