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Medical Application and Industrial Development Strategy of Laser Technology in China

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Abstract: Laser diagnosis and treatment technology have been successfully applied in the field of healthcare and have become an important part of precision diagnosis and treatment in modern medicine. This study focuses on the use of laser technology in medicine. We summarize the development status, trends, and problems associated with China's use of laser technology in clinical treatment, diagnosis, and industrialization, from the perspective of practical application. The study shows that China has made good progress in terms of laser treatment technology, medical laser diagnosis, and treatment equipment; however, overall, the clinical application of laser medical technology continues to lag behind global developments. The applied research on the technology still lacks original creativity, and the research and industrialization of medical laser equipment is at the low end of the scale. The key technologies and high-end equipment such as ultrafast lasers for precision diagnosis and treatment are still under foreign control. This study proposes that China should establish sub-disciplines under laser medicine, strengthen the construction of national science and technology innovation platforms for laser medicine, develop regulated standards and policies for laser medical equipment in a targeted manner, establish a framework to support the development of the laser medical equipment industry, and strive to make breakthroughs in key technology research for medical laser diagnostic equipment.
Keywords: laser technology; medicine; laser diagnosis; laser therapy; laser industry.

1 Introduction

Since the world's first ruby laser was developed in 1960, this new light source and the resulting new laser

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technology has found application in the medical field. After 60 years of development, laser medicine has developed into a new cross-discipline as a relatively complete and independent system, playing an increasingly important role in medical science. There are currently three major laser treatment technologies in clinical applications: high-level laser therapy, photodynamic therapy (PDT), and low-level laser therapy (LLLT) [1]. Simultaneous development includes optical coherence tomography (OCT) and laser diagnostic techniques with high sensitivity and resolution, including photoacoustic imaging, multiphoton microscopy, and Raman imaging [2]. In addition, with the development of related disciplines such as chemistry and biology, several biological probes and targeted labeling technologies have developed rapidly. The mutual integration of laser optics, materials science, nanotechnology, and biotechnology is constantly providing medical diagnosis and treatment with new development space.

With the transformation of modern medical models, the application field of laser medicine is moving forward from disease diagnosis and treatment to disease prevention, leading to the transformation of medical diagnosis and treatment models to those offering precision, minimal invasiveness, and non-invasiveness as technological breakthroughs. The development and application of laser diagnosis and treatment technology has promoted the industrialization of medical laser equipment, and a relatively mature medical laser equipment industry has evolved internationally. Compared to developed countries, there is a gap in China in medical laser core technology, industrial scale, promotion, and application. The high-end laser medical device market has long been occupied by imported products, and the corresponding technical service capabilities in China have not fully met the needs of national medical care.

In this study we systematically investigate the development status, prospects, and problems associated with laser technology in clinical treatment and diagnosis, and the laser medical industry in China. We propose measures to accelerate the development of China's laser medical technology and application industry, with a view to providing domestic technical equipment and medical applications with a development reference.

2 Current state of laser technology medical applications

2.1 Laser diagnosis technology

Laser diagnostic technology uses the basic optical properties of lasers, such as high monochromaticity, high light intensity, collimation, polarization, and several different interactions between light and matter (such as scattering, and absorption). These properties are used to measure the microstructure and physiological effects of biological tissues, biochemical molecular concentration distribution, and other key indicators to obtain information on the structure and function of biological tissues and analyze the occurrence and development of diseases. With the advantages of non-destructive imaging, high resolution, and rich contrast mechanisms, laser diagnostic technology has become an important part of modern medical precision diagnosis and treatment.

