LASER is the acronym for Light Amplification by Stimulated Emission of Radiation. Ever since it was coined, the term has stirred imaginations around the world. Today there is an anti-inflammatory drug with that name as well as countless methods and things, from laser-line to laser-sails, etc.
Invented by a thirty-two year old physicist, Theodore Maiman on 16 May 1960, the laser was not immediately accepted by the “official” academic-scientific community, which starting from the theories about its principles developed by Albert Einstein dating back to 1917 had spent considerable financial and intellectual resources to no avail (T. Maiman, *Laser Odyssey,* 2000).Therefore, Maiman never received the Nobel Prize. It was awarded to other scientists such as Townes, Schawlow and Prokhorov who had studied applications for the laser.

In medicine the laser followed the same path as all new technological discoveries, much like X-rays. First the technology was rejected as useless, then hailed as a panacea, then denounced and shunned because of harmful effects and then it was gradually accepted after adequate clinical testing. Since then X-ray technologies have developed to the point that a specialization was created, and probably the same will happen with lasers in the near future. As of today each field of medicine merely considers the laser a tool, like any other. Therefore, medical laser technology is evolving quickly but in a disorderly manner and with an enormous waste of financial and intellectual resources.

For this reason, fifty-one pioneers in the use of laser in various disciplines – including Maiman – have established an International Academy in Florence. The aim is to prevent the fragmentation of knowledge in line with the proposals of the European and international communities’ research programs. Each year a world congress is held present and compare totally different scientific and cultural situations. From 1997 to the present this meeting has always made new contributions which are most useful to the international scientific community. For the sake of convenience we will describe them briefly, broken down by specialty groups.

According to the application, lasers can be broken down into **diagnostic, therapeutic and surgical** (L. Longo, 1986). To these we must add **intense pulsed light**, which has been in use for a few years for therapeutic purposes. As we know, lasers are non-corpuslcar emissions of electromagnetic radiation with the peculiarity of being monochromatic, coherent, bright and directional at the same time. No other source of radiation currently known to physics has all four of these characteristics contemporaneously. Intense, pulsed light has brightness and a certain directionality, but it is neither coherent nor totally monochromatic. Therefore, while the laser beam can be adjusted at the tissue level and we can predict the amount of radiation absorbed by the tissues, this cannot be done with intense light because the radiation is not totally monochromatic, is not coherent and is not perfectly directional. Therefore, the amount of radiation that actually irradiates and is absorbed by the tissues is always different, at each instant, given identical tissues. Like intense pulsed light radiation, laser beams consist of photons and not solid corpuscles. As opposed to X-rays, for example laser beams are neither carcinogenic nor mutagenic. This hazard only exists if they are emitted in the Type A ultraviolet band. From photo-biological studies dating from the ‘fifties we know that this wavelength can give rise to genetic and oncogenic mutations (Fleury, *Traité de physique,* 1957).

LASERS IN DIAGNOSTICS
Lasers used: Excimer – Diode – Helium/Neon
(from 280 to 1000 nm)

All the current applications of diagnostic lasers are summarized in the table. We can distinguish the established and experimental uses. During Laser Florence 2000 Professor A. Hielscher of Columbia University, New York showed three-dimensional images of the human body obtained by optical tomography, which is a form of CAT where lasers are used in lieu of X-rays. Since 1997 Professor Tomasini of the University of Ancona has been measuring the vibrometry of the structures of the mouth obtained with lasers which are useful for determining and studying the state of dentition. The use of laser-Doppler to measure microcirculation in vivo is already an accepted technique while it is still in the experimental phase as regards studies of Raman spectrophotometry and measurements of the Kirlian effect. To summarize, the main applications of lasers in diagnostics are:

LASER DOPPLER: for determining the condition of the capillary microcirculation in vivo, accepted practice.

LASER SCANNING MICROSCOPY: three-dimensional microscopic examination of tissues, not yet a routine examination (P. Benedetti, Laser Florence 2003).

