"The importance of industry-science relation for the knowledge based economy: lesson learnt from RPIA", Brussells 5th Sept. 2006

# RPIA Project: OPTOMED Innovative optoelectronic technologies for ophthalmology


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*National Research Council of Italy*

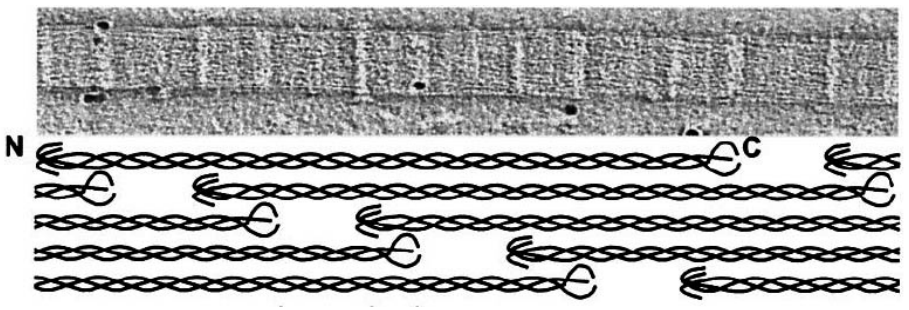
# Summary

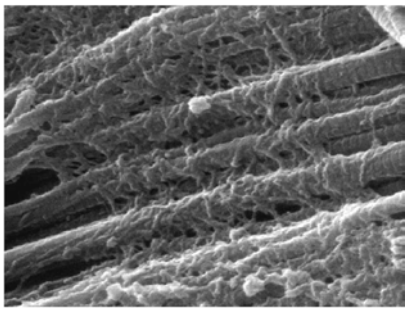
The OPTOMED Project aimed at the development and transfer of innovative instrumentation and methodologies used in Ophthalmic surgery to enterprises of Tuscany operating in the field of Opto-electronics and in hospital care in the most important university clinics and hospitals.

Specifically, the OPTOMED project has set up prototypes of new surgical diode lasers, instruments for ophthalmic diagnostics, and new pharmaceutical formulations of photosensitisers .

# Introduction:
# Laser-induced suturing of biotissue

- Welding (soldering) processes of biological tissues induced by laser radiation have been studied at the experimental level for applications in various surgical fields, e.g. to suture and repair blood vessels, nerves, tendons, skin, etc.
- They are based on laser-induced activation of the endogenous collagen, which behaves like a thermally activated glue



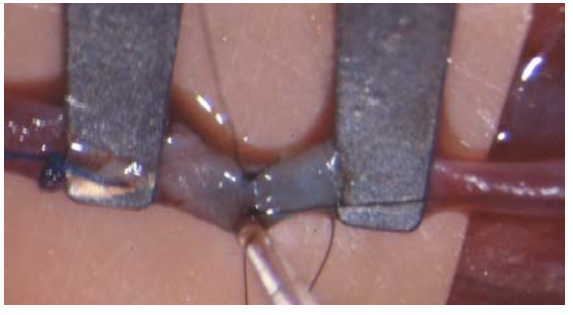



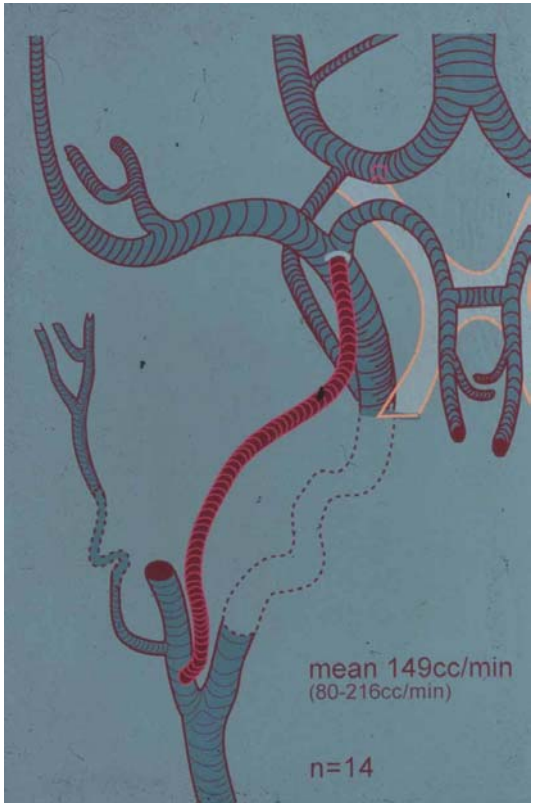
# Laser-induced suturing: Examples of surgical applications

