© Pediatr Med Rodz 2020, 16 (2), p. 165–170 DOI: 10.15557/PiMR.2020.0031

Jakub Kopeć, Przemysław Przewratil

Received: 18.06.2019 Accepted: 08.08.2019 Published: 30.06.2020

Laser therapy in paediatric surgery

Laseroterapia w chirurgii dziecięcej

Paediatric Surgery and Oncology, Medical University of Lodz, Łódź, Poland Correspondence: Jakub Kopeć, Tatarakowa 15/71, 91–495 Łódź, Poland, tel.: +48 664 313 466, e-mail: jdkopec@gmail.com

Advances in laser techniques used in medicine significantly expanded the pool of procedures as well as increased the Abstract frequency and ease of their use. Paediatric surgery is one of the branches of medicine open to use the dynamically developing laser technologies. Based on the current literature and our own experiences, we present a cross-sectional review of modern applications of laser therapy in the paediatric population. Laser therapy is often used complementary to other treatment methods and, in many cases, it becomes the main treatment approach in a variety of conditions. It is an indispensable element in the management of many diseases, both those health- and life-threatening as well as those responsible for cosmetic defects directly contributing to reduced quality of life of patients. This allows for a very short recovery time, with a low risk of adverse effects. The method is gaining popularity and is continuously improved. It is used, among other things, in the management of congenital and acquired vascular lesions, pilonidal sinuses, and scars. Undoubtedly, the future use of laser therapy in paediatric surgery will definitely expand to include further disease entities. A brief overview of therapeutic options for conditions in which laser therapy has become the leading therapeutic strategy can help general practitioners and paediatricians choose the optimal treatment strategy for their patients. Raising the awareness of general practitioners of indications for laser therapy may bring significant benefits for paediatric patients. Laser is becoming an increasingly available tool, which, considering the efficacy of laser therapy and a large number of indications, encourages referring patients to specialists performing such procedures.

Keywords: laser therapy, paediatric surgery, vascular malformations, scars, pilonidal sinus

Postęp techniki laserowej w medycynie spowodował istotne zwiększenie puli procedur i częstości oraz łatwości ich Streszczenie wykonywania. Chirurgia dziecięca jest jedną z gałęzi medycyny, która chętnie korzysta z dynamicznie rozwijających się urządzeń laserowych. Na podstawie przeglądu aktualnego piśmiennictwa i własnych doświadczeń autorzy prezentują przekrój nowoczesnych zastosowań laseroterapii w populacji pediatrycznej. Laseroterapia często uzupełnia już istniejące metody leczenia, a w wielu przypadkach staje się głównym sposobem terapii różnych rodzajów schorzeń. Jest nieodzownym elementem leczenia wielu chorób, zarówno tych zagrażających zdrowiu i życiu, jak i takich, które powodują defekty kosmetyczne bezpośrednio obniżające jakość życia pacjentów. Umożliwia bardzo krótki okres rekonwalescencji przy niewielkim ryzyku działań niepożądanych. Jest coraz bardziej powszechna i z dnia na dzień udoskonalana. Znajduje zastosowanie między innymi w leczeniu wrodzonych i nabytych zmian naczyniowych, torbieli włosowych, blizn. Nie ma wątpliwości, że w przyszłości zastosowania techniki laserowej w chirurgii dziecięcej będą się zdecydowanie rozszerzać na kolejne jednostki chorobowe. Krótki przegląd opcji terapeutycznych dla schorzeń, w których laseroterapia stała się wiodącą opcją terapeutyczną, może ułatwić lekarzom rodzinnym i pediatrom dobór optymalnej drogi leczenia dla ich pacjentów. Zwiększenie świadomości lekarzy pierwszego kontaktu na temat wskazań do laseroterapii może przynieść znaczącą korzyść pacjentom pediatrycznym. Laser staje się urządzeniem coraz łatwiej dostępnym, co - biorąc pod uwagę efektywność laseroterapii i dużą liczbę wskazań – zachęca do kierowania pacjentów do specjalistów wykonujących takie zabiegi.

Słowa kluczowe: laseroterapia, chirurgia dziecięca, malformacje naczyniowe, blizny, torbiel włosowa

INTRODUCTION

In the last few decades, laser technology has marked its presence in various fields of medicine, including surgery, ophthalmology, dermatology, and aesthetic medicine. Laser is used for cutting, coagulation, biostimulation, photodynamic therapy, and photoablation of diseased tissues. The dynamic development of laser devices used in medicine has encouraged us to review the progress in this field as well as the potential future benefits.

