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[LOGO: *Universita degli Studi, G. D'Annunzio, Chieti Pescara*]

MULTICENTRIC RESEARCH

TRIPLE THERAPY: REHABILITATIVE PROTOCOLS AND STANDARDISED USE OF HIGH RESOLUTION DIGITAL THERMOGRAPHY TO AID DIAGNOSIS AND ASSESSMENTS IN THE FIELD OF PHYSICAL AND REHABITATIVE MEDICINE

Coordinator: Prof. Raoul Saggini – Director of the Specialisation School of Physical and Rehabilitation Medicine at the Università degli Studi G. D'Annunzio di Chieti.

Participants: Rehabilitation Facilities (Universities, in an SSN Private and / or Private agreement, which have "Triple Therapy and thermographic camera" equipment)

40 centres distributed throughout the country and 20 or more centres located abroad.

Peripheral Coordinator: Centre Medical Officer

The centres included in this research project will be permitted to use the title: peripheral research centre of the University of Chieti

Duration of research study: 4 years

Research context: Painful pathologies with predominantly local manifestations, with nociceptive pain (post-traumatic, inflammatory, from chronic local ischaemia), mainly of the locomotor system, and of the neuropathic type, where this is mainly sustained by peripheral mechanisms.

Research Objective: to determine, through the use of thermography, the dosimetry for "Triple Therapy" laser therapy in relation to specific pathologies, to establish the specifications for using thermal cameras to support physiographic diagnosis, assessment and follow up.

Rehabilitation protocol:

The term ***LASER*** is an acronym derived from the letters for "Light Amplification by Stimulated Emission of Radiation" (amplification of light by amplified radiation emission).

Passing from being used in industry to applications in the medical field, lasers have found specific applications in the surgical, ophthalmologic, urological, dermatological, cardiovascular, neurological, gynaecological and tumour photo chemotherapy fields, as well as in the field of physical and rehabilitation medicine.

The physical principles on which laser therapy is based are: - ***The stimulated emission of photons*** i.e. the excitation of electrons with displacement to higher energy orbitals. The emitted photons have the same characteristics as the incident photons in terms of direction and frequency, and travel in phase with the excitation photons however, as with electromagnetic waves, there is no gap between the waves stimulating the emission and those emitted. - ***The inversion of electronic populations***, that is, the number of excited electrons exceeds the number of unexcited electrons (at thermal equilibrium, many of the atoms are in the ground state and few in the excited one). Contemporaneous de-energisation results in the coherent radiation that typifies lasers. Maintaining the process requires energy to be supplied continuously (which is referred to as "pumping"). The emission of energy will be neither random nor in any particular direction, but the photons emitted will have the same direction and the same wavelength as the photon inducing them.

Emitted photons can, in turn, hit other excited atoms and trigger a series of chain-stimulated emissions. In this way, via the subsequent collisions with excited atoms, the inducing photon produces a crop of photons, all of which have their own direction and wavelength.

This phenomenon is called a "light amplification process," because a single photon produces a group of photons that all have the same characteristics. For this process to take place the number of excited atoms must be high, and the population of excited atoms must be larger than the population in the ground state.

The light emitted by the laser is monochromatic, coherent, uni-directional and brilliant.

1) **Monochromaticity**

Electromagnetic radiation laser beams all have the same wavelength and hence the same colour. Lasers can be activated at all wavelengths, from infrared to ultraviolet. Ultraviolet wavelengths have been abandoned because they are considered teratogenic and carcinogenic.

2) **Coherence**

The laser wavefront does not change over time, and all of the waves making up the beam are in phase (i.e. have spatial and temporal coherence)

3) **Uni-directionality**

Unlike light from a light bulb, which spreads out in all directions, laser light propagates in one direction with almost parallel rays and therefore, with a very small divergence.

4) **Brightness**

Brightness (i.e. power) is the main property of lasers. The brightness of lasers is higher than that of the best traditional sources. This is due not so much to the high power emitted, as to the low divergence of the beam.

The architecture of a laser system refers to four fundamental elements:

■ the active medium;

■ the optical resonance cavities;

■ the pumping system, and

■ the laser beam carrier.

-The ***active medium*** is the complex of atoms and molecules that is raised from the ground state into the excited state, and from which the emissions are derived. Solid, liquid and gaseous lasers can be distinguished from each other, depending on the nature of the active medium used.