## Laser welding in cerebral bypass surgery

(work in co-operation with the Institute of Neurosurgery, Catholic Univ., Rome

- Laser welding for the suturing of cerebral arteries could offer significant advantages, such as the reduction of blood occlusion time (10 min. compared to 45 min. of conventional surgery), reducing the risk of cerebral damages

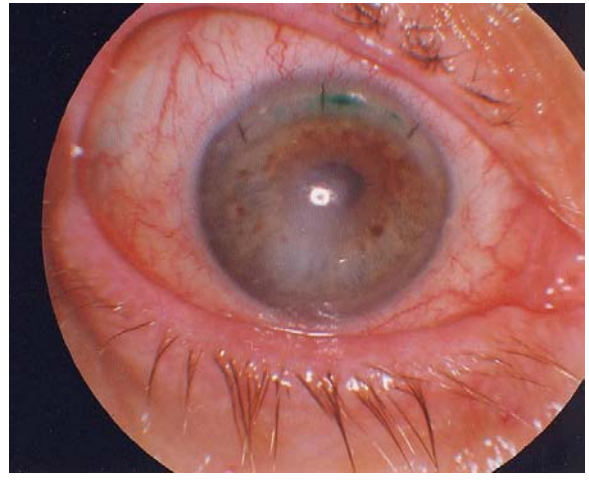




# Laser corneal welding ①

**Laser-induced welding (soldering) of corneal tissue is an original proposal made by Luca Menabuoni (ophthalmologist) and Roberto Pini (physicist), which received the approval of the Italian Health Ministry to perform both pre-clinical and clinical experimentations.**

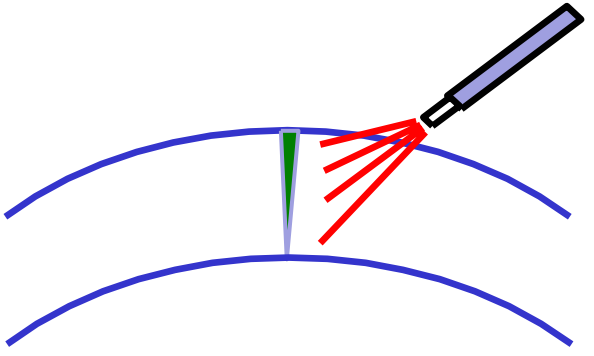
**It is proposed for use in the transplant of the cornea, in substitution of the conventional continue suture, as well as to close the corneal cut produced in cataract surgery.**



# Laser corneal welding ②

The laser welding technique is based on the application of a photosensitizer (i.e. a dye solution) in the corneal cut, followed by irradiation of the cut with a diode laser emitting at 810 nm. The role of the photosensitizer is to obtain selective and local absorption of diode laser radiation only by the cut edges, in order to activate corneal collagen and produce tissue fusion.

The repaired cut is water-tight, with a good mechanical resistance and no side effects (such as heat damage).



# Advantages of diode-laser corneal suturing

**Expected improvements of laser-assisted suturing in corneal surgery (especially in corneal transplant):**

- **Simplification of the sugical procedure and reduction of the intervention time (3-5 min. vs. 30-45 min.)**
- **Reduction of suture material and, consequently, of post-operative inflammation (foreign body reaction)**
- **Reduction of post-operative astigmatism**
- **Better and faster healing process (3-6 months as compared with 12-18 months of conventional surgery)**

# Objectives of the OPTOMED Project

- Design, construction and development of new demonstrative prototypes of lasers, photosensitizers, and intruments for ophthalmic diagnostics by Tuscan enterprises
- Conducting studies aimed at pre-clinical experimentation, validation of the developed technologies and related surgical methodologies
- Definition of clinical protocols by four of the main ophthalmic clinics of Tuscany.
- Evaluation of economical and social impact of the new technologies and surgical procedures in comparison with the traditional ones.
- Activities of diffusion, dissemination and training through meetings, conferences, exhibitions, and post-doc specialization courses.