PHOTODYNAMIC DIAGNOSIS (PDD): permits the selective identification of neoplastic cells with a substance that binds to them and is then stimulated by the laser.
It can be used together with photodynamic therapy (**PDT**), when the substance stimulated by the laser identifies and selectively eliminates the neoplastic cells.

Only a few centers in the world actually use this method, they are located mainly in England, Germany, USA, France, Japan and Lithuania. It was first presented by Tom Dogherty in the late ‘sixties. It has not yet become part of medical routine due to a series of drawbacks and limits: the relatively low fluorescent decay time of the substances and variable amounts of primary and secondary fluorescence according to the moment of use (poor stability); high costs and low availability in countries where these treatments are not permitted other than for experimental purposes; the impossibility of irradiating many deep tissues with lasers and the “shield effect” of the more superficial layers of the substance-tissue combination which necrotizes during irradiation and prevents the rays from penetrating deeper; only relative substance-tissue selectivity with the possibility that the photodynamic substance binds with other, cells – such as liver, skin and cancer – with high mytosic indices and/or does not bind with cancers cells that have little or poor vascularization. However, PDD and PDT are used mainly for the diagnosis and treatment of skin and hollow organ cancers. Today we are also trying to use these methods in the treatment of skin diseases such as acne, pigmented keratosis, vitiligo and eczema (Lancet).

OPTICAL TOMOGRAPHY: this is a form of CAT in which laser beams are used in lieu of X-rays and can give a three dimensional view of the irradiated area. There are few places in the world that offer this, (USA, Germany, France, Sweden and Japan), but it will be the technique of the future. The three dimensional images currently permit accurate study of the bones and muscles, but not yet fine structures (A. Hielscher, 2000).

OPTICAL BIOPSY: this method makes it possible to identify cells undergoing malignant transformations with a simple scan and no surgical incisions. It is useful for breast cancer, but is not yet used routinely. It is used mainly as a guide in traditional biopsies. (Harvard Medical School, Boston)
RAMAN SPECTROMETRY: each tissue has its absorption map of different colors. Lasers make it possible to draw these maps that change in each tissue just before it becomes diseased. It has been tested in Germany, USA, Sweden, Japan and Australia.

KIRLIAN SPECTROMETRY: each living being emits luminous radiation that can be measured and affected by laser beams and that can continue being emitted for varying lengths of time even after death. Experimental: USA, Russia, China, Saudi Arabia, Japan.

LASERS IN THERAPY
Lasers used: CO_2 – Neodymium / YAG – Helium/Neon – Diode
(10600 nm, 1064 nm, 632 nm, 532-1000 nm)

In the past, it was non-surgical applications of lasers that were most widely discussed and for several reasons. The effect was less immediate and less evident than in surgery, and they were only proposed by the Eastern Bloc countries (Mester, Alma Ata,) where lasers cost less than pharmacological treatments and so efforts were made to use them more frequently. In the United States testing of physical, non-surgical, treatments only began after Clinton became president, because up to then it had been challenged by the pharmaceutical industry. The early therapeutic lasers were inexpensive and were marketed wildly in Europe, even on television, so that they often ended up in the wrong hands. For some years now there has been ongoing scrupulous research conducted according to the accepted international rules of science. This, together with the review of countless clinical cases and surveys in the literature (Hode and Turner), has led to some rather surprising conclusions. For example, at Laser Florence 2002, the diode laser was successfully used to reduce glucose levels in insulin-dependent diabetics. This is a case of evidence-based medicine since the author, Professor P. Ramdawon, a resident of the Mauritius Islands did not support this clinical evidence with an adequate scientific demonstration according to the dictates of the Helsinki Declaration . Furthermore, the same method has been in use for about 20 years in several Eastern European countries, China and in Finland, and over the past year or so on Indian Reservations in Arizona. During Laser Florence 2002 and 2003 other groups discussed this topic, even though there is still not sufficient testing that would offer incontrovertible data. The effect of lasers on scarring in an experimental ulcer model where the fibroblast growth factors increased by 98% was demonstrated during Laser Florence 2002. This is a contributory cause that explains the extremely positive clinical effect of non-surgical lasers on scarring of ulcers and experimental wounds (Longo, Anders, Hode, Karu).

