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Stem cell treatment considerations with specialized lasers for improving/curing rheumatic affections

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Summary:

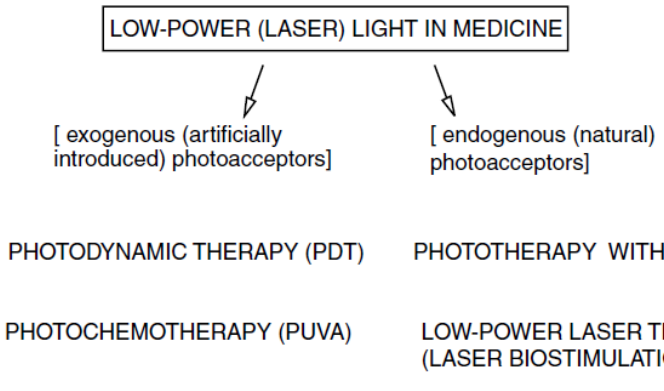
The following paper will present a way in which laser radiation may help improve the outcome stem cell interventions at the knee region in order to relieve and treat arthritis. Intervention with laser radiation is a painless one , that does not require hospitalization.

Considerations:

The succession of events for the overall procedure is the following : a decent amount of adipose tissue is harvested from the patient's abdominal region, tissue that contains a high amount of MSC. The amount that is harvested should be about 200grams. After that, the fat is deposited and injected in the knee region, according to the affected tissue/muscle. Once the fat is injected, the region is laser treated. The laser radiation from the LPL stimulates the injected fat and accelerates the procedure (stem cells from the adipose tissue, bond with the surrounding tissues and they transform in what they are needed – like an ace in a card game . A similar procedure, without the laser radiation and using only stem cells (without the fat), has been successful in England (Judith Brodie, chief executive of Arthritis Care)

The most frequently used mechanism of photon energy conversion in laser medicine is heating. Average heating of irradiated samples occurs with all methods of tissue destruction (cutting, vaporization, coagulation, ablation).

At low light intensities, the photochemical conversion of the energy absorbed by a photoacceptor prevails. This type of reaction is well known for specialized photoacceptors such as rhodopsin or chlorophyll. In medicine, light absorption by non-specialized photoacceptor molecules (i.e., molecules that can absorb light at certain wavelengths, but are not integral to specialized light reception organs) is used rather extensively . [1]



[1]

The absorbing molecule can transfer the energy to another molecule, and this activated molecule can then cause chemical reactions in the surrounding tissue. This type of reaction is successfully used in photodynamic therapy (PDT) of tumors. Alternatively, the absorbing molecule in a light-activated form can take part in chemical reactions, as occurs in treatment of skin diseases with psoralens and UVA radiation (PUVA). Importantly, in both PDT and PUVA therapy, the photoabsorbing molecules are artificially introduced into a tissue before irradiation.[1]

In the current article, we will be talking about low power laser therapy in order to treat arthritis. The principle of the low-power laser (LPL), is based on the theory of laser biostimulation.

There are a great number of mutually contradictory theories attempting to explain the biostimulating effect of laser light; however, none of them provide a scientifically acceptable explanation. This is the main reason why laser light has not come into general use to the extent which its efficiency would seem to deserve. Other reasons might be that a continuously operating laser providing the required output and beam diameter is rather complex, and that special skills are required during handling.
The special features of laser light are:
— monochromatism
— coherence
— possibility for producing extremely high output power densities
— polarization. [2]

A number of theories have been put forward on the mechanism of biostimulation at cellular level from light illumination (or irradiation) of various forms. Most of the literature have been focused on the more widely practices of applying the light from outside of the body targeting selected areas of the body. Very little have been proposed on the mechanism when blood in circulation is irradiated, either intravenously (injecting light into the vein – commonly practised in Russia, Germany and several European countries) or through the nasal cavity in our case.