# Partnership

- 2 Public Research Centers
- 4 Ophthalmic Clinics of Tuscan Universities and Public Hospitals
- 8 Entreprises ( 7 of them in “Area Obiettivo 2” )

Other co-operations with:

- 2 University centers of experimental surgery
- 2 Depts of the Faculty of Medicine of UNIFI
- 1 Dept of the Faculty of Electric Engineering of UNIFI
- 1 Dept of the Faculty of Pharmacy of UNIPI

# Partnership: Pubblic Organizations

**PUBLIC RESERCH CENTERS:**

- **Consorzio CEO - Unità CLAM (Centro Laser Applicazioni Mediche), Firenze – Group leader, project managing**
- **Istituto di Fisica Applicata "Nello Carrara" - CNR, Firenze – Technology transfer, preclinical researches, diffusion and dissemination**

**OPHTHALMIC CLINICS – Evaluation of preclinical tests, recommendation for clinical protocols :**

- **Clinica Oculistica II, Dip. Scienze Chirurgiche Oto-Neuro-Oftalmologiche, Univ. Firenze c/o P.Careggi**
- **Dip. Scienze Oftalmologiche e Neurochirurgiche, Univ. Siena**
- **U.O. Oculistica, ASL 4 Prato**
- **U.O. Oculistica, ASL 10 Firenze**

# Partnership: Private enterprises

- ACTIS srl, Firenze – Development of diode lasers
- Molteni Farmaceutici spa, Scandicci (FI) – Development of the chromophore
- ITAL TBS spa, Pisa – Analysis on clinical costs of the new procedures
- CSO- Strumenti Oftalmici srl, Scandicci (FI) – Development of corneal topographs and aberrometers
- Gestione SILO srl, Scandicci (FI) – Optical components and systems
- EUREL srl, Scandicci (FI) – Electronic components
- Loto d.i., Firenze – Fiber systems for diode lasers
- EL.EN. spa, Calenzano (FI) – Production and commercialization of diode lasers

# Activities: WG and WP

**The project was organized creating 3 woking groups (WG) and the activity was carried out in 15 months according to 6 working packages (WP). In brackets, the # of months (M) for each WP are indicated:**

| | |
|---|---|
| **WG1: Transfer and development of industrial products**<br>**Part.: Tech. enterprises + public research centres** | **WP 1 - Development of diode laser systems (M1-M7)**<br>**WP 2 - Development of the systems for ophthalmic diagnostics (M1-M8)**<br>**WP 3 - Development of photosensitizers (M4-M9)** |
| **WG2: Pre-clinical tests and validation**<br>**Part.: Research centres, university clinics, other university depts** | **ML 4 - In vitro and in vivo pre-clinical studies (M2-M11)** |
| **WG3: Medical, social and economical evaluations :**<br>**Part.: Research centres, university clinics, public hospitals, evaluation centres** | **ML 5 - Definition of criteria and protocols for clinical applications (M7-M14)**<br>**ML 6 - Evaluation of social and economical impact (M11-M15)** |

ACTIS
ACTIVE SENSORS SRL

LOTO
Scientific Instruments

El.En. Grou

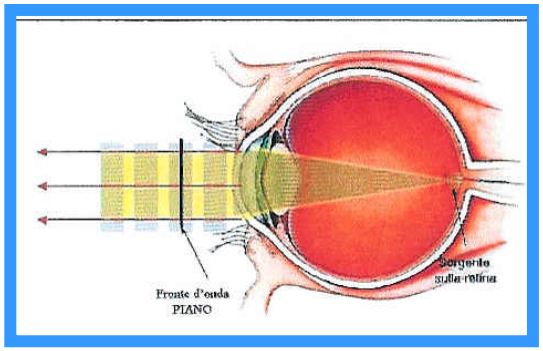
# The diode laser for cornea suturing

- AlGaAs diode laser @ 810 nm
- Fiber optic delivery system with fibers of 200/300 μm core diam.
- Hand piece to be used under surgical microscope

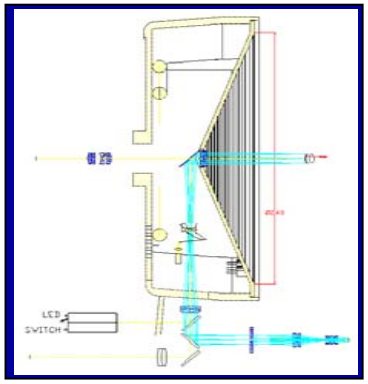

| | |
|---|---|
| Emission wavelength | 810 ±10 nm |
| Output power | 0.5-10 W * |
| Type of emission | CW and pulsed |
| Repetition rate (pulsed) | 0.5-500 Hz |
| Power emission stability | ±20 % |
| Aiming beam | 635 nm, 1 mW |
| User interface | Touch screen LCD |
| Size | 24x18x36 cm |

