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REVIEW

Modern trends in laser non-invasive reconstruction of biological tissues

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ABSTRACT

The article focuses on contemporary methodologies for laser-based, non-invasive reconstruction of biological tissues. It examines the mechanisms of laser-tissue interaction, including photothermal processes and the formation of new molecular bonds. A range of laser systems – neodymium-doped yttrium-aluminum garnet laser (Nd:YAG laser), carbon dioxide laser (CO2 laser), diode and their applications in vascular, micro- and plastic surgery are analyzed. The analysis is further enriched by a discussion of bioorganic solders, such as albumin and indocyanine green, and nanomaterials that have been shown to enhance bond strength and reduce thermal damage. Examples of successful applications of the technology for vascular and nerve repair, wound sealing, and plastic surgery are provided. Finally, future prospects are highlighted, including temperature control systems and personalized approaches. The text emphasizes the potential of laser methods as a minimally invasive alternative to traditional surgery.

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Introduction

Contemporary medicine is actively developing minimally invasive surgical methods, which are not only comparable in effectiveness to traditional approaches, but also provide less traumatic, reduced blood loss, minimal scarring, and shorter hospitalization and rehabilitation of patients. Thanks to the introduction of robotic systems, high-precision imaging, such interventions are becoming increasingly precise and safe, opening up new possibilities in the treatment of complex diseases. One of the most promising methods meeting these requirements is laser-assisted biological tissue reconstruction. This technology, based on the use of laser radiation in combination with biomaterials, demonstrates significant advantages over traditional surgical methods, such as suturing or stapling [1,2].

The aim of this article is to summarize current advancements in laser-assisted tissue repair, assess its benefits and limitations, and outline future research directions that could establish this technology as a standard in surgical practice.

Mechanism of interaction of laser radiation with biological tissues

When the process is exclusively laser-driven (laser tissue welding), it operates through a photothermal mechanism: laser energy induces structural rearrangements in the extracellular matrix components of connective tissue, leading to the formation of fusion bonds between opposing wound margins [3].

Thermal exposure induces unwinding of collagen's triple helices through hydrogen bond cleavage, resulting in denaturation and tissue contraction. Temperatures exceeding 60°C provoke covalent bond dissociation, disrupting the collagen fibers and modifying tissue characteristics, with complete relaxation achieved above 75°C [4,5].

The most common interpretation of the mechanism of operation of laser welding is the unravelling of collagen fibers at the cut ends, followed by intertwining of the fibers (interdigitation) across the cut under the action of laser radiation. As a result, fusion occurs either between the cut ends of collagen fibers or between their parallel edges. Also, new chemical bonds are formed during laser irradiation: formation of new covalent cross-links at the welding site and non-covalent interactions between unwound collagen filaments on both sides of the seam [6,7]. The operating temperature of laser welding is usually in the range of 60-65 °C.

Another effect occurring during laser welding of tissues is complete homogenization of the tissue (also called hyalinosis), in which the loose structure of collagen fibers is completely destroyed. In these cases, the temperature in the weld zone exceeds 75 °C. Denatured collagen and intracellular proteins photocoagulate, acting as endogenous glue (microsoldering) and forming new molecular bonds on cooling [8].

Photothermal soldering is based on the coagulation of protein solder due to a laser-induced temperature rise in the tissue. After cooling, non-covalent interactions between the solder and the collagen matrix in the tissue are responsible for the strength of the weld [9].

The higher the tissue's absorption coefficient, the more pronounced the photothermal effect. However, this also limits the penetration depth of laser radiation, making welding of deeper tissue layers considerably more challenging. Conversely, when tissues have low absorption coefficients, laser radiation can penetrate deeper, but the resulting photothermal effect is weaker, leading to lower tensile strength of the weld.

Laser systems for tissue reconstruction

One of the first lasers to be widely used in surgery is the Neodymium-doped yttrium-aluminum garnet laser (Nd:YAG laser) with a wavelength of λ=1064 nm. This wavelength coincides with the absorption peak of melanin and hemoglobin, giving it a hemostatic effect on soft tissue. At the same time, Nd:YAG laser radiation is poorly absorbed by water, allowing it to penetrate tissue to a depth of more than 5 mm. The benefits of the Nd:YAG laser also include its bactericidal and biostimulating properties. The positive effect of the Nd:YAG laser on cell proliferation and differentiation has also been demonstrated [10,11].