One extremely important point is that each effect of non-surgical lasers is closely dose-dependent to the extent that the same laser on the same tissue can have opposite effects. In fact, lasers used to stimulate scarring can also inhibit it. This is useful in cases of pathological scarring such as hypertrophic and cheloid scars, and for collagen disorders such as induratio penis plastica. In these cases we have see that the metal-sensitive proteinase of collagen increases by up to 80% after each laser irradiation, to reach the maximum after about three weeks or irradiation, while the TGF fibroblastic transformation factor remains unchanged until the third or fourth application using doses at least twice as strong as those used to stimulate scarring (Longo, LSM). Lasers and pulsed light are used in esthetic medicine for skin rejuvenation. In these cases an application of this radiation every 3-4 weeks, for an average of from 4 to 8 for each application succeeds in eutrophizing areas of dystrophic skin, reabsorbing discolorations and small wrinkles, giving the tissue a firmer appearance and making it more resistant to external agents. Several Anglo-Saxon authors have done histological studies using the punch method that reveal the reabsorption of the damaged collagen and other skin impurities, and their replacement with young collagen and revitalized tissue (LSM). The same authors have hypothesized a mild, dermal-hypodermal inflammation as the basis of these phenomena, but the same inflammation caused by violence, such as a slap does not produce the same effect. Therefore, we have proposed a totally different mechanism (Lubar, 2003): in vitro we have seen that light in the red wavelength is absorbed by cellular mitochondria, while infrared light is absorbed close to the cell walls as well as by tissues with complementary wavelengths. This makes the mitochondria produce a larger amount of H_2O_2, with a consequent increase in radicals oxygen stimulated (ROS), due to degradation of unstable H_2O_2. The small quantities of these radicals would “clean” the cellular cytoplasm enabling the cell to resume functioning at its best. Greater quantities of the ROS cause inflammation of the tissue with active hyperemia up to the toxic dose which causes the denaturation of cytoplasm and cell death. To summarize, the acceleration of tissue metabolism with the consequent acceleration of cellular metabolism and regeneration would be mediated by the light-induced ROS. A similar mechanism at the mitochondrial level has been proposed by other authors (Naviaux, Passerella, Wilden) for other types of non-surgical laser effects, such as reabsorption of ear inflammations.

Different clinical data have emerged from the double-blind trials conducted by various groups on rheumatic diseases and in sports medicine. Each year at Laser Florence the participants discuss the state of the art of this type of application, with representatives from WHO and the FDA who present their guidelines.

The complete list of laser applications in rheumatology and sports medicine is shown in the table.
To summarize, lasers are excellent local antiinflammatories and are useful wherever there is an inflammation that can be irradiated. According to some Russian authors, lasers could also be effective against bacteria, viruses and parasites by stimulating immune defenses and specifically the lymphocytes (Samoilova, Ovslannikov). But these statements have to be verified through adequate testing which has not bee done up to now.

Those same authors also propose intravenous laser treatment in which an optical fiber laser in a venous cannula needle is inserted in a brachial vein to irradiate all the blood in the body. It has been seen that this method increases both the number of lymphocytes and their activity and affects all blood-chemistry parameters.

Toshio Oshiro (Laser Florence 2003 Proceedings) uses lasers at the reflexogenic points that command the micro-vasomotor activity of the affected hemisoma. He checks the patient's map by remote thermography prior to irradiation, to detect any hypoperfusion of the affected areas and shows how these areas are normalized after the laser application. On the practical-clinical level this therapy is applicable to all types of inflammations and diseases where there is local hypoperfusion. This treatment also accelerates the venous-lymphatic draining of the tissues in areas particularly subject to

stasis such as the lower limbs. It also facilitates the *restitutio ad integrum* of areas subject to acute trauma such as sports injuries.
J. Anders et al. (Laser Florence 2004) have demonstrated the increased growth and reproduction of nerve fibers in vitro, that tie in with Levi-Montalcino’s discovery. This finding could lead to some benefits for patients suffering from paresis and neuralgia.