In solid state lasers, the active medium support comprises glass or pure mono crystal bars which are doped with atoms of active elements (neodymium, erbium, chromium, holmium, titanium; these being the actual light emitters). Pumping is of the optical type, with a wide-spectrum lamp. They can reach very high emission powers. Liquid-state lasers differ from those previously mentioned because the support for the active elements is a liquid rather than a solid.

The active media used are organic dyes (the most common being rhodamine G, coumarin and xanthene) which are dissolved in water or alcohol, or rare earth derivatives.

In the case of gaseous state lasers, the active medium can be a single gas or a mixture thereof. The most common solutions used to construct them are helium and neon blends (He-Ne), in which the active element is neon, to which helium atoms transfer the energy they have absorbed from electric discharges; alternatively, carbon dioxide mixtures with argon (CO2-Ar) or carbon dioxide with nitrogen and helium are used.

Finally, in semiconductor or diode lasers, the active medium consists of layers of materials of a different nature. Among the most commonly used is gallium-arsenic doped with aluminium atoms.

These achieve high yields, and are treated as smaller-sized lasers but, at the same time, cannot provide high power.

-Optical ***resonance chambers*** achieve signal amplification. Amplification is achieved thanks to two parabolic mirrors, one of which has the job of selecting photons that are moving in the same direction, while the other allows the laser beam to be emitted via a thin slit.

The presence of the resonance chamber always gives the laser beam the properties of coherence and collimation, thanks to which the radiance from such laser sources is always high, even if the radiant power is modest.

-The ***pumping system***, or energy source, has the task of energising the active medium atoms by raising their energy level, which stimulates them to create a metastable system so population inversion can take place. Among the most commonly used energy sources are: flash lamps, high voltage electric discharges, dynamic gas systems, chemical systems, other lasers or a series of several lasers to induce a cascade.

-The ***laser beam transport mechanism*** *(conduction systems)* is the means by which radiant energy reaches the point of application on the target tissue. Every laser has a transmission system. The ideal medium for diode laser transmission is a fibre optic. The atomic and molecular level reactions in biological tissues affected by the laser beam depend on many factors including: the light-generating system (continuous or pulsed), tissue affinity with the emitted wavelength, the type of treatment performed, the treatment mode, and the immune response of the patient.

The actual conditioning mechanism is determined by the optical properties of the target relative to the wavelength of the incident ray; hence the laser beams may be subject, to varying degrees, to the following phenomena:

- absorption;
- reflection;
- diffusion or refraction;
- transmission.

Absorption

This is the most important characteristic from a clinical perspective, since it is linked to the operation and therapeutic efficacy of laser beams. It defines the magnitude of the thermal effects that are transferred to irradiated tissues. Absorption can be selective, depending on the pigments and laser beam wavelength ranges they are sensitive to, or non-selective, as with water, which is the largest energy absorber in the infrared region of the spectrum (980 nm, erbium, CO_2).

Reflection

Laser beams that impinge on tissues that do not match their characteristics are reflected from the surface. When this phenomenon is modest, it is referred to as partial reflection; however, due to lack of affinity between laser beams and target surfaces, almost total dispersion of the incident energy by reflective phenomena can take place. This characteristic may be a safety issue for patients and staff working with lasers, because the photons can hit the retina of the eyes if they are not protected by appropriate eyeglasses to filter specific wavelengths from the laser in question.

Diffusion or refraction

When we refer to diffusion, we mean the way the beam spreads out at a tissue level, with a decrease in the energy density and the consequent limitation of the localised heating effect. The phenomenon is not always undesirable; in fact, it is used for polymerising composite resins for tooth fillings, and in dental whitening treatment.

Transmission

Transmission occurs when a laser beam crosses tissues without damaging them until it reaches the target.

Deep effects can be measured at the level of a tissue lesion, as can the therapeutic action, without involving the surface tissues.

Classifications

Lasers can be classified according to active material used, the emission mode, and power.

1*)* ***Classification based on active materials***

Depending on which substance is stimulated to obtain the laser light, we have Helium-Neon, Argon, CO_2 and Excimer devices.

2) ***Classification based on the mode of emission***

Light emitted by a laser can be continuous or pulsed. In the latter case, extremely short pulses (duration of 200 nanoseconds) are emitted but with high peak power.