* 50-1000 mW with the 1/10 optical attenuator accessory

# Corneal topograph+eye aberrometer




Total aberrometry: it measures the total modification of the light front wave propagating in the eye, including the astigmatism induced by the cornea + aberration on the retina due to light transmission in the eyeball

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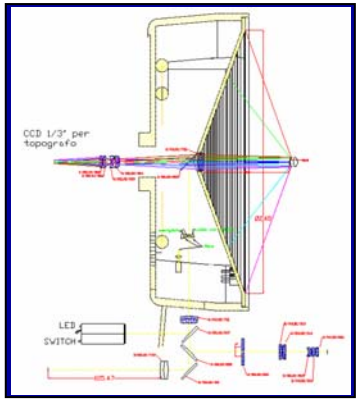
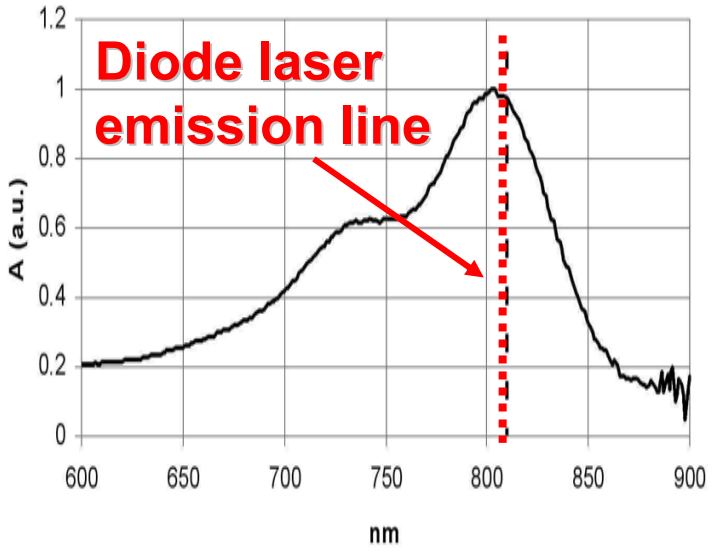



# Photosensitizer for corneal welding

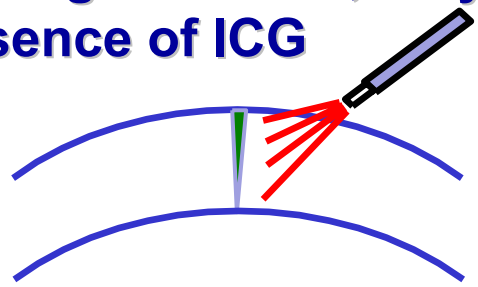
**Diode laser radiation at 810 nm is used in association with an exogenous dye (photosensitizer), i.e. a solution of Indocyanine Green characterized by high optical absorption of the diode laser light.**

## Absorption spectrum of ICG in corneal tissue




## Advantages in comparison with other laser approaches:

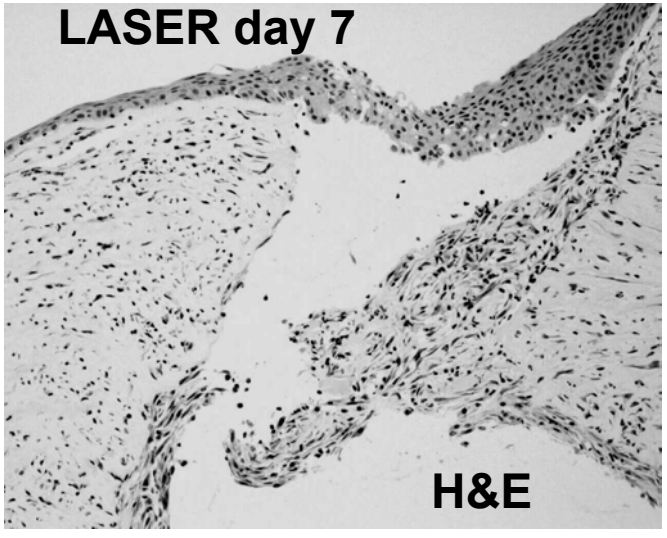
- Very low laser power (< 100 mW, 5-10 W/cm$^2$)
- Selective and localized welding in the cut, only in presence of ICG