With the continuous advancement of laser technology and the ongoing traction of the demand for clinical precision diagnosis and treatment, new technologies, mechanisms, and concepts in laser imaging continue to emerge. New diagnostic technologies such as non-contact, label-free imaging, and real-time *in-vivo* imaging have been gradually derived for clinical applications. Typical examples include OCT [3], photoacoustic imaging [4], laser speckle imaging [5], multiphoton microscopy imaging [6], confocal imaging [7], and Raman imaging [8]. As a representative optical diagnostic technology, OCT uses non-invasive near-infrared light as the light source to obtain real-time *in-vivo* retinal tomographic images similar to histopathology, which is widely used in the diagnosis of various ophthalmological diseases. In recent years, OCT has also been extended to medical disciplines other than ophthalmology, such as dermatology and stomatology. With the miniaturization of OCT equipment and its integration with catheters and endoscopes, future applications in cardiovascular diseases, gastrointestinal diseases, and early tumor diagnosis are expected to be further extended.

Although the above-mentioned laser imaging methods have played an important role in the direction of biomedical research, they inevitably have application limitations. Single-modality imaging methods can usually only obtain partial information, while the optical information obtained by different modal optical imaging methods is more complete. For specific diseases, the analysis results of different modal optical imaging methods are combined to form a multi-modal, multi-dimensional optical detection and monitoring platform, which is the key development direction of laser diagnostic technology in the future. The application range of laser diagnostic technology will continue to expand, from spot-on care and laboratory testing, to screening, diagnostic imaging, and treatment monitoring. The range could also include real-time *in-vivo* imaging and tumor boundary recognition during surgery. In the future, with the help of genetic engineering methods, optoelectronics and intracellular devices (such as micro

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and nano lasers) will be implemented to increase the integration of photosensitive functions for patients, thereby further expanding the application of laser diagnostic technology.

2.2 Laser treatment technology

2.2.1 High-level laser treatment technology

High-level laser treatment uses the photothermal effect of a laser to coagulate, vaporize, or cut biological tissues to achieve the purpose of eliminating pathological changes [9]. Since the ruby laser was successfully used in the photocoagulation treatment of retinal detachment in the 1960s [10], high-level laser treatment has been used in various clinical applications. Advantages of such treatment include reduced bleeding, precise positioning, no contact, sterile, and less damage to surrounding tissues. This technology has expanded rapidly in China and become the most mature branch of laser medicine and the fastest-growing. High-level laser treatment has been widely used in disciplines such as ophthalmology, dermatology, urology, gastroenterology, stomatology, and otolaryngology [1]. Furthermore, as a “light scalpel”, it has been a revolutionary breakthrough, changing traditional surgical methods and enabling the treatment of several intractable diseases. Intense laser therapy, as the key technology in modern ophthalmology, is regarded as the first choice for the treatment of many eye diseases.

Ultrafast lasers (such as picosecond and femtosecond lasers) have the characteristics of high selectivity and extremely precise cutting, and have gradually shown their application potential in medical applications and life sciences [11]. Femtosecond lasers can transmit light to the focal point without attenuation in transparent biological tissues, with little thermal damage to the surrounding tissues and high precision cutting accuracy. Compared with traditional therapeutic surgery and other laser surgery, femtosecond laser surgery has improved accuracy, safety, and stability, and is regarded as a relatively perfect clinical ophthalmic treatment method. Driven by medical demands such as ophthalmology and precision therapy, as well as the rapid development of surgical robotics technology, medical ultrafast lasers, and other new powerful laser applications are expected to grow to industrial scale, thereby providing new methods for the treatment of certain intractable diseases.

2.2.2 PDT

PDT is a new type of minimally invasive therapy to treat tumors that have emerged after surgery, chemotherapy, and radiotherapy. In the process of PDT, photosensitizers undergo a series of photophysical and chemical reactions under the activation of lasers of specific wavelengths to produce biologically toxic reactive oxygen species to kill target tissues, and then implement the targeted therapy [12]. Compared with traditional treatment methods, PDT has the advantages of high selectivity, minimal invasiveness, reusability, and effectiveness in the presence of almost any specific drugs. Furthermore, it can preserve the integrity of tissues and organs to the maximum level [13]. With continuous in-depth research on the mechanisms of PDT, the indications for PDT have gradually expanded from initial tumor treatment to the three major therapeutic areas of tumor-targeted PDT, blood vessel-targeted PDT, and microbial-targeted PDT. It is used in the treatment of malignant and precancerous tumors. Diseases, refractory microvascular diseases (such as age-related macular degeneration, port wine stains, and gastric antrum vasodilation), and refractory/drug-resistant microbial infections have good application prospects.