Pulsed emission frequencies can range from 100 to 10,000 Hertz. Pulse duration and peak power are fixed parameters that are specific for each device; the frequency can be set by the operator.

Lasers can either have continuous or pulsed emissions.

3) ***Classification based on power***

Lasers can also be classified according to their power. In relation to this parameter, these lasers can be sub-divided into:

a) **Power lasers**: these are the lasers with the highest power. The average power is tens of Watts. This group includes C02, Argon and Ruby lasers. They are used in surgery because they can destroy any irradiated tissues.

b) **Mid lasers:** these are of medium power and have a bio stimulating effect. They emit a power of a few Watts. This category includes pulsed emission Diode IIR lasers (power 5 Watts).

c) **Soft lasers**: these have a power of a few milliWatts and a bio stimulating action. This group includes Helium-Neon lasers (maximum power of 50 milliWatts).

Exposure times are important in laser treatments and are measured in minutes and seconds. The surface area being treated is another important parameter, because it allows us to determine the amount of energy needed for a bio stimulating or analgesic treatment, and is measured in square centimetres.

Power density allows the amount of output energy delivered to the surface area being treated to be quantified, and is measured in Watts per square centimetre.

The energy density allows the energy actually absorbed by the surface area to be quantified, and is measured in Joules per square centimetre. The total energy transferred is measured in Joules.

Therapeutic lasers

1) ***Helium-neon lasers***

A Helium-Neon laser comprises a mixture of helium and neon (in the ratio of 6: 1), contained in a Pyrex or silica tube. The active material is the neon; excitation is achieved via continuous electric discharge. The light emitting beam is continuous and has a power ranging from 1 to 50 milliWatts.

The wavelength is 6,328 A (red). At this wavelength, absorption of radiation by the tissues is poor, but penetration is good; despite this, Helium-Neon lasers exert their activity in the first few layers of the skin due to their low power. These lasers have a bio stimulating effect.

2) ***Semiconductor laser***

Semiconductor lasers are small, low cost devices. The active substance is usually a gallium arsenic alloy (GaAs); Pumping is performed by means of electricity. The Diodic IR laser is a member of this group. This laser emits a pulsed beam, which has a peak power of about 5 Watts and a wavelength of 9,040 A (infrared bandwidth). Experimental studies have shown that the energy of this laser is scarcely absorbed by the tissues and reaches a depth of about 3.5 cm. The Diodic IR laser has a bio stimulating effect.

3) CO_2 laser

CO_2 lasers use a mixture of CO_2, helium and nitrogen. Pumping is performed via an electric discharge. The wavelength of the emitted radiation is 106,000 A (infrared band). The high level of energy absorption by the tissues prevents the laser beam from penetrating deeply, so the action is only at a surface level. These are used in surgery because they have a power of many dozen Watts. There are also commercially available lasers that are "defocused", that is, that have a lower power, which are used in rehabilitative medicine.

Laser therapy is divided into contact therapy and scanning therapy and both types can use a mono-diodic or multi-diodic laser. In mono-diodic laser therapy, the hand pieces used are placed directly onto the skin.

These are used to stimulate of trigger points or loculatory areas and treatment requires the physical presence of an operator. Multi-diodic contact therapy, on the other hand, does not need an operator to be present. The use of scanning laser therapy, which also uses mono and multi-dimensional lasers, enables areas that are larger than the contact area to be treated, and to be performed automatically, without the presence of an operator.

Impact of laser light on tissues

The effects laser emissions have on tissues are determined by various factors, such as:

■ ***wavelength:*** in the electromagnetic spectrum between gamma rays (high frequencies) and radio waves (low frequencies) there are visible and invisible radiations that are involved in laser light. Most lasers are in the infrared range (diodes, CO_2, erbium). Every tissue has an optimal absorption coefficient in relation to a given wavelength: for example, 960 nm for blood (close to the 980 nm of diode lasers), 1064 nm for bone (Nd-YAG), and 1053 nm for dentine and enamel (Nd-YAG). Highly aqueous tissues absorb radiation at higher wavelengths, like erbium and CO_2, very well;

The tissue absorption of radiation with wavelengths ranging from 5,000 to 10,000 is minor, so this penetrates deeper as a consequence.

This explains why He-Ne (6.328 A) and diodic IR (9.040 A) lasers, whilst possessing a lower power, penetrate more deeply in the tissues than a CO_2 laser (106.00 A).