An example of a common explanation on the mechanism of light therapy in general is that by Harvard researcher, Hamblin, that reveal the activity of the cells upon exposure to certain low energy red light.[9] He expounds the theory that tissues have photoreactive proteins that will eventually stimulate the production of adenosine triphospate (ATP). ATP stores cellular energy, which is then released for biochemical processes occurring inside the cell. This explanation is shared by many researchers in the field.[10]

When we are physically hurt or ill in some way, the cellular damage and inflammation create additional singlet oxygen molecules, which is a reactive oxygen species (ROS). The homeostasis is unsettled and the body is signaled to restore the balance by stimulating the immune response system, increasing blood flow to the distressed areas, repair DNA and regenerate cells, etc . In other words it gets stimulated into the healing process. During this restoration, damaged cells die (“cell apoptosis”). This signalling process that stimulates the restoration is now recognized as “Redox Signalling”.
During this process, the ROS created act as Redox Signalling molecules. Eventually they create an antioxidative effect.[11] The body does not do anything differently than it normally does.
Cells exposed to light in the red spectrum mimics this response (but at controlled output energy level to avoid cellular damage).[12]

The process also signals the body's defence mechanism to activate the native antioxidants in the cells.[13] Meanwhile at this low energy level, the potential for oxidative damage by singlet oxygen is exceeded by the antioxidative therapy that it stimulates.

Clinical results with laser light have shown that the healing effect was independent of wavelength at 694 nm, 628 nm, 514 nm, 488 nm and 458 nm in the visible spectrum, as well as at 1060 nm in the infra-red. Recent measurements on liquid crystals illuminated by laser light have shown that the linearly polarized light can reorder the liquid crystal molecules. [2]

Linearly polarized light acts on the lipid bilayer of the membrane, whereby structural changes may occur, that is, the random distribution is replaced by a more ordered one. Consequently the surface features (for example, the surface charge distribution) and the lipid protein connections are supposed to be modified. This occurs because the electric field strength of the linearly polarized light changes the conformation of the lipid bilayer as it reorders the polar heads of the lipids.

As there is very close contact between lipids and proteins making possible energy transfer between them, the conformation change of the lipid bilayer may influence every cellular process connected with the cell membrane, that is, processes related to or taking place through the cell membrane. For example:
— the energy production of the cell,
— the immune processes, and
— enzyme reactions (this may include change of the active transport and activation energy of the enzymes).[2]

Several pieces of evidence show that mitochondria are sensitive to irradiation with monochromatic visible and near infrared (IR) light. The illumination of isolated rat liver mitochondria increased adenosine triphosphate (ATP) synthesis and the consumption of O2 (Kato et al., 1981; Passarella et al., 1984; Gordon and Surrey, 1960). Irradiation with light at wavelengths of 415 nm (Kato et al., 1981), 602 nm (Vekshin and Mironov, 1982), 632.8 nm (Passarella et al., 1984), 650 nm and 725 (Gordon and Surrey, 1960) enhanced ATP synthesis. Light at wavelengths of 477 and 554 nm (Kato et al., 1981) did not influence the rate of this process. Oxygen consumption was activated by illuminating with light at 365 and 436 nm, but not at 313, 546 and 577 nm (Vekshin and Mironov, 1982). Irradiation with light at 633 nm increased the mitochondrial membrane potential (Ψ) and proton gradient (pH), caused changes in mitochondrial optical properties, modified some NADH-linked dehydrogenase reactions (NADH is a reduced form of nicotinamide adenine dinucleotide) (Passarella et al., 1983) and increased the rate of ADP/ATP exchange (ADP is adenosine diphosphate) (Passarella et al., 1988a) as well as RNA and protein synthesis in the mitochondria (Hilf et al., 1986). In the case of state 4 respiration, the 351 nm and 458 nm laser irradiations accelerated the oxygen consumption of rat liver mitochondria; such acceleration was not observed with 514.5 nm irradiation.
On the contrary, in the case of state 3 respiration, the 514.5 nm laser irradiation activated the oxygen consumption of mitochondria. Activation did not occur with 458 nm irradiation, and 351 nm irradiation reduced the oxygen consumption in state 3 (Morimoto et al., 1994). The 660 nm irradiation increased state 3 oxygen consumption at both coupling II and III sites, as well as increasing the respiratory control ratio (Yu et al., 1996). It is also believed that mitochondria are the primary targets when the whole cells are irradiated with light at 630 nm (Hilf et al., 1986), 632.8 nm (Karu et al., 1995a; Bakeeva et al., 1993; Manteifel et al., 1997) or 820 nm (Herbert et al., 1989). Irradiation with light at 812 nm

(Loevschall and Arenholdt- Bindslev, 1994a) or 632.8 nm (Anders et al., 1995) altered the rhodamine 123 uptake by fibroblasts. These results were interpreted by the authors as inducting the perturbation of mitochondrial energy production (Loevschall and Arenholdt-Bindslev, 1994a) and membrane potential (Anders et al., 1995). [1]

Treatment with low power laser (LPL) is used as an invasive instrument in order to activate the endogenous growth factor, growth factor β1 (TGF-β1) of stem cells, which subsequently differentiate host stem cells to cause regeneration of tissue.