To study Nd:YAG laser tissue welding modes, Li et al. compared three techniques on porcine skin: continuous linear, zigzag, and segmented welding. The segmented method demonstrated superior outcomes, reducing thermal damage through intermittent exposure while preserving tissue regenerative potential. This approach achieved a weld strength of 0.37 MPa, outperforming linear (0.32 MPa) and zigzag methods, which exhibited energy concentration and heterogeneous joint strength, respectively [12].

The study of the effect of the Nd:YAG laser suture temperature on the tensile strength of the suture and the degree of denaturation of the reconstructed tissue showed that the strength of the sutures is maximum at a suture formation temperature close to 55 °C. At a temperature of 65 °C, the degree of protein denaturation becomes too great and the tensile strength of the sutures decreases [13].

The primary advantage of Nd:YAG lasers lies in their ability to penetrate deep into biological tissues. However, excessive energy density may cause uncontrolled thermal damage to surrounding tissues at depth. Consequently, the application of Nd:YAG lasers remains significantly limited in microsurgery and vascular surgery [14].

In contrast, the carbon dioxide laser (CO_2 laser) with a wavelength of λ=10,600 nm has found predominant application in microsurgery fields. This wavelength corresponds to water's peak absorption spectrum. Since water constitutes the primary component of most biological tissues, the laser energy gets predominantly absorbed in superficial tissue layers, with only exponentially diminishing energy available for deeper tissue heating [15].

A CO_2 laser system equipped with a fiber optic radiometer can be used for corneal integrity. Laser light is delivered via an optical fiber located directly over the treatment area. The system incorporates an infrared radiometer to monitor corneal temperature in real time, with the detector capturing thermal radiation from the tissue and transmitting the data to a computer. The laser targets only the superficial layers (less than 0.1 mm), thus avoiding damage to the deeper structures of the eye [16].

The most widely used lasers for soldering biological tissues are diode lasers with various wavelengths. Typically, semiconductor systems are more compact and consume significantly less energy than other laser technologies. The radiation from diode lasers is easily transmitted through fiber-optic delivery systems, which is crucial for applications in endoscopic surgery. However, the use of diode lasers has certain limitations, as their peak output power is significantly lower than that of CO_2 and Nd:YAG lasers. This drawback is minimized through the use of bioorganic solders and dyes that enhance tissue absorption [17].

In vascular surgery, an effective approach is the combination of a diode laser equipped with an optical fiber and a surgical microscope. One of the most commonly used wavelengths is $\lambda = 810 \pm 10$ nm. This wavelength interacts efficiently with indocyanine green (ICG), a cyanine dye incorporated into a chitosan patch. Initially, single pulses (100 J cm^2) were delivered to the tissue, with the fiber pressed firmly against the chitosan patch. Then, the patch was subjected to non-contact continuous-wave irradiation at an intensity of 20 W/cm^2 to ensure full adhesion of the patch to the outer vascular walls [18].

In the medical laser field, 970 nm radiation is widely used, especially for vascular repair. These units are equipped with a diode laser and a precision positioning system including a moving table with coordinate control (x, y, z) and a focusing lens with a fixed working distance of 18 mm, which ensures a stable laser spot diameter of 1.0 mm. The control mechanism is facilitated by a foot switch that incorporates a timer, while the integrated video system, equipped with a zoom function and an IR sensor, enables precise real-time control of the beam position, thereby mitigating the impact of human error. This configuration ensures a high degree of precision with minimal risk of damage to surrounding tissues [19].

To address the limited penetration depth of diode lasers, an intravascular approach was developed, utilizing a quartz fiber with a conical silver mirror to generate 360° ring radiation, delivered via a catheter to the anastomotic site. The procedure involved two sequential irradiation phases: primary soldering (0.41 W, 30 s, 1.52–4.1 W/cm^2) followed by reinforced treatment with additional solder application (0.55 W, 45 s, 2.04–5.5 W/cm^2). This method ensured uniform thermal diffusion across the vessel wall, achieving sutureless anastomotic integrity, as confirmed by histomorphological analysis demonstrating precise coaptation of vascular edges and controlled collagen denaturation within the irradiated zone [20].