LASERS IN SURGERY

Lasers used: CO_2 – Argon – Dye - Neodymium/YAG – Erbium/YAG – Diode – ProYellow – Nd-AG Q-Switch – KPT, Pulsed Light
(10600 nm, 488-510 nm, 2094 nm, 532-1000, 511-578 nm, 755 nm, 1064 nm, 1320 nm)

The first medical application of laser was in ocular surgery (Towns) in 1962.
A long road has been traveled since then and there is still a long way to go. Discussing all the surgical uses of lasers would require a book apart. Here we will focus on the main indications for these beams in the surgical treatment of diseases where they have been proven more effective and less invasive than traditional surgical techniques. We only have to emphasize a series of general concepts that are always applicable to laser surgery.

First of al, surgical lasers can cut and/or coagulate the target tissue through different mechanisms: *photothermal* where the light is transduced into heat; *isothermal photomechanical,* where the photons are transduced from luminous to mechanical energy; *photoacoustic,* luminous energy transduced into acoustical energy; *photoablative* where the luminous isothermal energy changes the tissue’s phase from solid to gaseous. These instruments offer the greatest advantages in microsurgery and simplify many otherwise very complex procedures. For example herniated discs are treated by percutaneous decompression under radiographic monitoring using an anesthesia needle with an optical fiber that transports a diode or Nd-YAG laser beam. The controlled irradiation heats a tiny portion of the disk to the vaporization point thereby reducing pressure and decompressing the herniated tissue (Choy, Ascher). This method has been accepted worldwide since 1984 was first used in Italy during Laser Florence 2002. Relapses have been reported in 3-5% of the cases treated, and they can be retreated with the same method.

The operation on calcified induratio penis plastica is also minimally invasive. Using the same procedure as for herniated discs hypodermic needle pierces the calcified plaque under radiographic or echographic control and a photoacousitic and/isothermal laser immediately disintegrates the plaque without damaging the surrounding tissue. This procedure was first performed here in Italy in 1986.
Today lasers are widely used endoscopically or intravenously for the photocoagulation of the saphenous vein of the lower limbs. This type of procedure is only logical if it is preceded by an accurate diagnosis and the circulatory physiopathology of the lower limbs is taken into due account. Otherwise, relapses are inevitable (Corcos, etc.) The use of laser to clear hollow organs occluded by vegetating processes is accepted and routine as is the elimination of intrahepatic metastasis via the percutaneous route.

Laser treatment of cutaneous angiomas of various classes is also an accepted procedure, it is only necessary to determine which method to use on a case by case basis. Telangiectases of the face are yet another specific indication for some types of laser, specially those with a complementary wavelength with tissue hemolgobins. However, only few telangiectases of the lower limbs can be treated with lasers without associated sclerotherapy. This is because this type of telangiectasis has a different genesis and etiology as well as being more difficult to attack because they are bigger deeper vessels with respect to the facial veins. Therefore, we prefer to use laser systems that are specific for hemoglobin but which can penetrate deeper even though they do not recognize the tissues. The difference between these laser treatments and acusectors is that the necrotic damage caused b these lasers (diode, neodymium-YAG) is immediately evident and limited to pigmented tissues, while the acusector causes post-thermal necrosis that becomes evident 48 hours later and can be double the magnitude of the immediately evident lesion. The difference between the acusector and laser marks has also been demonstrated on cadavers (Graev, Medicina Legale).