THE MECHANISM OF LASER ACTION AND TREATMENT TECHNIQUE

Laser action is based on a physical phenomenon known as stimulated emission, with different length and strength of the emitted wave, depending on the type of device, which in turn determines its use. Laser generates a beam of energy absorbed by the tissue in the form of heat, which may cut or coagulate the tissue. The frequency of the laser wave allows for controlling the size of the beam. Most medical lasers use wavelengths from infrared to ultraviolet. The longer the emitted wave, the deeper the penetration into tissue. The power of a laser is expressed in $J/cm^{2(1)}$. The most commonly used laser types include pulse dye laser (PDL), neodymium-doped yttrium aluminum garnet (Nd-YAG), and carbon dioxide (CO₂) laser. Due to its limited depth of penetration (1 mm), PDL is primarily used for superficial lesions⁽²⁾. Higher wavelength of Nd-YAG compared to PDL allows for deeper tissue penetration. The type of laser is initially selected based on the type, location and colour of the lesion as well as skin phototype, and then, depending on the efficacy of previous treatment⁽³⁾. Most laser therapy applications require repeated treatments to achieve the desired effect. Depending on patient's age, laser therapy may be performed under general or local anaesthesia, or after administering oral analgesics. If needed, an ointment, gel or cream containing an analgesic may be applied on the lesion under the dressing about an hour before the procedure. During laser procedure, every person in the room must wear protective glasses or use other means to protect the eyes against visible and invisible radiation. It is also important to perform a patch test to check for adverse effects.

INFANTILE HAEMANGIOMA

Laser therapy is one of the methods used for the management of infantile haemangiomas (IHs), which are the most common benign tumours of infancy, accounting for 5% of the population. Most haemangiomas resolve spontaneously⁽⁴⁾. Their clinical presentation varies and includes superficial, deep and mixed types. Haemangiomas are rarely found in the internal organs⁽⁴⁾. The decision on the need and type of treatment depends on the form, number, location and stage of the lesion. Between 20% and 30% of IHs require the use of propranolol due to their unfavourable size, dysfunction of the affected tissue, bleeding or ulceration⁽⁵⁾. Cases of propranolol-resistant IH, unfavourably located (respiratory tract, oral cavity, mammary gland, perineum, face) or complicated lesions require surgical treatment.

Laser therapy, which is also used in our department, is one of the available therapeutic options. Laser photocoagulation is intended to induce tumour involution⁽⁴⁾.

According to the available literature, laser therapy should be initiated already in infancy, and early treatment allows for either complete involution of the lesion⁽⁶⁾, or significant improvement of its colour⁽⁷⁾. Up to 80% of haemangiomas stop growing by 3 months of age. Most patients are reported for their first visit at the age of about 5 months, which is the period of the most intense or completed growth of haemangioma⁽⁸⁾. The energy needed to affect the tumour is lower in this patient population. Also, children have a greater capacity of tissue healing after each laser session.

The use of a dye laser affects the proliferative phase of haemangioma by slowing it down and enabling involution even in infants >6 months of age⁽⁹⁾. The use of PDL is currently recommended for:

- 1. early superficial skin lesions of the face;
- complex haemangiomas, to salvage the skin covering the lesion;
- 3. complications in the form of persistent ulcerations;
- 4. persistent telangiectasia or persistent postinvolution flat infantile haemangiomas⁽⁵⁾.

It is also recommended to use laser therapy for additional 8–18 months to manage persistent lesions. It significantly improves the size and colour of such lesions⁽¹⁰⁾.

The Nd-YAG laser, which ensures complete resolution of superficial lesions and shows high efficacy in the case of complex and deep haemangiomas in the growth phase, is an alternative for dye lasers. Treatment outcomes depend on age, tumour size and type of haemangioma⁽¹¹⁾. Lower absorption of laser energy at 1,064 nm by haemoglobin requires the use of higher energy, which may increase the risk of adverse effects⁽⁷⁾.