Diode lasers with wavelengths in the 1900–1950 nm range are increasingly used in microsurgery because their penetration depth closely matches the thickness of microvessel walls (about 150 μm), enabling precise, solder- and dye-free vascular welding. This wavelength is strongly absorbed by water, resulting in shallow tissue penetration and highly localized thermal effects, which minimizes collateral damage and allows for effective vessel sealing-making it ideal for delicate procedures like microanastomoses in hand surgery [21,22].

One of the most promising laser soldering technologies is the integration of temperature feedback into laser systems. Temperature feedback allows a preset temperature to be maintained in the weld area, preventing overheating and necrosis of the surrounding tissue. The basis of such systems is an infrared bolometric matrix sensor that scans the laser weld area and determines the temperature at the most heated point. The data received is transmitted to a microcontroller which, using a proportional-integral-differential controller, corrects the laser power to maintain the set temperature with high accuracy (up to 0.5°C). This avoids overheating the tissue and minimizes the thermal damage zone, providing optimal conditions for the formation of a strong and biocompatible joint. This technology is particularly effective in combination with biopolymer nanocomposite solders, as the feedback ensures uniform heating and stable transformation of the liquid dispersion into a solid framework material [23].

A comparison of the main types of laser radiation used in laser reconstruction of biological tissues is presented in Table 1.

Table 1. Comparison of laser systems for tissue reconstruction

Laser type	Wavelength, nm	Penetration depth, mm	Main advantages	Restrictions	Application
Nd:YAG [10-14]	1064	>5	Deep penetration, bactericidal properties	Risk of thermal damage	Dermatology
CO_2 [15,16]	10600	<0.1	High precision, minimal damage to surrounding tissues	Limited depth of penetration	Microsurgery, ophthalmology
Diode (near infrared) [17-20,23]	810-970	1-3	Compactness, safety, low cost	Low capacity	Plastic surgery, nerve repair
Diode [21-22]	1900	0.15	Spot treatment, no solder required	Narrow therapeutic window	Vascular microsurgery

Notes: Nd:YAG, neodymium-doped yttrium-aluminum garnet laser; CO_2, carbon dioxide laser

Materials for optimizing laser tissue reconstruction

The use of bioorganic solders in laser tissue repair significantly increased the strength of welds, reduced thermal necrosis of tissues and accelerated the repair process [23,24].

Blood protein serum albumin is the most widely used as a base for bioorganic solders. In experiments, bovine serum albumin (BSA) [13,25,26] and human serum albumin [24] are most commonly used. Albumin is a class of water-soluble proteins that have a globular structure. Albumin is found in the tissues of almost all animals and plants. Albumin acts as a bacteriostatic coating that simultaneously promotes attachment and proliferation of eukaryotic cells. These properties make albumin a major component of bioorganic solders [27].

In order to focus the laser impact in the incision zone and prevent thermal necrosis of the surrounding non-target tissues, a chromophore that absorbs the wavelength of laser radiation is added to the solder composition. The incorporation of chromophores enables the utilization of a more compact laser apparatus with reduced power, consequently reducing operational and financial expenditures while enhancing safety for the operating surgeon [28].

The most successful combination in laser soldering of biological tissues involves the use of ICG aired with an 810 nm diode laser ICG is a non-toxic fluorescent iodide dye characterized by rapid hepatic clearance. This pairing has gained widespread adoption because the peak absorption wavelength of ICG (800 nm) closely aligns with the laser's emission wavelength (810 nm), ensuring optimal energy absorption and efficient tissue bonding [28-30].

Another effective exogenous chromophore is methylene blue, which exhibits a peak absorption at 670 nm. methylene blue has found extensive use in oncology as a photosensitizer—when activated by laser irradiation, it promotes the destruction of cancer cells [31].

However, chromophores have several limitations: low stability in aqueous solutions, tendency to migrate into surrounding tissues (increasing necrosis risk), and absorption dependency on concentration, pH, and temperature [32]. To enhance stability, they are incorporated into biopolymer matrices such as chitosan. Chitosan films not only immobilize the dye but also promote healing by providing mechanical strength and electrical conductivity. Chitosan is a high-molecular-weight glucose polymer that is water-insoluble. Current research is actively exploring its applications in tissue engineering, gene therapy, and targeted drug delivery. ICG-doped chitosan films are used in laser-assisted end-to-end anastomosis. The anastomosis site is fully wrapped with a chitosan patch, which is then irradiated with a near-infrared laser [33].