The spectrum and curative effect of PDT are closely related to light parameters such as the wavelength, intensity, and illumination mode of the light used. Therefore, the light source is a key component of PDT. In the early application stages, incoherent light, such as incandescent lamps and high-voltage arc lamps, were usually used as radiation sources. Such light sources have shortcomings in terms of their spectral structure, power density, transmission system, and precise control. In view of the unique advantages of laser technology, lasers have become the light source of choice for PDT, which has significantly improved the effect of PDT in clinical applications.

PDT has a unique and complex mechanism of action, a wide range of treatment spectra, and different characteristics of specific treatment targets. The most active research direction in laser therapy is the systematic and in-depth research on different target diseases to achieve new therapeutic breakthroughs. The corresponding hot spots are the development of highly targeted and selective functional photosensitizers; PDT treatment in-depth improvement (such as two-photon PDT, and up-conversion nanomaterial PDT) [14,15]; the development and application of new PDT light sources; research on the mechanism and dose-effect of new indications of PDT; and precise control of the light dose in PDT treatment.

2.2.3 LLLT

LLLT is also known as low-intensity laser therapy or photobiomodulation therapy. When the laser acts on biological tissues, it does not cause irreversible damage, but stimulates the body to produce a series of physiological and biochemical reactions. These can regulate, enhance, or inhibit the tissue or body to achieve the purpose of curing diseases [16,17]. The most important feature of LLLT is that the treatment is non-invasive and painless, and its power density is usually in the order of milliwatts. Since the 1970s, the clinical application of LLLT has been widely used in Eastern Europe, the Soviet Union, and China. With the development of semiconductor lasers, lasers with multiple wavelengths, including red light and near-infrared light, have been used as light sources for LLLT treatment and are used in internal medicine, surgery, gynecology, pediatrics, ophthalmology, otology, stomatology, and other clinical disciplines. The benefits from treatment of a variety of diseases include promoting wound healing, pain relief, inflammation subsidence, tissue regeneration, and muscle fatigue relief. At present, clinical lasers are mainly HeNe/semiconductor lasers, with wavelengths in the red band (630–690 nm) and near-infrared band (760–940 nm), and the continuous output mode is mainly adopted.

Laser wavelength, laser dose, and continuous or pulsed laser output modes will produce different biological control processes. With an in-depth study of the mechanism of LLLT and the emergence and application of new light sources, the application fields of LLLT are also expanding. In addition to clinically mature applications (such as infection, inflammation, and pain management), ultraviolet and near-infrared pulsed lasers are used in some major chronic diseases, and the treatment and prevention of age-related diseases have shown good prospects. In recent years, LLLT has made some progress in the exploration of the prevention and treatment of neurodegenerative diseases. Given the lack of a safe and effective method to treat neurodegenerative diseases, LLLT has opened up a promising new direction, which is expected to drive the further development of low-level laser clinical applications and related laser technologies.

With the transformation of medical models and the expansion of the LLLT disease spectrum from common diseases to major chronic age-related diseases, related treatment fields are extending beyond disease treatment to include disease prevention. Furthermore, the main area of use is also changing from medical institutions to communities and families. This situation suggests the need for new and stricter requirements for the portability, miniaturization, and wearability of LLLT treatment equipment. It can be expected that wearable devices based on laser technology will play a more comprehensive and important role in disease treatment.