VASCULAR MALFORMATIONS

Vascular malformations are congenital vascular defects frequently mistaken for infantile haemangiomas. They affect 1–2% of the population, with equal incidence in both sexes. Their differentiation is based on the type of the source vessel and blood flow. These lesions are already present at birth, they grow proportionally with the child's growth and do not spontaneously involute. They develop as a result of impaired angiogenesis, vasculogenesis and lymphangiogenesis. Such lesions can be a major cosmetic problem for the patient, cause organ dysfunctions, and even be life-threatening for the child, leading to disability⁽⁴⁾.

1. Capillary malformations (CMs), commonly known as port wine stains, are the most common type of slow-flow vascular malformations, and are comprised of a capillary network in the skin and mucous membranes. They are usually located within the head and neck⁽¹²⁾.

166

PDL is the standard treatment for these lesions. Complete clearance of malformations is achieved in 10-20% of cases, whereas partial clearance of varying degree is seen in most patients, which is due to the deep location of lesions. Different therapies are increasingly often combined to improve treatment outcomes⁽¹²⁾. The best effects are achieved when the therapy is initiated in the first year of life, when the size of the lesions is the smallest, the child's skin is relatively thin and shows high regenerative potential⁽¹³⁾. Between 20% and 30% of lesions may fail to adequately respond to PDL treatment⁽³⁾.

- 2. Venous malformations are the second most common type of slow-flow vascular malformations. They are comprised of abnormal, dilated venous channels devoid of muscular tissue⁽⁴⁾. Venous malformations develop, among other things, in congenital defect syndromes, such as blue rubber bleb nevus syndrome (BRBNS) or Maffucci syndrome. Sclerotisation is the most common treatment form used for these lesions. Laser therapy is an alternative, yet common method⁽⁴⁾. Long-wavelength lasers (900-1,064 nm), such as Nd-YAG, which effectively close superficial lesions located in the subcutaneous tissue, are used. Repeated laser exposure at 8-12week intervals contributes to significantly reduced size and improved colour with minimal adverse effects. Small venous malformations usually involute, while larger ones reduce in size⁽¹²⁾. Nd-YAG laser is a promising alternative in the treatment of venous malformations in paediatric patients with critically located lesions, e.g. in mucous membranes, which respond best to treatment⁽¹⁴⁾. In our department, we also successfully use an endovascular diode laser, which is introduced directly into the lumen to close the vessel.
- 3. Lymphatic malformations are congenital lymphatic defects. The clinical presentation depends on their location and the nature of lesion. Malformations are classified as microcystic, macrocystic, and mixed. Due to compression on the adjacent organs and coagulopathic bleeding, internal organ lymphatic malformations may be life-threatening. Successful use of many types of lasers in the treatment of lymphatic malformations has been documented. The Nd-YAG laser is commonly used. In our department, we use the CO₂ laser for mucosal lesions; PDL is the best option for improving cutaneous lesions(15).

The treatment of lymphatic malformations requires a multidisciplinary approach considering patient's quality of life. Sclerotherapy is first-line treatment, especially for larger lesions⁽⁴⁾. Traditional surgery is the most effective solution for patients with life-threatening malformations, such as those involving the respiratory tract. Preliminary data indicate promising effects of percutaneous laser ablation. New pharmacological therapies using sildenafil or rapamycin are under trials(16).

4. Arteriovenous malformations are the rarest type of malformations. These lesions are characterised by rapid blood flow and are comprised of supplying vessels and dilated draining veins connected by fistulas. Vascular murmur heard during stethoscope examination is typical of these lesions. Schobinger stage 1 malformations require no treatment. Further stages are most often treated with embolisation of the focal lesion and surgery⁽⁴⁾.

Laser therapy is sometimes used as a coagulation technique during excision of this type of vascular lesions. This method for closing vessels without contacting their walls shows higher safety and, at the same time, similar efficacy compared to conventional methods⁽¹⁷⁾ (Fig. 1).

PYOGENIC GRANULOMA

Pyogenic granuloma is a benign vascular tumour usually found on the skin or the mucous membrane. It develops spontaneously at sites exposed to trauma or secondary to vascular malformations⁽¹⁸⁾. It usually presents as an isolated, fragile, polypoid or pedunculated red bump⁽⁴⁾. It may develop in children at different ages, but rarely in infants. Pyogenic granuloma is a rapidly growing lesion prone to mechanical injury, and thus bleeding. Surgical excision is the best treatment option as it ensures the lowest recurrence rates. Other methods include, among other things, ligation of the base of pyogenic granuloma, local coagulation with silver nitrate, electrocoagulation, and curettage^(4,18). CO₂ laser ablation is a practical and increasingly used alternative⁽¹⁸⁾.