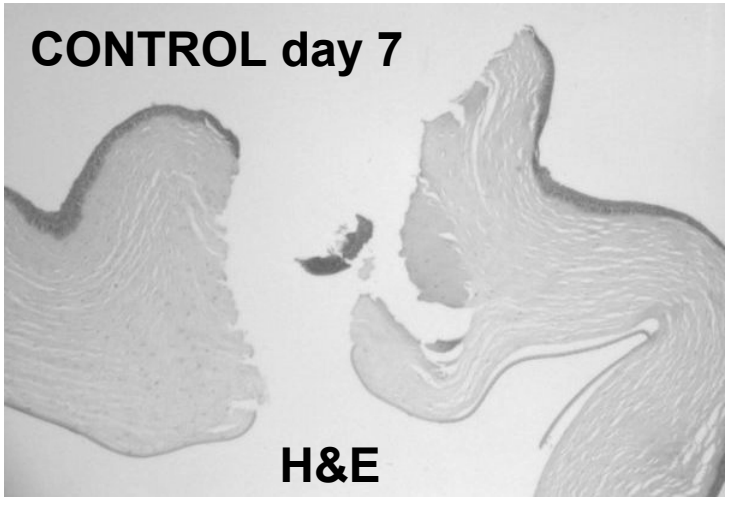


# Experimental studies on the healing process

**Results of histology exam. in a follow up study up to 90 days :**

- the healing process was found to develop in a shorter time and with less inflammatory and foreign-body reactions
- the architecture of the cornea regained an almost physiological aspect with continuity of epithelium and endothelium and regularly organized collagen fibers in the stroma .



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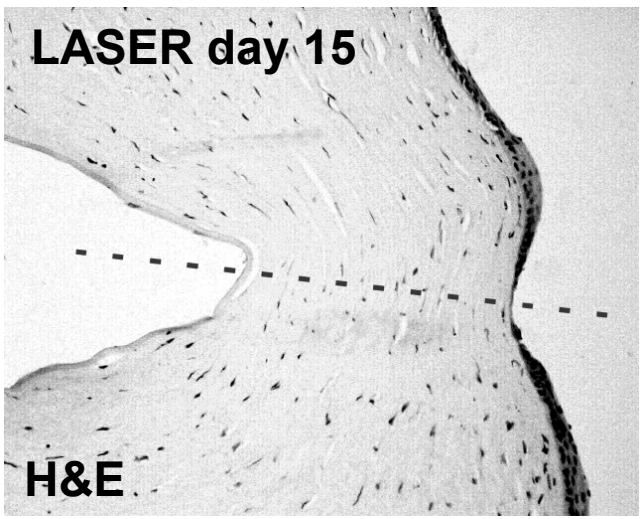


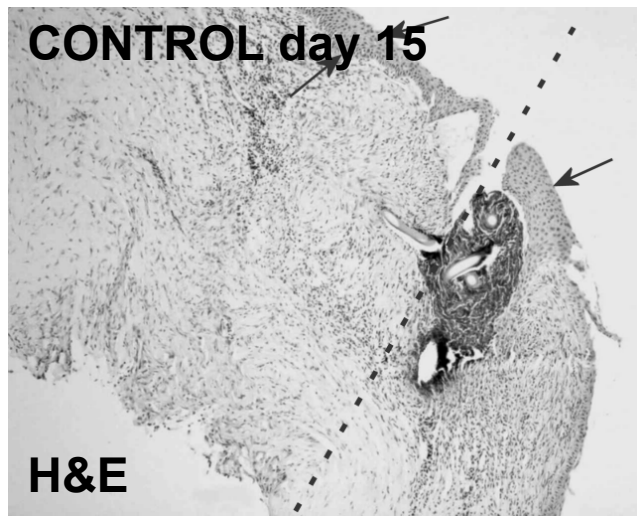

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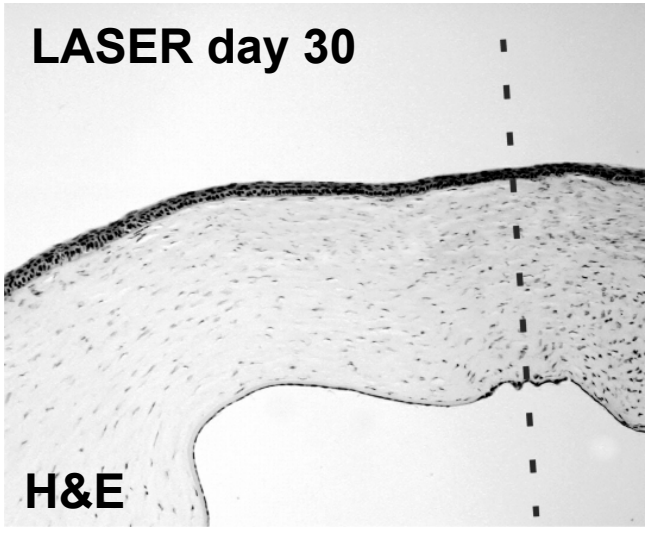


