Publishable summary

The MIRSURG project, comprising researchers from 9 European institutes and companies, was focused on the development of a laser source that will enable minimally invasive neurosurgery. The laser should emit at a wavelength near 6.45 µm and provide high single pulse energy and average power. The penetration depth at this wavelength will be comparable to the cell size (several micrometers), which will make it possible to avoid collateral damage when ablating the tissue. Conventional lasers for tissue ablation operate at wavelengths either near 2 µm or at 10.6 µm, evaporating the tissue as a result of the strong water absorption. The idea to perform neurosurgery with lasers emitting in the mid-infrared (mid-IR) spectral range near 6.45 µm, where non-aqueous resonant tissue absorption also comes into play, has been known for almost 20 years. However, suitable lasers operating at this wavelength could not be developed in the past.

Previous experiments in USA have verified that the use of mid-IR free-electron-lasers (FELs) at wavelengths near 6.45 µm, with a penetration depth of the focused beam comparable to the cell size and coupled both into the spectral wing of the water bending mode and the amide-II vibrational mode, results in tissue ablation with minimal collateral damage and very effective ablation rate. This finding is extremely important as a useful tool for minimally invasive human surgery. However, the clinical use of FELs is ultimately not viable due to large size, high cost, operational complexity and restricted access at a few multi-million-dollar accelerator-based facilities worldwide. Therefore, it is important to develop new technologies to replace the FELs for practical clinical applications in human surgery. If the promising results so far obtained with the mid-IR FELs could be reproduced or even improved using lasers based on more practical alternative technologies, then the engineering effort to develop compact, inexpensive, table-top laser systems suitable for clinical use will be well justified.

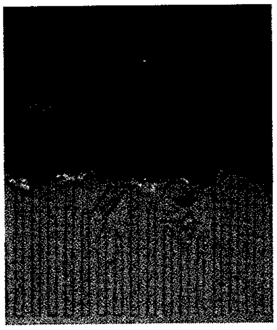
Thus, the main objective of MIRSURG was to develop advanced table-top solid-state photonic sources for a specific wavelength in the mid-IR spectral range, as a practical, reliable and cost-effective alternative to large-scale FELs, for an important application in biomedicine (health): minimally invasive surgery (MIS).

Several attempts to develop non-FEL alternatives had largely failed to meet the necessary requirements in terms of pulse energy and repetition rate. In fact, no suitable lasers exist that emit in this wavelength region. Frequency conversion in nonlinear optical crystals, however, makes it possible to transform the wavelength of powerful near-IR lasers into the mid-IR to reach the target wavelength of 6.45 µm. The main strategy in the project MIRSURG was to exploit nonlinear optical techniques (optical parametric oscillators, OPO) in combination with novel near-IR laser pump sources (near 1 and 2 µm) and new materials (e.g. orientation patterned GaAs), to obtain an unprecedented energy level near 6.45 µm at a repetition rate of 100 Hz. Two basic approaches, differing in the time structure, can provide less than few µs (macro) pulse duration. The project MIRSURG encompassed four distinct elements: (1) Material research; (2) Pump laser development; (3) OPO development; and (4) Validation in tissue ablation experiments.

The MIRSURG project was focused on the design and realization of solid-state laser systems operating near 6.45 µm with temporal structure suitable for MIS. The requirements, as derived from the unique experience with FELs and some very preliminary and mostly unsuccessful experiments with three alternative sources can be summarized as follows:

- the pulse duration may vary from a few ns (single pulse version) to a µs (macro-pulse version).
- there is minimum pulse energy for efficient tissue ablation in the mJ range at 6.45 µm.
- effective MIS will require a sufficiently high pulse repetition rate and hence an average power of ~1 W. Variable repetition rate will enable to study its influence in soft tissue ablation.

The material research within MIRSURG focused on nonlinear optical crystals suited to meet the requirements of MIS with unprecedented advantages, including easier availability. The route followed in this project was built on former demonstrations of Orientation-Patterned Gallium Arsenide (OP-GaAs), relying on a special epitaxial growth step (based on Hydride Vapour Phase Epitaxy or HVPE), fast enough to obtain hundreds of microns-thick layers on substrates pre-patterned with the suitable Quasi-Phase Matching (QPM) period.



Thick OP-GaAs crystals for mid-IR frequency conversion

Thicker and thicker samples have been fabricated during the project (top: various samples after dicing and polishing), reaching 1.2 mm with an excellent patterning duty cycle (bottom: side view after etching of a 1.2 mm thick OP-GaAs sample with a period suited for mid-IR generation around 6.45 µm. In phase with the gradual increase in thickness over the project duration, the latest efforts have enabled to fabricate the first OP-GaAs samples with a thickness >1.2 mm. OP-GaAs thus provides a unique opportunity to design new mid-IR OPOs based on a material developed in Europe.