PILONIDAL SINUS

Pilonidal sinus is an inflammation of the subcutaneous tissue most often located in the gluteal cleft. It usually affects adolescent Caucasian males. The aetiology of pilonidal sinus is not clearly defined. Hair penetration into the sacral fistula and the resulting inflammation around the foreign body are usually the direct cause. Patients most often report with a symptom of a fluctuant, painful nodule in the coccygeal/sacral region⁽¹⁹⁾. Pilonidal sinus has high recurrence rates (>30% of cases) and significantly reduces the quality of life^(20,21). Surgical excision is a common treatment method for pilonidal sinus. Unfortunately, recurrence rates after this type of treatment are high (5-20%)^(22,23). Laser hair removal is an alternative treatment method. Due to appropriate wavelength, the laser emits energy absorbed by the tissue in the form of heat at an appropriate depth in the absorber - hair follicle melanin; therefore, better effects are achieved in patients with dark hair, which contains more pigment. Laser hair removal decreases recurrence rates by reducing the thickness and the amount of hair in the gluteal cleft, and thus improving hygiene in this region⁽²¹⁾.

It may be used as the primary method or incorporated as a permanent part of postoperative care⁽²³⁾. Usually, about 6 procedures performed at 3-6-week intervals are recommended. Studies among adult patients have shown that laser hair removal reduced recurrence rates for pilonidal | 167



Fig. 1. **A.** *Infantile haemangioma of the face in a 3 months old child.* **B.** *Venous malformation of the forehead – 8 months old child.* **C.** *Capillary-lymphatic malformation of the left lower extremity in a 6 months old child.* **D.** *Capillary malformation of the face in a 15 years old boy*

sinus by up to $80\%^{(20)}$. No need for hospital stay is an advantage of this method⁽²⁴⁾.

Primary intervention using the Nd-YAG laser may replace conventional surgical excision. Postoperative recovery period may be longer, whereas patients after Nd-YAG laser procedure return to activity already after one day, with similar efficacy of the procedure. The penetrating depth and direct action on hair follicles are advantages of the Nd-YAG laser⁽²²⁾. Ultrasound monitoring of the irradiated site, which helps determine the presence of hair and assess treatment efficacy, may play an important role in such procedures⁽²⁵⁾.

SCARS

Any injury penetrating the skin to the dermis, regardless of the mechanism, leaves a scar after healing⁽²⁶⁾. There are three types of scars: atrophic, hypertrophic and keloids⁽²⁷⁾. Scars may be accompanied by pain, hyperalgesia, and pruritus. Advances in laser therapy have enabled the introduction of alternative and effective treatment of both scars, and the accompanying symptoms⁽²⁸⁾.

Adjusting an appropriate type of laser to treatment stage and type of scar allows for maximising the therapeutic effect. Owing to the phenomenon of photothermolysis, PDL acts on the smallest capillaries present in immature scars, causing their coagulation. More mature scars are treated with CO_2 laser, which causes evaporation of water accumulated in the abnormal form of collagen. Irradiated scar tissue undergoes ablation, enabling deposition of normal collagen⁽²⁹⁾.

PDL used at an early stage of scar formation helps improve erythema, reduce pain, pruritus, scar volume and improves scar surface texture. Fraction lasers (e.g. CO_2) induce remodelling of tissue, whose structure becomes similar to that of healthy skin in terms of the content ratio of different types of collagen. The achievable depth of tissue penetration combined with treatment efficacy established the gold standard in the treatment of scars⁽²⁶⁾.

Postoperative management of a scar treated with laser should be individualised and it should consider the use of individually adjusted compression garments (pressotherapy) and other forms of physical therapy⁽²⁹⁾.

Laser-assisted drug delivery (LADD) may be an alternative scar treatment. LADD is based on temporary disruption of the scar tissue barrier during fractional photothermolysis. Combining topical steroids with laser therapy increases penetration depth and absorption of these substances⁽²⁸⁾. LADD has not been sufficiently studied⁽²⁶⁾.