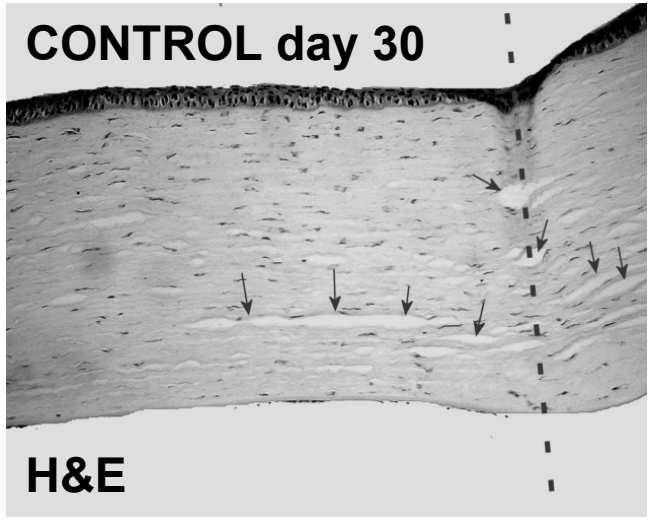

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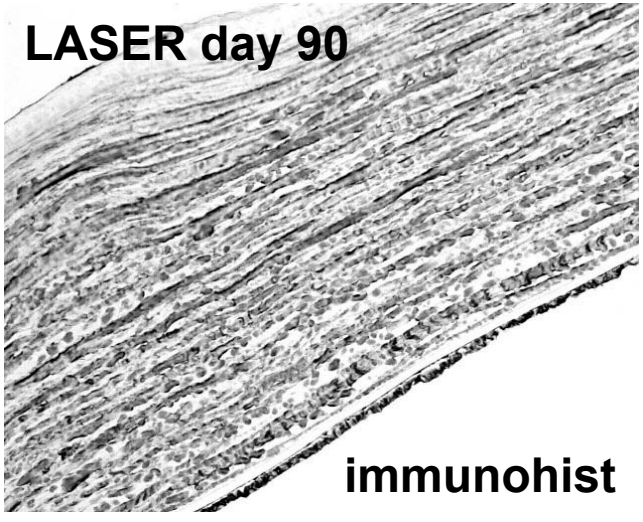


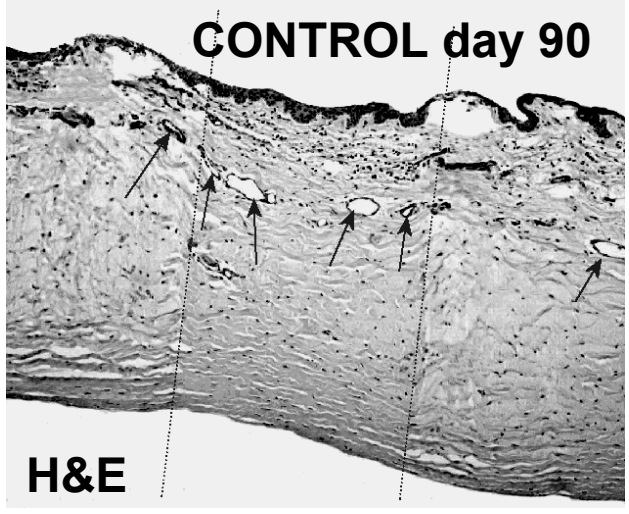

# Promotions of the OPTOMED Project

**The project was promoted and publicised by means of:**

- **A brochure (in Italian and English) printed in 2000 copies, which was used in all the public occasions of diffusion.**
- **A web site, reporting the objective of the project and the link with the parters**
- **Participation to 5 meetings and exhibitions**
- **5 scientific articles**
- **Several communications to national and international scientific conferences**
- **About 20 Press reports, articles in national newspapers, interviews**

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# Beneficiaries of OPTOMED results ①

**The project has developed a network of public and private partners which enabled it to attain innovation transfer in various application fields. Beneficiaries could be identified as follows:**