An alternative technology to prevent chromophore run off into the surrounding tissue walls is the creation of frameworks based on polycaprolactone (PCL) and ICG by electrospinning. Electrospinning represents a method for the production of fibers in the nano- and micrometer range that is undergoing active development. Electrospinning frameworks find application in targeted drug delivery [34], tissue and cell engineering [35], supporting cell adhesion and the delivery of growth factors, and promoting wound healing [36].

To fabricate the PCL scaffold, PCL was first dissolved in chloroform while ICG was dissolved in methanol. Each solution was stirred for 24 hours to achieve homogeneity. The solutions were then combined to obtain a final ICG concentration of 0.1 wt.%. The soldering scaffolds were produced via electro-spinning. A high voltage was applied to the polymer solution to generate a fluid jet, resulting in the formation of long, thin fibers. During deposition, the solvent evaporated, causing the fiber diameter to significantly decrease from 100 μm to 3-9 μm. The jet was ultimately deposited onto a grounded collector, forming a random non-woven fibrous scaffold. Prior to laser soldering, the fabricated scaffold was soaked in a 40 wt.% BSA solution and air-dried for 15 minutes. The resulting scaffolds were flexible and moderately adhesive, making them suitable for use around vascular anastomoses [36].

Although polymer frameworks have greatly improved the efficiency of laser soldering, when PCL melts under laser irradiation, a significant portion of the chromophore penetrates into healthy tissue, leading to thermal necrosis [37].

The development of research in the field of nanoscale particles has made a significant contribution to the improvement of modern medicine in general, and surgery in particular. Addition of nanoparticles to solder leads to increased absorption of laser radiation by solder, localization of irradiation in the area of weld formation and prevention of thermal damage to surrounding tissues

Encapsulating ICG silicon dioxide (SiO_2) nanoparticles prevented chromophore migration from the repair site into surrounding tissues and increased the tensile strength of welded joints [33]. The porous nanoshells were created by polymerizing silicon around cetyltrimethylammonium bromide micelles. To counteract electrostatic repulsion between negatively charged ICG molecules and the SiO_2 nanoparticle framework, the nanoshells were coated with polyallylamine hydrochloride. The positively charged polyallylamine hydrochloride retains ICG within the pores through electrostatic attraction [38].

Gold nanoparticles are widely used in tissue engineering due to their high absorption capacity, stability in physiological environments, and biochemical versatility[33].Gold nanoparticles were employed to create a nanocomposite solder. Polyethylene glycol-modified gold nanorods were centrifuged in phosphate buffer. Hyaluronic acid was then added to the resulting suspension to achieve a final concentration of 3 wt.%. The solder mixture was continuously stirred for 48 hours to obtain a homogeneous burgundy paste. The gold nanorod-based solder demonstrated low diffusion through the tissue matrix and highly localized laser energy absorption at the weld site. But it should be taken into account that gold nanoparticles can aggregate in biological fluids, which reduces their photothermal efficiency and consistency of tissue repair [39-42].

The addition of carbon nanotubes (CNT) to solder not only addresses the issue of laser radiation localization in the welding zone but also significantly enhances the tensile strength of welded seams [43]. Carbon nanotubes are actively used in regenerative medicine and diagnostics due to their size, which matches the main components of the cellular matrix, and their properties, which are comparable to protein structures [44]. CNT-based biopolymers exhibit low cytotoxicity and have a positive effect on cell differentiation and proliferation [45-46].

