A Flash of Light for Health

Scientists are increasingly specializing in narrower fields, and communication is often difficult between physicists researching elementary particles and those studying semiconductors, not to mention between physicists and biologists or doctors. This makes interdisciplinary work difficult. And yet sometimes they succeed. One thread of work underway at the PAS Institute of High Pressure Physics offers a good example.

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For twenty years now our Institute has been working on laser diodes made of GaN, InN and AlN nitride layers and their alloys. These relatively new semiconductor materials have enabled the production of energy efficient visible light sources, revolutionizing lighting technology. In 2014, three Japanese scientists, Isamu Akasaki, Hiroshi Amano and Shuji Nakamura, received the Nobel Prize in Physics for the discovery of nitride-based laser diodes. The gallium nitride crystals produced in our Institute, containing very few defects (dislocations), made it possible to obtain blue laser diodes. These are layered structures built into the p-n junction, which, when powered with current above threshold, emit coherent light with a narrow spectral line. Prior to the "nitride era," such diodes were produced from other semiconductors and emitted light at longer wavelengths, from 630 nm to 2500 nm. Nitride lasers have made it possible to obtain wavelengths from 350 nm to 530 nm. The race is on to extend this range into the ultraviolet, as well as yellow and red light.

Sending light to the optic fiber

While participating in the European BRIGHTER project we encountered medical groups looking for fiber-coupled laser sources to use in Photodynamic Therapy (PDT) for treating cancer. In simplified terms, this method involves injecting a patient with a photosensitizer that accumulates predominantly in tumor cells. After illumination with a laser at the selected wavelength a photochemical reaction occurs in tumor cells, destroying them. The wavelength depends on the photosensitizer, but is generally located in the red part of the spectrum, from 630 nm to 690 nm. In most medical applications, it is best to use fiber lasers because the fiber can be fixed in the needle, inserted into the vein, and when irradiating the skin or the

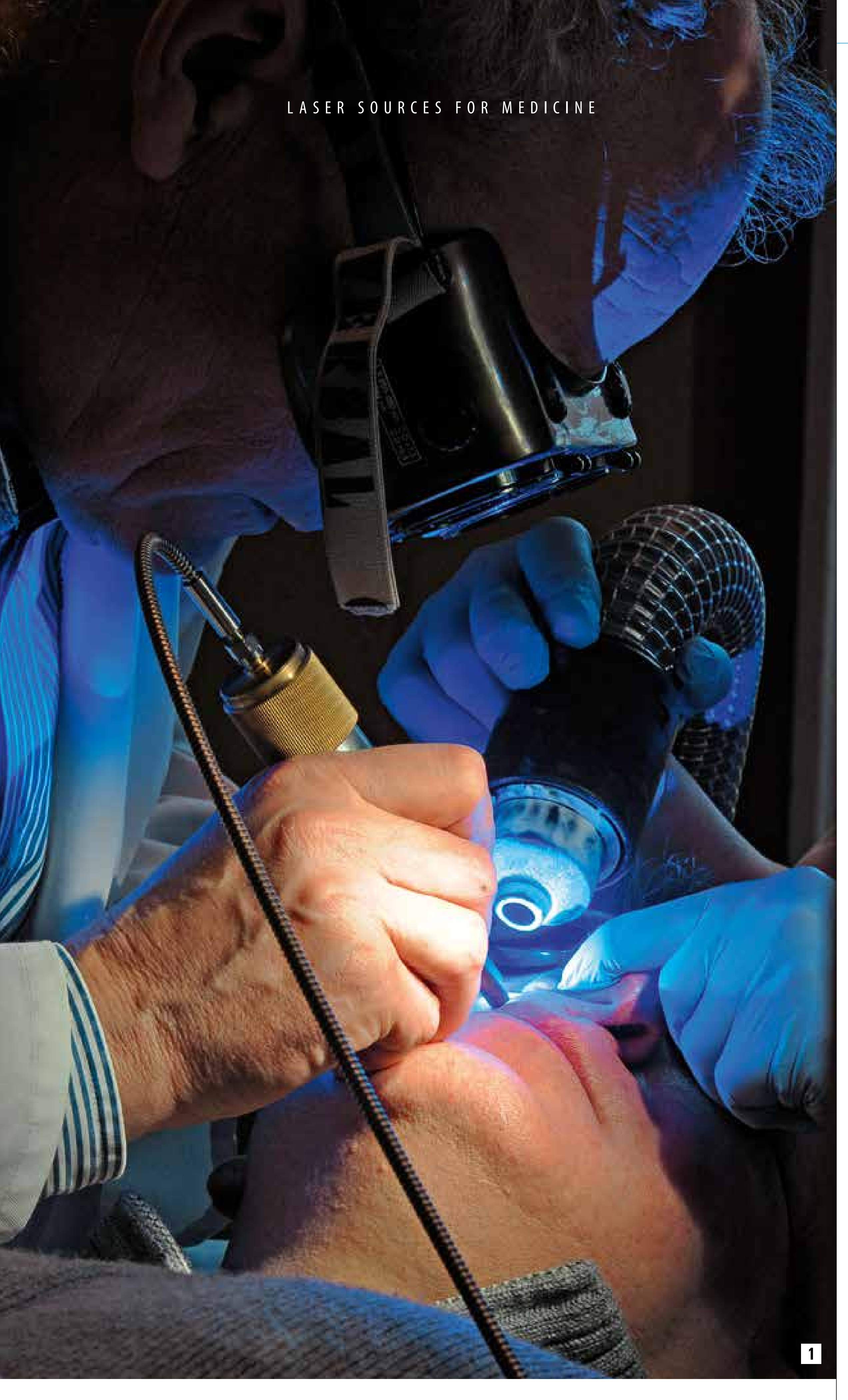
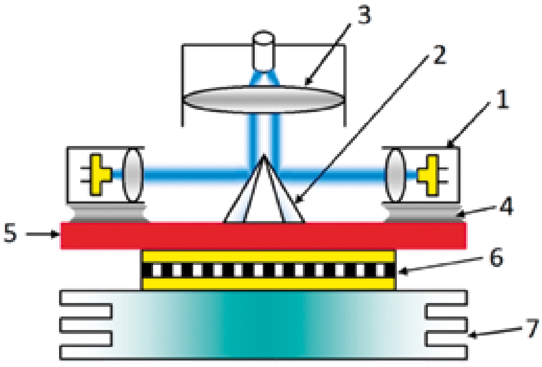