2.3 Laser monitoring technology

Medical monitoring technology based on light-emitting diode (LED) light sources has gradually emerged because of their ability to monitor important physiological indicators such as blood glucose and blood oxygen. Compared with LED light sources, laser light sources have better optical characteristics and can provide new non-destructive and precise monitoring methods. They can realize minimally invasive or non-invasive monitoring, combine high sensitivity, high selectivity, and long-term stability, and significantly improve the precision of medical monitoring results. With the transformation of medical treatment models, the “hospital treatment + family health monitoring” model will be the developing trend, and precision laser monitoring technology will become an increasingly important development direction for medical monitoring equipment.

In terms of extremely sensitive laser health monitoring, laser monitoring technology based on breathing gas, urine, and blood is the focus of future development.

In terms of miniaturized laser health monitoring, there are three major development directions: (1) portable laser monitoring technology, miniaturization, and integration of laser monitoring systems, such as portable blood glucose and blood pressure monitors; (2) wearable laser monitoring technology, and design of laser monitoring equipment suitable for human wear such as a wearable smart laser monitoring watch; (3) endoscopic laser monitoring technology, combining laser technology for molecular, cell, and tissue level detection with the current mature endoscopic technology for real-time monitoring of tissues in the body.

In terms of intelligent laser health monitoring there are also three major areas of development: (1) laser monitoring functions based on big data, and artificial intelligence technology will become a powerful tool for automated processing and analysis of biomedical big data; (2) small size, light weight, and low voltage devices in response to dynamic medical testing needs and laser light sources with low power consumption, improving the physical indicators of diagnostic lasers, and equipment battery life to meet user experience requirements; (3) future laser diagnosis and treatment methods will develop in the direction of implantation, exploring the biocompatibility of new lasers such as micro-nano lasers and degradability.

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3 The development trend of China's laser medical industry

According to the Allied Market Research report [18], the world laser medical market was worth 5.116 billion USD in 2016 which is expected to increase to 12.586 billion USD in 2023, with an average annual growth rate of approximately 13.6%; the United States, Europe, Israel, and Japan rank among the world's leading markets. The global market share of laser medical devices is led by North America who account for approximately 35%, with 25% for Europe and the Middle East, 20% for the Asia-Pacific region, and approximately 15% for China. Internationally, the medical laser industry consists of more than 40 commercialized products with annual sales exceeding 1 billion USD.

China's laser medical industry lags behind developed countries in terms of scale, core technology, promotion, and applications. China currently imports most of its laser medical equipment. For example, high-end ophthalmic treatment equipment is exclusively sourced from foreign companies. Domestic laser medical equipment consists mainly of CO_2, Nd:YAG, and semiconductor lasers. The main applications include dermatology, general surgery, urology, and cardiovascular diseases, but still exclude ophthalmic diagnosis, detection, and treatment. Domestic equipment has been used in the field of dermatology and urology; however, the manufacturer is small with only one product line. China's laser medical device industry is currently concentrated in Beijing, Shanghai, Guangdong, Hubei, and Jilin, and consists of approximately 200 registered laser medical device companies.

Meanwhile, it should be noted that basic research and technological innovation in the medical application of laser technology in China have developed rapidly in recent years. In 2019, the National Natural Science Foundation of China had 82 major national scientific research instrument development projects, 16 of which were related to laser medical treatment. The funding for laser medical treatment amounted to 118 578 700 CNY which represents 20.44% of the total funding provided by the Foundation. There are several domestic medical laser companies who focus on technology research and development (R&D), and breakthroughs have been made in key technologies at different levels related to laser power, stability, and accuracy, and the localization of laser medical devices has steadily accelerated. In addition, there has been significant progress made in the R&D of power and core components of domestic medical lasers. With the continuous enhancement of China's scientific and technological innovation capabilities and the overall breakthrough of key laser technologies, China's medical lasers have broad application prospects, and the corresponding industrial development trends are as follows:

(1) China's laser medical industry is dominated by small- and medium-sized private enterprises, which have increasingly become a relatively active market for innovation and entrepreneurship.