1) **The industrial sector:**

   **Technologies related to innovative pharmaceuticals and instruments with applications in ophthalmology, which were previously developed as prototypes in the Tuscan scientific axis, were transferred to a group of enterprises working in the fields of laser technology, optics and electronics components, ophthalmic instruments, pharmaceutical products, economic consulting and planning for the Health System. All of them have the capacity to engineer, mass produce and market such products and instruments**

# Beneficiaries of OPTOMED results ②

2) **The medical field:**

**Instruments, pharmaceutical products, and innovative procedures were created and tested in four important university clinics and hospitals in Tuscany, thus involving the final target consumers during the actual development phase. This enables the project to guarantee that the products are a valid match with its intended consumers in the appropriate contexts, thus favouring their distribution and use on a large scale.**

# Beneficiaries of OPTOMED results ③

3) The public health system, in terms of both economic and social advantages.

3.1) Economic advantages:

- a reduction in length of average hospital stays (surgery in a day hospital as opposed to longer hospitalization);
- smaller expenses due to the lower number of checkups necessary during the healing process
- lower relapse rate
- reduced expenditure for eyeglasses and vision correction

3.2) Social advantages referred to health benefits for patients and to improvement in their quality of life. Specifically:

- technical/surgical advancements in corneal transplants and in the suturing of corneal wounds
- more efficient healing with less astigmatism

# Positive aspects of multidisciplinarity

- OPTOMED's managing was carried out by research centers, which hinged on their previous experiences in co-ordinating quite large and multidisciplinary research projects.
- Beside researchers and industrial engineers, the working groups included also the end users, i.e. ophthalmic surgeons, which provided an immediate validation of the instruments during design and engeeniring phases. This helped to harmonize demands of the end users and engineering constrains, shorthening the time-to-market of the products.
- The management had strong interactions with the Regional steering committee by means of the group of experts nominated by the Tuscany Board in order to verify the accomplishment of the results. This also helped a transversal coordination with other projects carried out in the same program frame.

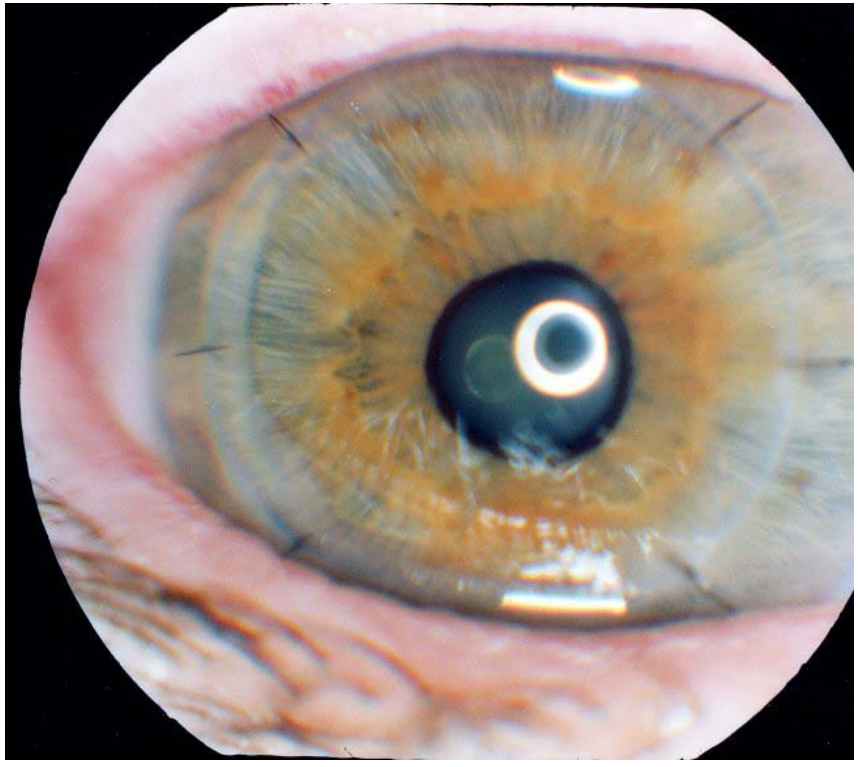
# Obstacles in terms of design and implementations

- **MANAGING PROBLEMS: Small enteprises and hospital clinics who had no previous experiences in co-ordinated projects felt the participation to a common strategy as a constrain or a lose of time. Moreover, they encountered big problems in facing bureaucratic and administrative managing of the project. A simplification of administrative procedures would help in the future to improve this figure.**