Fig. 1
Vascular laser therapy in the Dermatology Clinic at the Medical University of Warsaw.

Fig. 2
Vascular lesions on the skin.



Schematic side view of the 8 laser diodes coupler for the optical fiber: 1 – laser module (with collimating lens), 2 – mirror pyramid, 3 – optical lens focusing the light of 8 lasers in the optical fiber, 4 – solder in which the laser module is positioned, 5 – dissipating heat copper base, 6 – base cooling Peltier plate, 7 – radiator.

eye it is more convenient to use a flexible fiber optic scope than mirrors.

After the BRIGHTER project ended, we tried to couple light from laser diodes into an optic fiber. We developed a method of inserting eight laser beams into one optic fiber. Modules with laser diodes are arranged on a circular copper base, which is cooled from the bottom by Peltier plates, one of which cools and the other heats when the current flows. The laser modules require precise positioning on the copper base, so that the beam focused in the optic fiber enters a core measuring 0.2-0.4 mm. We achieved this goal by positioning the modules in a low melting solder. Once the solder hardens, we achieve a continued injection of about 90% of the light output to the fiber core. Thanks to a mirror pyramid, the laser modules are spaced apart and the beams of the eight lasers are positioned near the optical axis of the lens focusing the light into the optic fiber. This allows us to achieve a high light output in the optic fiber, or to mix several wavelengths in one fiber.

Lasers in medicine

After creating the prototype, we needed to check whether our laser source could be useful in medical treatment. At one of the laser conferences I met Dr. Jacek Szymańczyk from the Dermatology Clinic at the Medical University of Warsaw, and Prof. Piotr Ziółkowski from the Wrocław Medical University. I showed them the prototype of our "8 laser diode coupler" and succeeded to interest them in a joint research project. Dr. Szymańczyk has used lasers for many years to treat skin lesions. These were argon or dye lasers, requiring large power supplies and water cooling. Meanwhile, laser diodes, being extremely efficient light sources, are small and easy to power. In addition, the wavelengths emitted by our sources are strongly absorbed by hemoglobin and melanin, two important chromophores in human skin.

In Wrocław, clinical trials are being conducted on mice treated with light from a lamp and from a laser beam.

The laser light absorbed by hemoglobin should allow coagulation of the blood vessels without heating the neighboring tissues. This gave rise to the idea of using our lasers to treat angiomas, or blood vessel abnormalities.