(2) China's laser medical industry is shifting from solely domestic sales to the global market. In particular, driven by the Belt and Road initiative, more and more domestic laser medical device companies have obtained US Food and Drug Administration (FDA) and European Unified (CE) medical qualifications, enabling them to steadily increase their export share.

(3) With the implementation of the registration system in China, certification and production, R&D, and manufacturing are becoming separated, and third-party manufacturing has become a development trend. In the future, large-scale industrial clusters will be formed in areas where the laser medical industry is concentrated.

(4) With the advancement of China's medical reform, the upgrading of resident consumption, and the improvement of quality of life, the domestic medical market has a stronger demand for high-quality laser medical equipment.

4 Problems with the medical application of laser technology in China

Overall, the current medical application of laser technology in China is at a low level, and the traction driven by clinical needs is insufficient. The use of laser technology is fairly typical; originality of design is lacking, and the combination with clinical research is not sufficient to move the industry forward. The situation requires high standards and high-quality clinical needs. Although domestic research on basic and clinical applications such as vascular targeting, PDT, and low-light therapy have maintained China's competitiveness, the development of medical lasers and their industrialization for laser medicine is clearly lagging behind developed countries.

At present, in developed countries, approximately 10% to 15% of surgical operations use lasers instead of traditional surgical instruments such as scalpels. With the expansion of laser technology in the field of medical applications, this proportion continues to increase. In contrast, China's laser medical industry research is following developed countries and trying to synchronize development. In laser equipment with high technical barriers, such as ophthalmic laser equipment, there are few competitive domestic companies. This is due to the long R&D cycle for laser medical equipment, with high technical barriers, and a high risk of failure. R&D of laser medical technology and equipment for clinical use is not popular with investors. In the fields of dermatology, urology, surgery, and other equipment with low technical difficulty, domestic equipment has succeeded in securing a large share of the low-end market. In emerging laser medical fields such as tumor PDT, low-light medical treatment, and oral cavity, there are no dominant equipment companies in China or abroad.

China’s laser medical industry as a whole is currently in a state of tracking and imitation, with low technical advantages, little added value, and a small share of the high-end market. The corresponding medical applications of laser technology are facing significant difficulties.

(1) There is no secondary discipline in laser medicine. Although laser medicine has many unique characteristics such as strong technology, high comprehensiveness, wide coverage, and universal clinical applications, the lack of clear discipline attributes has made China’s education system unable to establish a secondary discipline focused on laser medicine. As a result, there is a lack of professional talent and subject development is falling behind.

(2) Industry concentration was not high. There are currently about 200 laser medical device companies in China, mainly small- and medium-sized private enterprises, and apart from a few National Equities Exchange and Quotations companies, there are no main board listed companies; most companies have only one or two medical laser products, with low levels of production.

(3) The industrial structure is inappropriate. Domestic laser medical products are concentrated in the middle and low end of the value chain, while high-technology, high-value-added products are rare. Low production volumes of low value products are dominant resulting in low returns on investment. Consequently, many companies remain at the stage of imitation, and lack the willingness and ability to independently innovate.

(4) The combination of production, study, and research has not reached economic levels. The resources of the laser medical industry have not been fully integrated with powerful intellectual resources and abundant clinical resources. The main body of the enterprise in the ‘production, study, and research’ combination is obviously missing, causing a disconnect between research and the market, and existing resource advantages are difficult to reflect at the industrial level.

(5) The market cycle of domestic laser medical equipment is long. The average market cycle of medical devices in China is three to five years, while the market cycle of medical devices in developed countries and regions such as the United States and the European Union is generally only one to two years.