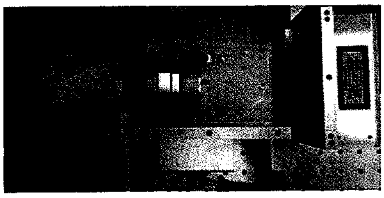
On the other hand, periodically poled oxide materials of the KTP family, with specially designed properties, are interesting for the first stage of cascaded OPO schemes. The fabrication and characterization of this family of crystals was also part of the material studies in the project, benefiting from the experience in that kind of QPM devices. The periodic structuring technology developed for KTA and thick samples of KTP and Rb:KTP solid solutions was essential for fabrication of active elements used in the first stage of the cascaded OPO experiments performed.

Finally, these efforts were complemented with characterization and evaluation of several more rarely used wide band-gap semiconductors (obtained from external collaborators) applicable in OPO schemes for direct conversion from 1 µm to 6.45 µm by birefringent phase-matching. Important properties, besides the transparency, dispersion and second order nonlinear coefficients, are the damage threshold and the two-photon absorption (TPA). During the third period, two new (discovered after the start of the project) wide band-gap mid-IR crystals, $BaGa_4S_7$ and $BaGa_4Se_7$, were identified and their linear and nonlinear optical properties as well as damage threshold characterized. An active element of $BaGa_4S_7$ has been manufactured and coated for OPO tests.

Some of the proposed approaches based on direct or cascaded synchronous OPO pumping (SPOPO) with picosecond pulses, require powerful pump sources with special time format. The novel concept developed was the amplification of a macro-pulse of several hundreds picosecond pulses, obtained with fast acousto-optic modulation from a low-power cw diode-pumped mode-locked oscillator at 1064 nm: a 450-MHz, 6-ps laser, specifically developed and engineered to allow easy and reliable operation. This oscillator has been further optimized and fully integrated within the laser system.

In the all-diode-pumped solid-state amplifier system, starting from a 1-µs long pulse train with 45 nJ energy, the two-slab $Nd:YVO_4$ low-power pre-amplifier side-pumped by two 200-W qcw arrays has shown single-pass amplification up to 1.3 mJ. High-energy amplifiers were employed to further boost the macro-pulse energy: a $Nd:YVO_4$ slab pumped by a 1.3-kW stacked array and two Nd:YAG multi-pass post-amplifiers each pumped by a 2-kW stacked array. As much as 50 mJ in the macro-pulse train at 50 Hz have been achieved. The repetition rate could be increased in principle up to 100 Hz. Resonant saturable absorber mirrors (RSAMs) have been used for the first time in such a high-energy picosecond system to suppress effectively background noise and self-oscillation tendency due to the extremely high amplifier gain. Accurate numerical modeling of the laser system showed that RSAMs pose the most significant efficiency limitation, suggesting up to 80-mJ output energy if they can be avoided and concepts for this were considered.

Another concept followed in the pump laser development relied on the fact that the efficiency of an OPO in general increases for pump wavelengths which are already close to the wavelength that has to be generated. Therefore, as an alternative to lasers emitting at ~1 µm, Tm:YAG lasers emitting at ~2 µm have been chosen as the OPO pump sources, as they are very efficient due to direct diode pumping at around ~800 nm, using a cross-relaxation process which doubles the quantum efficiency. Novel cavity geometries were developed and tested. In particular, a dual end-pumping scheme based on total internal reflections and minimized heat deposition has proved to be promising, yielding a maximum pulse energy of the Q-switched Tm:YAG laser up to 13.6 mJ at a pulse duration of 400 ns or 13.2 mJ at a pulse duration of 300 ns, with a diffraction limited beam quality at any operation point. At a later stage the pump diode source was upgraded to 300 W and the achievable average output power was almost doubled. Therefore, even though the upgraded laser set-up is still to be completed, it promises to achieve the required energy in Q-switched cavity-dumped operation (30-40 mJ to achieve ~5 mJ OPO output at 6.45 µm) as soon as new laser rods and electro-optical switch are delivered and installed in the laser oscillator.



All-solid-state Ho:YAG laser

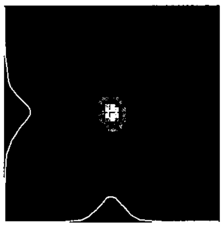
Compact plane-plane cavity of the diode-pumped Ho:YAG laser operating in cw regime with both pump diode stack and rod water cooled. The resonator mirrors were positioned as close as possible to the Ho:YAG rod leading to a total cavity length of ~60 mm.