1) **Type of tissue irradiated:** absorption is greater in tissues that are richer in water.

2) **Beam inclination:** the beam must be perpendicular to the irradiated surface, to avoid the phenomenon of reflection.

■ **Beam power and density**: whilst power expresses the amount of energy per unit of time, density is the energy that, for a period of time, is incident on a unit of surface area perpendicular to the radiation beam. Put simply, if 2 W are carried by a fibre of 200 microns diameter, or by a fibre of 600 microns diameter, it will have two different effects on the irradiated tissue if the irradiation time is kept constant;

■ **Laser/tissue interaction time**: this is a fundamental parameter for determining the effects of radiation on tissues.

For each type of intervention, it is the rehabilitation medicine physician who has to decide the appropriate energy / exposure time for obtaining the desired effect on the tissues being treated, without involving the adjacent ones. Movement of the terminal or hand piece and pulsing the radiation (adjusted via laser software) are the operating tools used to reduce irradiation times;

■ angle of incidence: as you move away from the 90° angle from the surface to be irradiated, the laser beam's power density automatically decreases; moving away from the angle of incidence, in fact, reflection of the electromagnetic emission increases and decreases its diffusion and absorption;

■ distance from the application field: the more you move away from the application field, the more radial defocusing there is, reducing the amount of energy irradiated into the tissue; for example, at a 2 mm distance with 4 W power output from the fibre optic, 0.5 W is obtained on the irradiated tissue with a consequent regenerative action.

Biological effects

The biological effects of lasers are influenced by the power and duration of the irradiation. At high power, lasers cause water to evaporate and carbonise the tissues; with a lower energy input, the photo-thermal effect causes the phenomenon of irreversible protein denaturation.

The wavelength of the laser beam incident on bio tissues should be between 600 and 1,400 nm; this interval is defined as the therapeutic window.

With even lower doses, the lasers cause chemical reactions; using very low doses, they exert a bio stimulating action.

Photo-evaporation phenomena, photo-thermal effects and photo-chemical reactions are generated by power lasers, bio stimulating actions are specific to mid and soft lasers.

The biological effects of mid and soft lasers are as follows:

1) ***Mitochondrial stimulation***

Laser light can stimulate mitochondria and accelerate ATP production. The increased production of ATP recharges the cells for which, if these are damaged by inflammatory, traumatic or degenerative causes, they begin to perform their physiological functions.

2) **Activating the microcirculation**

Laser therapy has an intense vasoactive action on the microcirculation. Activation of the microcirculation favours better nutrition and improves the drainage of catabolites from the tissues.

3) **Activation of lymphatic peristalsis**

Laser light accelerates lymphatic peristalsis, which facilitates the absorption of interstitial fluids and reduces flogistic and post-traumatic oedema.

4) **Hyperpolarization of nerve fibre membranes**

Experimental studies have shown that therapeutic lasers induce a hyperpolarisation of nerve fibre membranes. This effect seems to be linked to closure of the membrane channels for potassium ions, caused by changes in surface lipoproteins. Hyperpolarisation causes the excitation threshold of pain receptors to increase.

5) Therapeutic lasers transform prostaglandins into prostacyclin PG12, which have an anti-inflammatory, anti-oedema and antalgic action.

Therapeutic effects

The biological modifications induced by laser light cause the following therapeutic effects:

1) **<u>Destructive / ablative effect</u>**

Power lasers, via the evaporation process, can destroy pathological tissues without damaging the surrounding healthy tissues or altering local defences; they also allow organic tissues to be cut without bleeding.

Because of this, power lasers have found a wide range of applications in surgery.

2) **<u>Bio stimulating effect</u>**

The bio stimulation effect can be obtained with mid- and soft lasers. This effect has been deduced from the clinical observation that lasers accelerated the healing of ulcers or torpid sores.

Lasers promote tissue repair by increasing the cell's metabolic activities, activation of the micro circulation, and, according to some authors, by stimulating the mitotic activity of cells as well.

3) **<u>Anti-inflammatory and anti-oedematic effect</u>**

Therapeutic lasers reduce local inflammation and oedema. These effects are secondary to the action of PG12 prostacyclin and the activation of lymphatic peristalsis.