Scar treatment requires a diversified, integrated therapeutic approach; however, prevention of scar hypertrophy remains the most important and effective method⁽²⁷⁾. Laser therapy should be considered at least supplementary to the already used methods⁽²⁹⁾.

LITHOTRIPSY

Laser lithotripsy is a common, globally used method for breaking apart kidney and biliary stones. The most frequently used lasers for this procedure include, among other things, dye laser, which, introduced through a cystoscope, disintegrates yellow stones with a green light beam, leaving the adjacent tissues intact. However, this method is ineffective in the case of colourless stones, such as cystine stones, disintegration of which requires a photosensitising dye. The holmium-YAG laser (Ho-YAG) acts through a photothermal effect. This type of laser induces vaporisation of the liquid medium, in which a stone is suspended, which enables the laser beam to directly reach the target⁽¹⁾.

BEZOARS

Laser therapy is also effective in the case of bezoars. Small, soft bezoars can be dissolved using appropriate means, which is time-consuming and likely to cause complications. Different endoscopic techniques are used to remove bezoars. If such methods fail, the lesion must be removed surgically, which involves the risk of complications. Endoscopic lithotripsy using the Nd-YAG laser may solve some of the clinical problems caused by bezoars. It involves inducing microexplosion using a tip of a gastroscope equipped with a laser, which leads to bezoar fragmentation⁽³⁰⁾.

COMPLICATIONS

Skin hypopigmentation, especially in the case of dark phenotype, pain, hyperalgesia and irritation are the most common complications of laser therapy. Furthermore, burns, skin atrophy, scarring, bleeding lesions, and local ulcers (especially in the case of vascular lesions) may occur. However, complications are uncommon, and most of them are transient and reversible^(5,7).

CONCLUSIONS

Currently we are witnessing the greatest expansion in laser technology in medicine. Laser therapy is often used complementary to the already existing treatment methods and, in many cases, it becomes the main treatment technique in a variety of diseases. It is an indispensable element in the treatment of health- and life-threatening diseases as well as those responsible for cosmetic defects directly contributing to reduced quality of life of patients. Laser therapy allows for a very short recovery time, with a low risk of adverse effects. The method is increasingly popular and continuously improved. Undoubtedly, the future use of laser therapy in paediatric surgery will definitely expand to include further disease entities.

Conflict of interest

The authors do not report any financial or personal connections with other persons or organisations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

References

- 1. Azadgoli B, Baker RY: Laser applications in surgery. Ann Transl Med 2016; 4: 452.
- Shen L, Zhou G, Zhao J et al.: Pulsed dye laser therapy for infantile hemangiomas: a systemic review and meta-analysis. QJM 2015; 108: 473–480.
- 3. Brightman LA, Geronemus RG, Reddy KK: Laser treatment of port-wine stains. Clin Cosmet Investig Dermatol 2015; 8: 27–33.
- 4. Przewratil P: Naczyniaki i malformacje naczyniowe. In: Bagłaj M, Kaliciński P (eds.): Chirurgia dziecięca. PZWL, Warszawa 2016: 985–1000.
- 5. Darrow DH, Greene AK, Mancini AJ et al.; Section on Dermatology, Section on Otolaryngology–Head and Neck Surgery, and Section on Plastic Surgery: Diagnosis and management of infantile hemangioma. Pediatrics 2015; 136: e1060–e1104.
- Asilian A, Mokhtari F, Kamali AS et al.: Pulsed dye laser and topical timolol gel versus pulse dye laser in treatment of infantile hemangioma: a double-blind randomized controlled trial. Adv Biomed Res 2015; 4: 257.
- Chinnadurai S, Sathe NA, Surawicz T: Laser treatment of infantile hemangioma: a systematic review. Lasers Surg Med 2016; 48: 221–233.