Ho-lasers, due to their longer wavelength and shorter pulse durations, are more efficient in pumping OPOs near 2 µm, but pumping them with conventional laser diodes is impossible. The concept followed in this project was based on in-band pumping of Ho:YAG without the use of an intermediate Tm-laser. Ho:YAG is a particularly attractive laser material for achieving high energy in Q-switched operation, owing to its long storage time in the upper laser level. Key components for the proposed new technology development were 1.9-µm (AlGaIn)(AsSb) laser diode arrays.

In cw free-running operation of the direct-diode-pumped Ho:YAG laser oscillator, 55 W of output power at 2.122 µm were achieved. The slope efficiency reached 62% with respect to the incident pump power. In Q-switched operation, pulse energies of 7 mJ at a repetition rate of 500 Hz were initially achieved limited by damage of the coatings of the resonator elements. A new resonator design for low repetition rates was developed and successfully verified solving the damage problem. Pulse energies and peak powers exceeding 30 mJ and 300 kW were achieved for 100-200 Hz repetition rates in absolutely damage free operation. As demonstrated by preliminary OPO experiments, such laser performance could be already exploited for 6.45-µm generation of the target energy output. Nevertheless, the pulse energy is still scalable with a single amplifier stage.

During the last period of the project substantial progress has been made in the development of OPO sources for the generation of mid-IR radiation to reach the target wavelength of 6.45 µm using direct single-step or cascaded two-step conversion schemes. In the first approach, involving single-step conversion of a pulsed picosecond SPOPO, for the first time $CdSiP_2$ (CSP) was employed with direct 1064-nm pumping. Under 90° phase-matching, the first such SPOPO produced quasi-steady-state idler micropulses near 6.4 µm with an energy as high as 2.8 µJ at 100 MHz. The train of 2 µs long macro-pulses, each consisting of 200 micropulses, follows at a repetition rate of 25 Hz, which corresponds to an average power of 14 mW. This average power was scaled up by a factor of ~2.5 to 35 mW after optimizing the amplification stage of the pump system, reaching a macro-pulse energy of 1.4 mJ at 6.4 µm. CSP was compared directly with type-I and type-II $AgGaS_2$ (AGS) crystals for similar parameters such as length and showed superior performance (lower threshold and higher damage resistivity). The same nonlinear crystal CSP was employed also in a highly compact (~30 cm long), efficient and high-energy picosecond SPOPO at 450 MHz repetition rate pumped directly by the diode-pumped laser system developed within the project and described above. This SPOPO can be tuned over 486 nm across 6.091-6.577 µm. Idler macro-pulse energy as much as 1.5 mJ has been obtained at 6.275 µm at a quantum conversion efficiency of 29.5%, and >1.2 mJ over more than 68% of the tuning range, for an input macro-pulse energy of 30 mJ. Both the signal and idler beams exhibit good beam quality with TEM_{00} spatial profile.

In the second approach, using direct single-step pumping of a pulsed nanosecond OPO, one focus was the demonstration of a 90°-phase-matched singly resonant OPO based on CSP and pumped at 1064 nm, to produce idler pulses near 6.45 µm with an energy as high as 0.47 mJ (highest in this wavelength range for any non-oxide material pumped at ~1 µm). Subsequently this OPO was operated at 100 Hz increasing the average power. The high nonlinearity of CSP was exploited also for optical parametric generation (without cavity) yielding similar idler pulse energy at 6.125 µm for sub-6 ns duration and average power of 52 mW at 100 Hz, at much higher conversion efficiency. For the first time such scheme was realized with pump pulses as long as 8 ns. Since only a fraction of the available 250 mJ of pump energy at 1064 nm was applied – scaling of the idler energy and output power to ~2 mJ/200 mW will depend in the future only on the availability of larger aperture CSP or can be simply realized by beam recombining. Based on the characterization results in the materials research section, an OPO was realized also for the first time with a $BaGaS_2$ crystal, demonstrating that similar pulse energies (average power of ~50 mW at 100 Hz for the idler at 6.217 µm) can also be achieved with low-nonlinear but resistant to optical damage wide band-gap nonlinear crystals. Substantial progress was achieved in the third period in realizing nanosecond cascaded down-conversion scheme which also employs a commercial high-energy Q-switched Nd:YAG laser as a pump source. Large aperture periodically poled crystals developed within the project were employed for building the first down-conversion stage. Here the 2.1 µm radiation at an average power of 3.2 W and at a repetition rate of 100 Hz was generated. The output of the first frequency conversion stage pumped $ZnGeP_2$ (ZGP) OPO in a non-planar RISTRA cavity. Good spatial beam quality mid-IR pulses tunable between 6.27 and 8.12 µm with pulse length of 5 ns and maximum energy of 0.9 mJ (peak power reaching 180 kW) at 6.45 µm were achieved.