4) **<u>Analgesic effect</u>**

Mid and soft lasers induce analgesia because they raise the threshold of excitability of algoreceptors and produce an anti-inflammatory action. An action on "Gate control" and the release of endogenous opiates has also been hypothesised. In some experiments, it has been observed that the laser's analgesic action can be cancelled out by simultaneously injecting naloxone, an endorphin antagonist.

All of the premises involved will perform specific rehabilitation protocols for the various pathologies, and the data they gather, along with the evaluations will be sent to a centralised database at the University of Physical Medicine and Rehabilitation at the Universita G. D'Annunzio di Chieti.

The ***Triple Therapy laser is a scanning diode laser with 2 laser sources***:

Source 1: Ga Al As (Gallium, Aluminium, Arsenic)

Power: 10 W

Wavelength: 805-811 nm

Frequency: 1-10,000 Hz

Duty cycle: 50%

Source 2: Ga Al As (Gallium, Aluminium, Arsenic)

Power: 15 W

Wavelength: 1,061-1,067 nm

Frequency: 1-10,000 Hz

Duty cycle: 50%

It's possible to work with specific pre-set programs for individual pathological scenarios, or change the application parameters to manual mode, according to the patient's pathology and characteristics

Every site that joins the project will receive a treatment protocol for the illnesses included in the study, to generate comparable data, which will then be sent to the headquarters in Chieti – ***Centro Universitario di Medicina Fisica e Riabilitativa Universita G. D'Annunzio,*** **Chieti - with the assessment forms attached.**

Thermography

Thermography is based on the principle that skin temperature varies from area to area, as a function of the circulatory or cellular processes that occur inside the body.

It is a technique for capturing images in the infrared region. It is based on a well-known physics principle, under which any body with a temperature above zero absolute (- 273ºC) emits energy in the form of radiation, with an amplitude and frequency that is a function of its temperature: in the case of humans (35-40ºC) the frequency is in the near infrared, so it is imperceptible to the human eye.

Medical thermography, since it was started over forty years ago, has been through more and less fortunate periods. In the 1970s it was used in a myriad of diagnostic applications, collecting both consensus and criticism, and was abandoned due to poor or dubious results. The reason for the disappointing results was partially attributed to the limitations of the equipment available then, and the excessive and occasionally inappropriate choices of the types of diseases to be examined. Nowadays, thermography is referred to as tele thermography, and is so called because it uses thermal cameras to shoot at varying distances, in contact thermography (using photo-cromatographic glass plates placed on surfaces under examination) and is now not used.

Over the years, the literature has reported studies into the detection of tumours, determinations of the sites and extension of inflammatory processes, the depth of tissue destruction from burning and freezing, and also into applications in physical medicine and rehabilitation. The limitations of these studies are due to sample sizes and the lack of standardisation in the thermal cameras used, which makes comparing the results difficult.

Skin temperature can vary between 23 and 36 degrees. Under normal conditions, the variation depends on the skin itself, the subcutaneous tissue, and the amount of fat and muscle mass. In addition to these differences, there are others which are caused by abnormal diseases or physiological states. When conducting thermograms, the degree of skin pigmentation does not pose any problem; however, spurious effects caused by visible light and the reflection of low-wavelength infrared rays are possible.

Some products used for cosmetics, like lipsticks, nail polish and powder, make the skin appear lighter because the emissive power of these materials is lower than that of the skin.

Standard Data Logging Protocol:

To ensure homogeneity of the results, the parameters for the external factors have to be standardised:

if the room which is to contain the irradiation has dark-coloured walls, the light has to be attenuated, the temperature maintained at around 25ºC, with no air currents and without resorting to heat or cooling sources with a marked temperature difference compared to ambient values; the humidity must be around 65%. To conduct the examination under homogeneous conditions and therefore in the absence of any stimulating effects, patients have to be informed:

- to stop taking any medications, avoid intense physical exercise and physical and/or manual treatments the day before;

- to avoid exposure to the sun and / or tanning lamps for 2 days prior to the analysis;

- to avoid smoking, drinking alcohol, or eating cold foods or snacks for five hours beforehand;

- not to use cosmetics, ointments or dressings;

- to wear light and non-constricting clothing;

- to arrive at the clinic at least 30 minutes before the test;

- to remove all of their clothing in the dressing room (you can wear baggy and light cotton shirts) and stay at room temperature (25ºC) for 15 minutes;

- to remain still during the scan.

A scan will be performed before the Triple Laser session and immediately afterwards, with these external parameters kept constant.

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