In dermatology there are two types of lasers that are very useful for dermoabrasion or peeling since they are absorbed by tissue water so that the vaporization of various epidermal layers does not necessarily mean that they are carbonized. Furthermore, in addition to being extremely superficial and pre-programmable they also make it possible to see the various epidermal layers during the procedure in a practically exsanguine field. These are the computerized CO_2 laser and the erbium-YAG laser. The erbium is used for more superficial peeling since its absorption peak in water is approximately ten times greater than that of the CO_2 laser and the small vessels are not coagulated. The CO_2 laser is mainly used for deeper dermoabrasions and where direct microcoagulation and contraction of the collagen (shrinkage effect) are indicated. This enters the field of esthetic medicine with laser resurfacing of wrinkles, creases, deep acne scars, rhinophyma, xanthoma, xanthelasma and other superficial flaws. But the same method is also used in other areas such as surgical cleansing of skin sores and decubitus ulcers, performed with topical anesthesia and enormous savings of blood and healthy tissue. Photo-excisions of moles are only justified if there is no need for surgical suturing, otherwise healing after thermal laser cutting is longer than after incisions made by scalpels. It is always possible to do histological examinations of bioptic specimens from edges of the removed tissues and the margins are always clearly evident. The advantage over scalpels is in the saving of healthy tissue and the less visible surgical scar.

The CO_2 laser is an excellent photo-excisor as well as selective coagulator. Therefore it is used to remove warts and condylomas and for treating ingrown nails without have to make recourse to complete nail removal.
A series of lasers that emit mainly visible light are only absorbed by chromophorous tissues, whose color is of wavelengths complementary to the lasers’ and they only affect on these chromophores which are their target according to the theory of selective photothermolysis. The relativity of this theory is in the fact that the human body is composed of differently colored overlapping tissues. Hence absolute selectivity is rare, and it is not sufficient that the beam be absorbed by a tissue of complementary color, the dose of radiation must be such that it has the desired effect on these tissues, be it a surgical or merely “therapeutic” effect. Furthermore, the chromophorous tissue does not always coincide with the target. This is what happens in the blood vessels of the lower limbs: the chromophore for the laser with a wavelength ranging from 532 and 577 nm is hemoglobin, but the target is the vessel wall. Therefore, the Hb only allows the major concentration of the radiation in the

lumen and triggers a process of micro-thrombosis and thereby, indirectly destroys the target.

The theory of selective photolysis is valid in the treatment of skin pigments and tattoos where we almost always use lasers with a wavelength of a complementary color to the lesions. To concentrate the radiation on the target we try to reduce exposure to the radiation to the indispensable minimum in order to respect the skin’s thermal relaxation time which is defined as the interval during which a tissue spreads 50% of the heat it receives from irradiation to the surrounding tissues. The thermal relaxation time changes for each tissue and is strongly influenced by a series of exogenous and endogenous factors, including the patient’s neuro-endocrinological condition. At the epidermal level, the more we respect the skin’s thermal relaxation time the more we respect the epidermis. Since these are skin lesions with dyes, we can greatly affect the absorption and concentration of laser beams that emit in the red and nearby infrared to circumscribe the lesion’s surface and thus reduce radiation doses and consequently discomfort for the patients during and after the procedure and shorten healing time. This concept is applied in the treatment of leukoplasias of the mouth, where Mashberg’s solution usually used for the diagnosis is also used as the photo-absorbent so that a minimum dose of a complementary wavelength laser is sufficient for selective destruction of the leukoplastic tissue without discomfort for the patient (Longo and Marangoni). In the treatment of pigmented lesions we often use the Q-Switch lasers. At this time there are two, the neodymium-YAG and the Alexandrite lasers. The Q-Switch is a special type of emission in which the energy of the laser source is released contemporaneously on the tissue for durations of nanoseconds or picoseconds. The advantage is that the laser is extremely selective and superficial. The drawback is that if the lesion is thick only the first layer will be coagulated and hence many applications are needed to eliminate it.
Depilation for hypertrichosis and hirsutism or for cosmetic reasons is done using a laser that emits close to the infrared and with pulsed light from 590 to 1200 nm. None of these systems gives permanent results because hair regrowth depends mainly on its nature. Malformed hairs never grow back after they are eliminated. Hairs sensitive to steroids will always grow back because, under hormone stimulation, the totipotent stem cells in the skin will always be differentiated into hair bulbs in that specific area. The advantage in