A three-dimensional nanocomposite for tissue integrity restoration was obtained by irradiating a biopolymer dispersion based on BSA and CNT with a pulsed femtosecond laser at a wavelength of λ = 810 nm. To create the nanocomposite, single-walled carbon nanotubes (SWCNT) with an average diameter of 1.4–1.6 nm and a length of 0.3–0.8 μm were used. An aqueous dispersion of SWCNT with a concentration of 0.001 wt.% was mixed with BSA powder until a protein concentration of 25 wt.% was achieved. The mixture was then sonicated in an ultrasonic bath until complete homogenization (for 40–60 minutes). The dispersion was irradiated with an unfocused laser beam. The pulse duration was 140 fs, with a frequency of 80 MHz. The laser output power was set to 2 W [47]. When using laser soldering technology for biological tissues in combination with this nanocomposite dispersion, the restoration strength achieved was 10 times higher than the tensile strength of sutures soldered using a solder based solely on BSA and ICG [23].

A description of the main components of solders used in laser reconstruction of biological tissues is presented in Table 2.

Table 2. Main compounds used in laser tissue reconstruction

Material	Purpose	Advantages	Disadvantages	Examples of applications
BSA [25-27]	Solder base, regeneration promoter	Biocompatibility, accessibility, promotion of cell proliferation	Low strength without additives	Vascular anastomoses, nerve repair
Chitosan [32,33]	Biopolymer matrix for solders	Biodegradability, antibacterial properties, healing promotion	Insoluble in water, requires modification	Anastomosis patches, drug delivery
ICG [28-30]	Chromophore for focusing the laser	High absorption at 800 nm, non-toxic, rapid clearance from the body	Migration into surrounding tissues, low stability	Plastic surgery, wound sealing
Carbon nanotubes [23,43-47]	Enhancing weld strength	High mechanical strength, biocompatibility, regeneration stimulation	Potential cytotoxicity at high doses	Reconstructing connective tissues
Gold nanoparticles [39-42]	Localization of laser action	Stability, high absorption capacity, biological inertness	Aggregation in physiological fluids	Skin reconstruction
Silicon nanoparticles [38]	Carrier for chromophores	Prevent dye migration, increase seam stability and strength	Complexity of synthesis, potential toxicity in case of improper functionalization	Vascular surgery, deep tissue soldering

Notes: BSA, bovine serum albumin; ICG, indocyanine green

Practical application of laser tissue reconstruction technology

The gold standard in vascular anastomosis is the classic suture method, but this method of tissue repair is time-consuming and in many cases is associated with hypoxia and tissue damage, as the supply of oxygenated blood to the operated and surrounding vessels is cut off during suturing. In addition, the effectiveness of microsurgical sutures depends on the skills of the surgeon. Laser methods of vascular repair have an advantage over suturing because they reduce the risk of stenosis, foreign body reaction and inflammation, require less surgical time, are less traumatic to surrounding tissues and limit the thrombogenicity of the anastomosis. Laser soldering provides immediate watertight wound closure [23,48].

Studies on laser-assisted tissue repair were conducted on porcine aortas. The vessels were divided into identical rectangular samples with an area of 3 cm^2 and cleaned of excess connective tissue to achieve a sample thickness of approximately 1 mm. For vascular anastomosis, two samples were pressed firmly together, and a polyetherimide membrane soaked in a solution of BSA (2 wt.%) and ICG (0.002 wt.%) was applied. The membrane was positioned to overlap approximately 10% of the surrounding healthy tissue. The weld was then treated with a diode laser at a wavelength of λ = 810 nm and a temperature of 80°C for 30 seconds [49].

The potential application of laser technologies for gum and oral mucosa restoration is being actively studied. For ex vivo experiments, pig gum tissue and oral soft tissues were used. The tissues were divided into samples with an area of 6 cm^2, and the average sample thickness was 1 mm. A 2 cm long incision was made in the center of each sample. ICG was applied to the incision, followed by exposure to laser radiation at a wavelength of λ = 808 nm. The results demonstrate that the use of an 808 nm diode laser in combination with ICG enables effective laser welding of oral soft tissues. The optimal bonding strength was achieved at an ICG concentration of 9% and a laser power of 4.5 W (10 Hz), with the weld strength comparable to that of conventional suturing. The average surface temperature reached 74 ± 5.4 °C, while the thermal damage zone remained within 333 μm. Histological analysis confirmed the localized thermal effect, indicating minimal collateral tissue damage [50].