Our lasers could also be used to treat skin pigment lesions, appearing as dark brown spots. This in turn requires light absorbed by melanin. The range of emission by nitride laser diodes seems adequate for both hemoglobin and melanin. Keep in mind that strong light absorption means shallow penetration into the tissue, so depending on the depth on which the diseased vessels are located, different wavelengths may be effective. In addition to the wavelength, the length of the laser pulse may be significant. The same dose of light can be obtained at a short pulse at high power, or at a longer pulse at low power. A number of dermatological papers have recommend the use of a short pulse at high power. They should have sufficient time to heat the objects in the tissue selectively absorbing the laser light without heating the neighboring tissues. That is why we decided to use our lasers with both DC power and short pulses.

Testing the light sources

Dr. Szymańczyk put us in touch with Accuro, headed by Piotr Tuchowski. This company has previously assisted Dr. Szymańczyk in adapting lasers for dermatological treatment. Prof. Ziółkowski, head of the Department of Pathomorphology at Wrocław Medical University, has been using filter lamps in the photodynamic method and was interested in using lasers with emission wavelengths matched to new photosen-

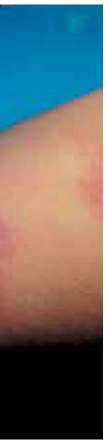


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Fig. 3
Green laser light source (520 nm) with 5 W power.

sitizers. Thus we created a consortium consisting of the PAS Institute of High Pressure Physics, the Medical University of Warsaw (WUM), Wroclaw Medical University (UMW) and Accuro. Despite our differing specialties there was good communication between us and working together was a pleasure (I hope not only for me). It is easy to work in a group of kind and friendly people.

After a few months we developed a proposal for the project "New laser sources and their applications in dermatology" which received funding through the Applied Research Program competition organized by Poland's National Center for Research and Development. The project plan included producing laser sources to use in medical treatment for several lengths of light: 410 nm (violet), 450 nm (blue), 520 nm (green) and 638 nm (red). These sources were to be tested in vascular therapy in Warsaw and Wrocław, and in photodynamic therapy of cancers in Wrocław. After the project was approved it turned out that clinical trials could not be financed by the program, and that compensation for doctors could not be paid from this grant! Despite this, our dermatologists decided to work without pay and the project began in April 2015. We are currently midway through a three year project, but so far the results look promising.

We have produced about ten laser sources achieving higher light output than originally planned: 40 W for blue, 5 W for green and 8 W for red. Our lasers work in both continuous and pulse mode and the treatment parameters are set on a special touch panel. In addition, the laser is equipped with a power meter so that the doctor can check the irradiation parameters before the procedure. The therapeutic tip allows the size of the laser spot to be adjusted from 0.5 to 5 mm. Large spots up to 10 cm in diameter can also be obtained using a special diffuser. The purpose of the clinical trials is to determine optimal exposure parameters, such as laser power density, wavelength or pulse duration, for different types of medical conditions. We plan to include about 100 angioma patients and 50 patients undergoing photodynamic skin cancer therapy in the trials. Studies on each patient last several months because they require multiple irradiations. Thus at this point it is too early to discuss the results of the therapy. In Wrocław, clinical trials are being conducted on mice treated with light from a lamp and from a laser beam.

Accuro has developed a cold air cooler. The site on the skin is cooled before exposure to light, which alleviates pain. An important part of the project is the certification of our equipment so that they can be used in hospitals and aesthetic medicine clinics.

Plans for the future

We hope that our laser sources will find uses in other medical fields, in addition to dermatology. We can use different wavelengths than the ones used so far and we can mix many wavelengths in the optic fiber. For example, by mixing red, green and blue light, we have obtained high intensity white light in the optic fiber.

Today, the medical laser market is dominated by American, Israeli and Chinese companies. We would like to be present on this market with our Polish devices.

In conclusion, it may be worth mentioning the red-tape obstacles involved in working with medical institutions. In scientific projects, state-run hospitals, financed by the National Health Fund, are considered commercial enterprises. This means that in grants they must provide 30–40% of the funding from non-state budget resources, that is from the funds obtained from their own commercial activities. Because hospitals generally do not have such resources, they cannot actually participate in clinical trials as partners or consortiums! Only higher education institutions are treated as scientific institutions. This is how we were able to use the grant with the participation of WUM and UMW. In the meantime, hospitals often have good laboratory facilities and are interested in participating in research. It is a pity that they are not allowed to take part in the trials.

Witold Trzeciakowski
Photography by **Jakub Ostałowski**

Further reading:

http://www.ist-brighter.eu/project.htm

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