the use of this method is that it is subjectively and objectively well tolerated by the patient so that even the entire surface of the skin can be treated at the same time and relatively few applications are needed over the span of a few months to obtain results.
Today vitiligo and psoriasis are treated with excimer lasers, reinforcing the fact that these methods create fewer hazards of carcinogenesis with respect to traditional techniques because the light is more filtered and directional and each application is progressively shorter. However, they are still ultraviolet rays which strike the target in greater concentrations therefore the lower level of risk and greater efficacy still remain to be proved.
Laser treatment of angiomas is considered elective. It is only a matter of selecting the type of laser to use on a case by case basis (Apfelberg and Aster).
In gynecology lasers are routinely used for cervical conization in cases cancer with the enormous advantage of conserving the function of the cervix in the event of pregnancy. It is also used for mini-invasive surgery of cervical dysplasia, to excise condylomas and it has been experimented in the treatment of vulvar dystrophy. Lasers can also be used to monitor endometrial function during menstruation and pregnancy (Vaitkuviene et al.) and are being tested for applications to increase fertility.
In gastroenterology and bronchology lasers are used in endoscopic procedures, or clear the esophagus and colorectal tract occluded by chronic vegetating processes such as cancer, to excise neoformations such as polyps and papillomas and to coagulate small hemorrhages. In proctology they are used for the complete removal of hemorrhoids and anal fistulas, to coagulate anal fissures and to sacrum dissection in the treatment of rectal cancer. The main advantages in this area are the reduced healing time and a better post-operative course. In the case of fistulas, there is also nearly a total lack of relapses (Longo-Corcos). Lanzafame et al. also use lasers for treating gallstones and for percutaneous gall bladder removal - usually the Nd-YAG or 810 nm diode laser and occasionally the alexandrite laser.
In otolaryngology lasers are commonly used for specific indications. Laser treatment is indicated for hypertrophy of the turbinate, nasal polyps, chronic sinusitis, laryngeal conditions, diseases of the vocal chords, dizziness, tinnitus, TMJ syndrome and snoring. An excellent paper on the use of lasers in otology was recently written by V. Oswal et. al, Neoplasia of the mouth. Mainly the 532 nm, 810 nm 1064 nm lasers are used.

Ophthalmology is the field in which lasers have revolutionized all diagnostics and treatment to the point that all ophthalmologists should be able to use them. There are many indications from the treatment of myopia to the treatment of macular degeneration of the retina and hemorrhages, secondary cataracts and many other highly specialized applications that go beyond the scope of this paper.
Dentistry is constantly developing new applications and each year the world’s main groups (Lynn-Powell, Brugnera, etc.) meet to establish the guidelines to follow beyond the current trends.
In urology A. Hofstetter and Reza Malek have demonstrated the practical uses of photodynamic treatment of tumors of the bladder and lower urethra, prostatectomy with 532 nm and Nd-YAG lasers and laser treatment of stones in the final section of the urethra treated with laser. In cardiovascular medicine lasers have been used to clear obstructions in the coronary as well as peripheral arteries and in experimental modes for dissolving atherosclerotic plaques.

LASER TISSUE WELDING
Laser tissue welding is being used experimentally in microsurgery to seal small vessels without suturing in the USA, Germany, Israel, Japan, Australia and other country.

The use of lasers in medicine and surgery is growing constantly and rapidly. However, up to now no truly valid guidelines have been drawn up for all the applications other than the U.S. Food and Drug Administration rulings on efficacy, safety of use and protection. Used in inappropriate situations and by inexpert hands lasers can cause serious harm. Therefore, it seems clear that a post-graduate specialization focusing exclusively on medical-surgical lasers is needed to train physicians in order that they may flank other specialists to use these beams in the optimum manner, exactly the way radiologists do with X-rays.