Peripheral nerve injuries are one of the most common consequences of motor vehicle accidents and work-related injuries, resulting in sensory and motor impairment. Despite the advances made in neurosurgery over the last 10 years, effective reconstruction of peripheral nerve injuries is still a major challenge in regenerative medicine. A comparison of sciatic nerve repair using traditional needle-and-thread sutures versus an 810 nm diode laser (500 mW) with a protein solder based on 25 wt.% ICG and 62 wt.% BSA showed that the average operation time was significantly shorter in the laser repair group compared to the suture group. Electromyography revealed no differences between the experimental groups. However, the sciatic nerve function index was significantly better in the laser-repaired nerves compared to sutured nerves after 12 weeks. Histological evaluation showed no difference in inflammatory processes between the groups but demonstrated faster and more effective restoration of the peripheral nerve outer layer (epineurium) following laser repair compared to the suture method [51].

The most dangerous postoperative complication in thoracic surgery is alveolar air leaks. However, there is still no optimal method for eliminating leaks. Laser soldering enables the formation of airtight seams, overcoming the limitations of traditional suturing. For lung sealing, a semiconductor pulsed diode laser with a wavelength of 808 nm was used in combination with a semi-solid solder based on 50 wt.% BSA and 0.1 wt.% ICG. In vivo studies were conducted on 14 pigs, where two types of lung injuries were created: a linear incision and a circular incision. The protein solder was applied to the incision site and irradiated with the laser. In all cases of laser repair (except for two requiring repeat closure), no postoperative air leaks were detected. By the seventh day, all animals showed complete healing of the lung lesions with fibrous scar formation and only minor inflammatory reaction in the adjacent lung tissue [52].

Due to its ability to rapidly provide tight wound closure, laser soldering is suitable for leak prevention in gastrointestinal surgical treatment. A gold-based nanocomposite solder (Au nanorods) and collagen at a wavelength of 800 nm was used for laser soldering. The pulsed mode of laser sealing with a pulse duration of 130 fs and an interval of 12.5 ns ensures minimal heating of adjacent tissues, which prevents thermal damage. As a result, the suture strength reaches 42% of the natural tissue strength, and the tightness is 64% of the physiologic norm [53].

One of the most promising applications of laser-assisted tissue repair is in plastic surgery, as laser soldering enables precise suture formation without scar formation. Studies, including experimental work on rats, have demonstrated that laser-assisted edge joining using solder composed of BSA, ICG, and SWCNT results in significantly less noticeable scarring. For instance, Scar assessment scale evaluation on postoperative day 21 showed only 1 point for the laser method compared to 4 points for conventional sutures. Laser treatment stimulates healing processes, as confirmed by histological data: experimental groups exhibited earlier appearance of hair follicles and reduced inflammatory infiltration compared to control groups [54].

Discussion

Improvement of laser systems, aimed at the introduction of temperature feedback, providing precise control of tissue heating (up to 0.5 °C) and minimizing thermal damage. Integration of Proportional–integral–derivative controller and infrared sensors allows to optimize the soldering process safety and efficiency of the technique.

To increase the strength of laser repair and enhance the proliferative properties of repaired tissues, new generation biocomposite solders include albumin, collagen, carbon nanotubes and nanoparticles (gold, SiO_2). These materials not only increase connection strength (up to 4±0.4 MPa), but also stimulate tissue regeneration, shortening healing time. Innovative approaches, such as encapsulation of dyes in nanoparticles or polymer matrices, solve the problem of chromophore migration and reduce the risk of necrosis of surrounding tissues.

At this stage of development, laser reconstruction is moving towards personalized solutions, including the selection of laser parameters and solder composition for different tissue types. This trend is supported by the development of machine learning to predict weld strength and optimize exposure modes [55].

Despite the successes, challenges remain, such as standardization of techniques, ensuring long-term stability of compounds, and scaling of technologies for mass clinical application. Further research should focus on: in-depth study of molecular mechanisms of regeneration under laser exposure, development of universal biosimilars with programmable properties, and multicenter clinical trials.

Conclusion

Contemporary technologies of laser restoration of biological tissues demonstrate rapid development, opening new perspectives for reconstructive and plastic surgery.

Laser reconstruction of tissue is bringing the era of sutureless surgery closer, where precision, minimal invasiveness and aesthetics are becoming the standard. Already transforming approaches to wound care and reconstructive surgery, this technology may become the gold standard in plastic and microsurgery in the near future.

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