Any surgical intervention carries a degree of risk however the surgical procedures used for stem cell therapy are the same as those for routine hip or knee arthroscopy operations. There is a theoretical risk of infection, but this is low and surgery is in any event covered by antibiotic treatment. As for the stem cells, these are derived from the patient's own blood or marrow, so there is no risk of rejection or disease transmission.

In the worst case scenario, the intervention won't work. Nothing will happened, but on the best case scenario, the regenerative process starts and healing is bound to occur. If the stem cells are placed in a certain area, they can't get to other parts of the body.

Another part of the complications process can appear from local anesthesia. In order to extract the body fat using the liposuction method, a local anesthesia might be needed to numb the area of the extraction. Pacients should be tested before the intervention for anesthesia allergies.

To understand the operation of the laser requires a knowledge of the energy levels associated with atoms, ions and molecules. In thermal equilibrium, the energy levels are populated according to the Boltzmann distribution, which forbids the conditions in which an upper level might have a greater population than a lower level. Because, for lasing, an upper level must be more highly populated than the lower level, lasing will not take place. Lasing can take place only when a material is not in thermal equilibrium. This non-equilibrium is created by an excitation source sometimes called a "pump" source. Just as thousands of atoms, ions or molecules can be laser materials, numerous pump sources can excite the materials. In many cases, the gain produced by the pumped laser material is low. To make a device, it is necessary to use an optical resonator to repeatedly reflect the signal through the amplifying material to add to the intensity. [1]

Wavelength and output power are important factors when taking in account a laser generators, though two other factors are important as well: type of operation (continuous or pulsed) and the affected area.

Choosing between a CW(continuous wave) and a pulsed operation depends a lot on the chosen laser and how it copes under different environments: it's not easy to choose when it comes to biological material. It does not behave like other materials such as metal.

As for choosing how the beam is concentrated (either in a point or affecting a bigger area) it is beneficial if it's concentrated in a small area. During the procedure the laser beam should move all along the area that needs healing, a couple of times (4-5), to be sure that the effect is embedded.

Choosing a laser comes down to documentation , balancing what is needed versus the budget that is a available.

The table bellow shows a list of vibronic lasers. Vibronic solid-state lasers, i.e. lasers based on vibronic solid-state gain media, allow for wavelength tuning over large ranges, and also the generation of ultrashort pulses.[1]

TABLE 1.4 Vibronic Lasers

Type	Pump source	Operation	Wavelength (nm)
Alexandrite	Arc lamp	CW	730–810
Alexandrite	Flashlamp	Pulsed	701–858
Ce-YLF	KrF Excimer	Pulsed	309–325
Co-MgF2	1320 nm Nd:YAG	Pulsed	1750–2500
Cr-LiCaAlF6	Laser or lamp	Pulsed or cw	720–840
Cr-LiSrAlF6	Laser or lamp	Pulsed or cw	760–920
Emerald (Cr doped)	Laser	Pulsed or cw	720–842
Fosterite (Cr doped)	Laser	Pulsed or cw	1167–1345
Thulium-YAG	Laser	CW	1870–2160
Ti-Sapphire	Usually laser	Pulsed or cw	660–1180

A good choice would be the Ti-Sapphire laser. The following pictures are from a catalog (from a firm that produces such lasers).