5 Suggestions and strategy

5.1 Establishing laser medicine as a secondary discipline

The interdisciplinary nature of laser medicine, the complexity of laser interactions with tissues, and the professionalism of laser treatment promote higher professional requirements for laser medical practitioners. They must be proficient in the professional medical knowledge required for laser diagnosis and treatment, as well as have a professional background in laser medicine. In China, the first-level discipline of clinical medicine lacks a second-level discipline in laser medicine, implying that clinical medicine undergraduates’ education lacks relevant professional courses. Only a few colleges and universities have postgraduate enrollment qualifications for laser medicine, and because there are no secondary subjects, they can only recruit students from other disciplines. These factors have resulted in a scarcity of talent, a complex structure of practitioners, and uneven education in laser medicine in China.

Laser medicine has gradually developed into a unique, relatively complete, and vibrant frontier interdisciplinary subject. With the gradual integration of laser medicine and clinical medicine, the current talent training model of medical schools has been unable to match the country’s fresh demand for advanced laser medicine professionals. We recommend that a second-level discipline of laser medicine be established under the first-level discipline of clinical medicine to build a complete undergraduate–master–doctorate training system. This is an important measure for promoting the cross-integration of medical engineering and ensuring the long-term development of laser medicine in China.

5.2 Building a laser medicine technology innovation platform

Relying on key and characteristic clinical hospitals, we should consolidate the respective advantages of universities, scientific research institutes, and high-tech enterprises to establish a national research center for the

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clinical transformation of laser medicine. The center would be different from national key laboratories for photoelectric research and would be guided by actual clinical needs. It will gather superior domestic research forces, focus on close collaboration with enterprises to promote industrial development, and focus on laser diagnosis, treatment, and monitoring. The core key technologies involved would help in the clinical transformation, demonstration, and promotion of laser diagnostic and treatment technologies in China.

5.3 Accelerating the establishment of medical device regulations

We recommend that medical device regulations include laser medical equipment (such as optical coherent imaging equipment used in ophthalmology and dermatology) that have a clear working mechanism, a finalized program design, a mature production process, and no serious adverse event records in the *Catalog of Medical Treatment Devices Exempted from Clinical Trial*. Moreover, the requirements for clinical trials of products with high maturity and low risk should be further reduced, allowing companies to invest more energy in new product development and quality assurance. We further recommend the comprehensive promotion of a medical device registration system, the separation of production and certification, and the provision of a standardized and convenient environment for laser medical devices to accelerate product innovation and shorten the R&D cycle. The protection of intellectual property rights needs to be strengthened and patent laws and regulations implemented to protect innovation achievements in the development of laser medical devices and to stimulate an incentive for innovation.

5.4 Supporting industries related to laser medical equipment

The long R&D cycle, high technical barriers, and high risk of failure of laser medical devices make social capital investors cautious. Therefore, government policies and support are critical. We recommend that local governments support the establishment of laser medical industry parks and give full play to the research strength, production, and manufacturing capabilities of local universities and research institutes. An environment needs to be established that encourages product sharing between the military and civilians, and necessary financial support needs to be provided, as well as tax relief and other preferential policies to promote the laser medical device industry. The government also must provide support for laser medical industrial parks and third-party manufacturing platforms of laser medical equipment, and provide policy support and maintain continuity in terms of land, capital, taxation, talents, etc. They must provide financial and legal public services compatible with industrial development and promote the sharing of public resources and their efficient use. Focus is needed on substantive key technological breakthroughs, and the medium- and long-term steady development of the industry, to cultivate well-known brands and leading enterprises.

5.5 Strengthening R&D of key core technologies

There is still a gap between China's clinical laser medical technology and international standards. For example, the stability and safety of femtosecond lasers in China have not yet reached medical standards, and the key parts of domestic ultrafast lasers are mostly dependent on imports (such as chirped mirrors and nonlinear crystals). We recommend that we use the new national system for key technologies under market economy conditions to break through the current bottleneck of laser technology medical applications through the continuous support of national fund projects and focus on solving problems related to the most promising key technologies of the laser medical industry.

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