- **TECHNOLOGY PROBLEMS: During the development of the project we realized that only innovations that were almost mature for the industrial development had the major possibilities of success. Sometimes the innovation appeared "too innovative" for the industrial process, especially when research centers proposed the whole design of new devices. For example, we realized that we could more effectively achieve the goal of industrial production of a new laser for corneal suturing by modifying and implementing existing laser devices, rather then proposing completely new technology.**

# Perspectives of *future* developments

- **Production of a pre-series of diode lasers for clinical tests (*6*)**
- **Clinical phase: tests of corneal transplant (*20*)**



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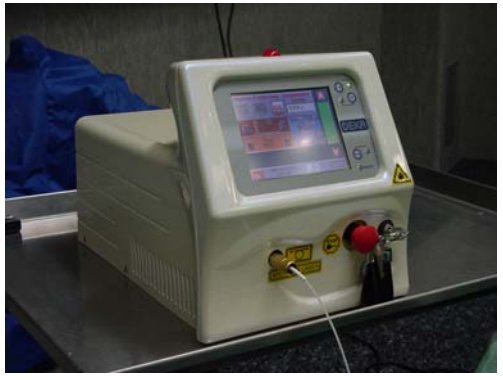
- Design of new instruments for ophthalmic surgery



# Perspectives of *future* developments

- Production of a pre-series of diode lasers for clinical tests (*6*)
- Clinical phase: tests of corneal transplant (*20*)
- Design of new instruments for ophthalmic surgery
- New Projects and Networks:
  - REGIONE TOSCANA Giunta Regionale — OPTONET
    Network for Optoelectronics in Tuscany
  - Programme Interreg IIIB MEDOCC Pour la cohésion des territoires de l'Europe du Sud — FEDER — ROM Réseau Optique Méditerranéen
    Network of Optics of Mediterranean Countries
  - Azienda USL 4 di Prato — OPTOWELD
    Clinical Project on laser-assited “Lens Refilling”

# Thanks to scientific co-operators:

| | |
|---|---|
| Prof. Riccardo Pratesi | Facoltà di Fisica, Univ. Firenze |
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| Prof. Leonardo Masotti | Facoltà di Ingegneria, Univ. Firenze, Presidente CEO |
| Dr. Monica Monici | Ricercatore CEO |
| Dr. Francesca Rossi | Ricercatore CEO |
| Dr. Franco Fusi | Dip. Fisiopatologia Clinica, Univ. Firenze |
| Dr. Giovanni Agati | Istituto di Fisica Applicata - CNR |
| Dr. Guido Toci | Istituto di Fisica Applicata - CNR |
| Prof. Ugo Menchini | Clinica Oculistica II, Dip. Sci. Chirurgiche Oto-Neuro-Oftalmol., Univ. Firenze |
| Dr. Rita Mencucci | Clinica Oculistica II, Azienda Careggi |
| Dr. Gianni Virgili | Clinica Oculistica II, Univ. Firenze |
| Dr. Fabrizio Giansanti | Clinica Oculistica II, Univ. Firenze |
| Prof. Aldo Caporossi | Dip. Scienze Oftalmologiche e Neurochirurgiche, Univ. Siena |
| Dr. Cosimo Mazzotta | Dip. Scienze Oftalmologiche e Neurochirurgiche, Univ. Siena |
| Dr. Silvia Tampucci | Dip. Biorganica, Univ. Pisa |
| Dr. Susi Burgalassi | Dip. Biorganica, Univ. Pisa |
| Prof. Avio Maria Perna | Laboratorio di Chirurgia Sperimentale, Azienda Careggi |
| Dr. Paolo Santoro | S.O. Oculistico, ASL 10 Firenze, I.O.T. |
| Dr. Giovanni Laganà | S.O. Oculistico, ASL 10 Firenze, I.O.T. |
| Dr. Ivo Lenzetti | S.O. Oculistico, ASL 4 Prato |
| Dr. Maurizio Corsani | S.O. Oculistico, ASL 4 Prato |
| Dr. Pierpaolo Gini | S.O. Oculistico, ASL 4 Prato |
| Prof. Gabriella Vannelli | Dip. Anatomia, Univ. Firenze |
| Dr. Stefano Ambrosini | Dip. Anatomia, Univ. Firenze |
| Dr. Bernardo Innocenti | Dip. Meccanica e Tecnologie Industriali, Univ. Firenze |
| Dr. Damiano Fortuna | Dip. Cardiotoracico, Univ. Pisa |

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