SolsTiS

Ultra Narrow Linewidth CW
Ti:Sapphire Laser

Applications

- Atom trapping and cooling
- High-resolution spectroscopy
- Squeezed light
- Quantum optics

Features

- Low amplitude noise
- Narrow linewidth
- Sealed and fully automated design
- Broad tuning range with one optics set (up to 300nm)
- Custom wavelength ranges available, e.g. < 700 nm or >1000 nm, please enquire
- Simple 'dial a wavelength' for wavelength setting
- High precision 'dial a wavelength' option (requires wavemeter)
- Terascan wide scan version (requires wavemeter)
- Instrument control by Ethernet (ICE) for hands off use
- Easily purged in minutes
- Frequency doubler / mixer accessories available
- Fully integrated beam pick off and fiber launch accessories available

Specifications [1]

Model	Power (W) [2]
SolsTiS 4000	> 4.0
SolsTiS 3500	> 3.5
SolsTiS 3100	> 3.1
SolsTiS 2000	> 2.0
SolsTiS 1600	> 1.6
SolsTiS 1200	> 1.2
SolsTiS 1000	> 1.0
SolsTiS 700	> 0.7
SolsTiS 500	> 0.5
SolsTiS 300	> 0.3
SolsTiS 100	> 0.1

Tuning Range (nm) [3] [4]	-XS	-R	-F	-XF	-XL
SolsTiS 4000		725-875	(725-975) +/-15		
SolsTiS 1200 to 3500	670-710	725-875	725-975	700 - 1000	950-1050
SolsTiS 500 to 1000		725-875	725-975		
SolsTiS 100 to 300		745-855			

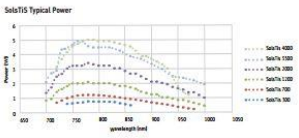
Linewidth [5]	
SolsTiS SRX (Scanning Reference Cavity)	< 50 kHz
SolsTiS PSX (Passive Scanning)	< 5 MHz
SolsTiS LX (Etalon Lock)	< 5 MHz
SolsTiS PX (Passive Etalon)	< 5 MHz
SolsTiS BRF (BRF Only)	< 20 GHz

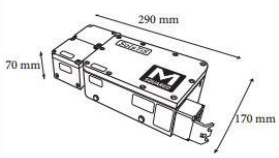
Scan Range [6]	> 25GHz, measured at ~780nm, scan stitching option available
Amplitude Noise	< 0.1% RMS above pump noise, added in quadrature
Spatial Mode	TEM_{00}
Beam Radius	< 0.4mm, $1/e^2$ intensity (nominal, at output port)
Beam Divergance	< 1.5 mrad, far field, half angle
Polarisation	Horizontal (pump & output beam)
Laser Head Dimensions [7]	<29 x 17 x 7cm (<11.5 x 6.7 x 2.6 inches), L x W x H
ICE-BLOC™ Controller Dimensions	34cm x Half Rack x 2U, L x W x H
AC Power	90 - 264 VAC, 2.5 A max.
Cooling	Supplied closed-loop water
Environmental Requirements	Operating temperature range: 16-30ºC Max. relative humidity: 80% non-condensing, up to 30ºC
Laboratory	Mounting surface: optical table Air free of dust (laminar air flow box recommended)

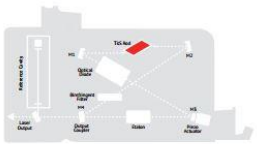
Notes

1. Unless stated otherwise, all specifications apply to: the peak of the tuning curve; ambient temperature change of < +2ºC; after 30-minute warm-up; provided the pump laser is operated at its nominal rated output power & meets its published specifications; & provided SolsTiS is not operated on or near strong atmospheric absorption lines without purge.
2. Unique integrated pump packages are available for models up to SolsTiS 3500, intermediate output power levels available
3. Other custom tuning ranges are available - please inquire for specific wavelengths.
4. All ranges available with 'dial a wavelength' and high precision wavemeter control option
5. RMS values. Linewidth specification applies relative to reference cavity and also absolute linewidth. Relative linewidth measured indefinitely and absolute linewidth measured over a period of 100µsec.
6. SRX and PSX models only. Typical 25GHz scan < 0.1 seconds. Terascan option for narrow linewidth scan of full wavelength range.
7. Laser head only. Includes reference cavity. Excludes Pump Optics Module, baseplate used with integrated pump lasers, or riser blocks in configuration using separate pump.

Typical Tuning Curves







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10.14/SolsTiS V15

The next step of this article is to make a series of tests, using a certain type of laser that satisfies all the presented parameters, to see how certain tissues behave under certain conditions. Once we find the conditions (if again again we get the same results-the results we want), once we are in control of the testing, we can move to clinical trials and hopefully ending with a viable and interesting procedure to cure arthritis.

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