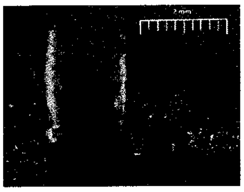
6.45 µm output beam profile of the ZGP RISTRA OPO at ~5 mJ pulse energy

The unique properties of the RISTRA cavity resulting from the 90° image rotation per round trip allow for highly-symmetric beam profiles with improved beam quality – an important factor for high-efficiency fiber coupling.

Finally, the same RISTRA cavity with the ZGP crystal was pumped by a ~30 ns diode-pumped laser system at 2.053 µm. With maximum pump energy of ~45 mJ, the idler output energy reached 6.4 mJ at 100 Hz, at a slope efficiency of 17%. At 200 Hz the idler output energy of 5.45 mJ was obtained which gives an average power of 1.09 W at 6.45 µm, realizing the primary objective of the entire project. A linear OPO, employing OP-GaAs and pumped by a Tm^{3+}:YAG Q-switched laser, both developed within the project, was also realized, showing promising performance at 100 Hz.

During the last period, the fiber transmission and comparison experiments have been finalised. The preferred fiber for the 6.45 µm wavelength and pulse characteristics proved to be a solid core silver bromide fiber. Although this fiber does not have the highest transmission of all tested fibers, it is the most practical as to usability in a clinical environment (moist and water) and mechanical properties such as stiffness and bending radius with constant reliable energy output. Hollow waveguides showed the highest transmission but are relatively stiff and have high losses when curved. The hollow open ends of the fibers require a permanent gas flush to prevent contamination and damage which is not practical in a clinical environment.

With the successful OPO development, the energy levels have finally become significantly above the ablation threshold of biological tissues and serious tissue ablation experiments could be performed. The imaging set-ups developed were transported and integrated in the laser set-ups. Experiments performed with different types of biological tissue and tissue phantoms showed efficient ablation/cutting with hardly any coagulation. Histological analyses confirm these macroscopic observations. The tissue ablation characteristics were comparable with the tissue ablation experiments performed with two reference lasers (pulsed CO_2 laser at 10.6 µm and Er:YSGG laser at 2.79 µm). The reference lasers create relatively large thermal damage zones. However, this cannot be ascribed solely to different wavelengths. Experiments with the reference lasers revealed that increasing the pulse length from the µs to the ms region increased the thermal effects significantly. This observation was consistent with the results comparing the CO_2 laser (50 µs pulse), the Er:YSGG laser (700 µs pulse) and the 6.45µm system developed within the project with an idler pulse length of ~30 ns. Therefore, additional research has to be performed in the future to exclude this pulse width variation.



Macroscopic image of ablation/cut in muscular tissue at 6.45 µm

Bovine tissue was exposed to the 6.45 µm OPO source with 4.7 mJ, 300 µm spot at 100 Hz while moving the tissue through the idler beam. Although the repetition frequency was relatively high, the thermal buildup was minimal. This can be partially attributed to the short pulse length of about 30 ns.

With these tissue experiments the primary goal of the MIRSURG project has been achieved: a table top laser system (much smaller and cheaper than a FEL) has been developed that can effectively ablate biological tissue at a wavelength of 6.45 µm with a pulse length in the ns range. Although the average power targeted (>1 W) has been achieved at 200 Hz, the >5 mJ pulse energy available is more than sufficient for the tissue ablation itself (threshold established at ~1 J/cm^2) and the repetition rate that can be chosen (200 Hz, 100 Hz or less) will depend in real applications on the speed necessary to achieve the required effect.

The MIRSURG website www.mirsurg.eu served to inform about the project MIRSURG, both the partners and the interested (expert) public. The website describes aims, content and work packages of the project in general, and lists the partners (with links) that are involved. It is the main and unique instrument for dissemination of knowledge in the sense that it contains complete information on the results produced within MIRSURG. The pages related to the results obtained are regularly updated. In addition to the Recent Highlights, at present the website contains full texts of all Press Releases, Publications in Journals, Presentations at Conferences, as well as a list of seminars/lectures/courses and unpublished reports with links to the corresponding media/events. The website will continue to exist also after the end of the project and will be updated in the next two years with results obtained and published by the partners.

In the last period (1.5 years), 52 scientific papers were published in peer-reviewed journals disseminating results obtained within the MIRSURG project. Results from the research were reported also in 48 conference presentations during the last period. Finally, a total of 8 Ph. Theses were or are still being carried out fully or partially supported by the MIRSURG project.

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