- 8. Zhang W, Li F, Yang Y et al.: Hemangioma treatment with pulsed dye laser distinct parameters used between neonatal and nonneonatal patients. J Cosmet Laser Ther 2016; 18: 389–392.
- 9. Kessels JP, Hamers ET, Ostertag JU: Superficial hemangioma: pulsed dye laser versus wait-and-see. Dermatol Surg 2013; 39: 414-421.
- **10.** Dementieva N, Jones S: The treatment of problematic hemangiomas in children with propranolol and 940 nm diode laser. J Pediatr Surg 2016; 51: 863–868.
- Zhong SX, Tao YC, Zhou JF et al.: Infantile hemangioma: clinical characteristics and efficacy of treatment with the long-pulsed 1,064-nm neodymium-doped yttrium aluminum garnet laser in 794 Chinese patients. Pediatr Dermatol 2015; 32: 495–500.
- **12.** Craig LM, Alster TS: Vascular skin lesions in children: a review of laser surgical and medical treatments. Dermatol Surg 2013; 39: 1137–1146.
- 13. Rajaratnam R, Laughlin SA, Dudley D: Pulsed dye laser doublepass treatment of patients with resistant capillary malformations. Lasers Med Sci 2011; 26: 487–492.
- 14. Murthy AS, Dawson A, Gupta D et al.: Utility and tolerability of the long-pulsed 1064-nm neodymium:yttrium-aluminumgarnet (LP Nd:YAG) laser for treatment of symptomatic or disfiguring vascular malformations in children and adolescents. J Am Acad Dermatol 2017; 77: 473–479.
- **15.** Defnet AM, Bagrodia N, Hernandez SL et al.: Pediatric lymphatic malformations: evolving understanding and therapeutic options. Pediatr Surg Int 2016; 32: 425–433.
- **16.** Amodeo I, Cavallaro G, Raffaeli G et al.: Abdominal cystic lymphangioma in a term newborn: a case report and update of new treatments. Medicine (Baltimore) 2017; 96: e5984.
- 17. Cenzato M, Dones F, Marcati E et al.: Use of laser in arteriovenous malformation surgery. World Neurosurg 106: 746–749.
- Wollina U, Langner D, França K et al.: Pyogenic granuloma a common benign vascular tumor with variable clinical presentation: new findings and treatment options. Open Access Maced J Med Sci 2017; 5: 423–426.

- Wałęga P, Romaniszyn M: Torbiel pilonidalna. Med Prakt Chir 2013; 5.
- Lopez JJ, Cooper JN, Fischer BA et al.: Safety and tolerability of laser hair depilation in pilonidal disease: a pilot study. Surg Infect (Larchmt) 2017; 18: 890–893.
- 21. Marza L: Reducing the recurrence of pilonidal sinus disease. Nurs Times 2013; 109: 22–24.
- 22. Suárez Valladares MJ, Rodríguez Prieto MA: Neodymium-doped yttrium aluminium garnet laser to treat primary pilonidal cysts: an alternative treatment. Br J Dermatol 2018; 178: e127–e128.
- 23. Segre D, Pozzo M, Perinotti R et al.; Italian Society of Colorectal Surgery: The treatment of pilonidal disease: guidelines of the Italian Society of Colorectal Surgery (SICCR). Tech Coloproctol 2015; 19: 607–613.
- 24. Khan MAA, Javed AA, Govindan KS et al.: Control of hair growth using long-pulsed alexandrite laser is an efficient and cost effective therapy for patients suffering from recurrent pilonidal disease. Lasers Med Sci 2016; 31: 857–862.
- 25. Dragoni F, Moretti S, Cannarozzo G et al.: Treatment of recurrent pilonidal cysts with Nd-YAG laser: report of our experience. J Dermatolog Treat 2018; 29: 65–67.
- **26.** Krakowski AC, Totri CR, Donelan MB et al.: Scar management in the pediatric and adolescent populations. Pediatrics 2016; 137: e20142065.
- 27. Kuzański W, Andrzejewska E: Jak uzyskać estetyczną bliznę u dziecka. Med Prakt Chir 2017; 4: 33–40.
- Waibel JS, Wulkan AJ, Shumaker PR: Treatment of hypertrophic scars using laser and laser assisted corticosteroid delivery. Lasers Surg Med 2013; 45: 135–140.
- **29.** Hultman CS, Friedstat JS, Edkins RE et al.: Laser resurfacing and remodeling of hypertrophic burn scars: the results of a large, prospective, before-after cohort study, with long-term follow-up. Ann Surg 2014; 260: 519–532.
- 30. Mao Y, Qiu H, Liu Q et al.: Endoscopic lithotripsy for gastric bezoars by Nd:YAG laser-ignited mini-explosive technique. Lasers Med Sci 2014; 29: 1237–1240.